ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 04 | April - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY TO DETERMINE THE CLINICOEPIDEMIOLOGICAL PROFILE OF CYTOMEGALOVIRUS SEROPOSITIVE INFANTS

Paediatrics

Dr Juhi Kapadia Final Year Post Graduate student, Department of Pediatrics, Sawai Man Singh Medical College, Jaipur

Dr Vijay Agrawal MD Pediatrics, SMIMER, Surat

Dr Dhaval Kapadia Associate Professor, Department of Pediatrics, Sawai Man Singh Medical College, Jaipur

Dr Sonika Meena Final Year Post Graduate student, Department of Pediatrics, Sawai Man Singh Medical College, Jaipur

ABSTRACT

Background: Cytomegalovirus (CMV) is an enveloped double stranded DNA herpes virus belonging to herpesviridae family and is a leading cause of viral infection in new born and infants with variable clinical manifestations. The Objective was to study the clinical and epidemiological profile of CMV seropositive infants admitted in tertiary care hospital of Rajasthan. **Materials and Methods:** A Cross sectional observational study was done in Department of Pediatrics, SPMCHI, SMS Medical college Jaipur on 42 infants The various epidemiological , biochemical and hematological parameters along with their associated morbidity was studied. **Results:** Most of the infant with CMV were aged 1 to 3 months (71.43%). Males (76%) outnumbered females (24%) and 86% were from rural background. Microcephaly was seen in 52% of cases which was statistically significant ($p < 0.001$). Among the various clinical manifestations jaundice was seen in 95% of cases and was also most common cause of morbidity followed by pneumonia. **Conclusion:** CMV is a virus which can be a potential killer or a silent companion occuring in rural community. The most frequent cause of morbidity was jaundice involving liver with raised liver enzymes and poor synthetic function.

KEYWORDS

Cytomegalovirus, Jaundice.

INTRODUCTION

Cytomegalovirus (CMV), an enveloped double stranded DNA herpes virus belonging to herpesviridae family and is the leading cause of infection among children with seroprevalence ranging from 45 to 100%[1]. Ten percent of infected newborns will be symptomatic. Mortality among this subset can reach 30% and 90% may suffer serious sequelae[2] . It is also known as human herpesvirus 5 (HHV-5) and like other herpes viruses it becomes latent after a primary infection but can reactivate with renewed viral shedding or from a new strain[3] . Congenital CMV (cCMV) has a birth prevalence of 0.2%–2.5 % worldwide varying by geographical region according to the level of CMV immunity in the pregnant women in that population[4].

CMV is an enveloped, double-stranded DNA β herpes virus. Primary entry occurs via mucosal site, followed by a viraemic phase where the viral infection occurs[5] . This virus gets secreted in bodily fluids such as saliva, urine, breast milk and genital secretions and cause further transmission. Maternal to Fetal transmission of virus occurs via placental cytotrophoblasts that are permissive to CMV replication and post natally via genital secretions and breast milk.[6]

The various clinical manifestations of CMV infection includes adverse pregnancy outcomes such as still birth, neonatal death, IUGR, preterm birth. Symptomatic infants presents with petechia, thrombocytopenia, hepatosplenomegaly, jaundice, microcephaly, seizures, developmental delay, sensorineural hearing loss, vision loss, optic atrophy, strabismus and chorioretinitis.[7,8]

Maternal infection with CMV can be detected by CMVspecific IgM antibody indicating a recent maternal CMV infection. However, reactive CMV IgM antibodies may be detected upon both primary and non-primary infections. Therefore, IgM positivity and low-affinity CMV IgG antibodies indicate a recent primary infection, and when detected before 12–16 weeks of gestation indicate a high risk for congenital infection[9,10]

The confirmation of CMV infection in infants can only be made with certainty before the third week of life. After this it is difficult to distinguish congenital infection and infection acquired in postnatal period.

The gold standard for the diagnosis of congenital CMV infection in newborns has traditionally been viral culture of urine and saliva. However this being time consuming so as an adjunct we use PCR amplification of CMV DNA from saliva or urine which is a rapid method to diagnose CMV infection.[11,12] Detection of CMV-specific IgM in neonatal serum may also disclose congenital infection. However IgM antibodies are only present in 20– 70% of infected newborns.

METHODS

The study was a cross sectional observational study conducted in the Department of pediatrics, SPMCHI, Sawai Maan Singh medical college Jaipur in admitted patients with positive cmv serology and with symptoms of the disease. The duration of study was one year from august 2021 to August 2022.

Inclusion Criteria:-

Patients were enrolled full filling all the following criteria:

1. Age less than 12 months.
2. Infant diagnosed as suffering from CMV infection based on presence of specific IgM/IgG CMV antibody titres,urine for RT-PCR.
3. Newborns presenting with microcephaly, IUGR, hepato splenomegaly, rash neurological abnormality (presenting as poor tone and decreased motor function and abnormal head lag), petechiae or purpura, and/or hearing loss. (stigma of congenital CMV infection).

Exclusion criteria:

The following patients are excluded from our study

1. Age more than 12 months
2. Metabolic liver disorders.
3. Congenital /acquired immunodeficiency.
4. Rash of a known skin disorder/systemic illness.
5. Thrombocytopenia due to IEM, chromosomal disorders and congenital thrombocytopenia.
6. Hepatosplenomegaly due to known causes like malaria, liver disease, haemolytic disease or surgical causes.

The enrolled patients were evaluated for various epidemiological , hematological i.e Hemoglobin, WBC count , platelets and biochemical factors i.e SGOT, SGPT, Serum bilirubin levels etc. Neuroimaging along with anthropometry was also studied .

RESULTS

Out of the 42 infants included, 31 (73.81%) infants had urine PCR positive, 4 (9.52%) infants had blood PCR positive , 8 (19.05%) infants had IgM positive and 7 (16.67%) infants had IgG positive serology. In mothers of these babies 21 (50%) had IgG positive and (14,28%) had IgM serology. Majority (71%) of them were in the age group 1 to 3 months in them males outnumbered females by huge margin. Growth

was severely compromised with wasting present in 19% of patients and microcephaly was seen in 52.2 % .Length for age was less effected 53% were normal.(table 1)

Majority (83%) belong to rural community and among them 74% mothers were educated up to 8th standard. Higher maternal age 78.5% and multigravida 85% was seen. Most of the mothers (71%)belonged to lower socio economic class. In antenatal history of mothers fever was present in 19% of them.

The most common clinical presentation was jaundice (95%) followed by abdominal distension (61%) and fever(59%).(Table 2). Among the various haematological parameters anaemia was present in 66 percent infants which was statistically significant . Mean haemoglobin was 9.09 $\pm$ 2.76 . 1 in every 10 infants had severe thrombocytopenia less than 50000/mm3 and mean platelet count were 2.95±2.21. Most of the infants (30.95%) had bilirubin less than 5mg/dl and 1/3rd had bilirubin levels more than 5 mg/dl. SGOT and SGPT were severly deranged in most of the infants. USG findings(table 3) and Haematological and biochemicals parameters were compared between survived and expired babies.(table 4)

Table 1: Clinical and demographic characteristics

Parameter	Number of infants	Number of infants	Number of infants	Mean SD
Age	<1month (30)	1 to 6months (11)	More than 6months(1)	3.14±1.49
Weight for length kg	Normal(22)	<-1 SD (12)	<-2 SD (8)	4.20±1.50
Length for age cm	Normal (20)	<-3 (22)		38.95±5.15
Head circum ference cm	Normal (22)	<-1 SD (12)	<-2 SD (8)	56.91±6.24

Table 2: Clinical presentation of seropositive infants

Symptoms	No. Of cases	Percentage
Fever	25	59.52%
Jaundice	40	95.24%
Rash	3	7.14%
Seizures	2	4.76%
Pneumonia	19	45.24%
Abdominal Distension	26	61.90%
Lymphadenopathy	0	0.00%
Hepatomegaly	10	23.81%
Splenomegaly	2	4.76%
Bleeding	1	2.38%

Table 3: Usg Findings Among Infants With

USG findings	No. of Infants	Percentage
Hepatosplenomegaly	16	38.10%
Hepatomegaly	10	23.81%
Ascites	5	11.90%
Splenomegaly	2	4.76%
Lymphadenopathy	2	4.76%
Normal	7	16.67%

Table 4: Hematological And Biochemical Parameters In Survived Vs Expired

Parameter	Survived n=32	Expired n=10	p value
Hemoglobin (gm/dl)	9.62±2.79	7.39±1.90	0.0063 (S)
Platelet count (x 10^6/dl)	3.67±2.33	1.66±1.10	0.0005 (S)
Total Bilirubin level (mg/dl)	11.09±8.56	11.50±9.86	0.9066 (NS)
Direct Bilirubin level (mg/dl)	6.01±4.42	5.87±5.32	0.9403 (NS)
Albumin level (g/dl)	3.38±1.05	3.31±0.73	0.8458 (NS)
ALP level	469.38±412	899.60±1086.17	0.0667 (NS)
SGOT level (IU/L)	259.50±337.77	241.50±202.08	0.8744 (NS)
SGPT level (IU/L)	214.75±513.99	133±111.98	0.6231 (NS)
TLC/m^3	14.37±9.15	15.98±10.69	0.6449 (NS)

DISCUSSION

CMV is a most common viral cause of congenital infections, up to 90% of newborns with congenital CMV infections have no clinical symptoms at birth, and only 5% have disease affecting the neurologic, hematopoietic, respiratory, gastrointestinal, and other organ systems that results in high mortality and long-term consequences. In preterm and small-for-gestational-age newborns, liver dysfunction is the most prevalent clinical manifestation of symptomatic congenital CMV infection.13

In our study 83.33% of our patients were from rural background which in contrast to the observation of Mohammad et al14 who reported 86.3% cases from urban community. So this suggests that regional distribution is highly variable. Also in our study 72% females had age less than 25 years suggesting that lower maternal age is a risk factor for congenital CMV infection, similar to Stagno et al15 who reported lower maternal age as risk factor for cCMV infection. Primary infection in young mother infects the fetus more than secondary infection and greater exposure to virus in this age group. Most of the mother belonged to low socioeconomic status 71.43% and 83.3% were from rural background.

Higher parity is a risk factor for cCMV. Multigravida (82%) outnumbered primigravida (16%). IgG prevalence in mothers of infected infants was 50% and IgM prevalence was 14.28% similar to this Khairi S. I., Intisar K. S. et al,16 (97.5%) and 12(6.0%) were CMV IgG and CMV IgM positive, respectively.

In our study Jaundice was the most common presentation (71.43%), followed by abdominal distension (61.90%) and fever (59.52%). Pradeep Singh et al17 in their study Fever was the most common presentation (66.66%), followed by difficult breathing (46.66%). Pneumonia was the most common morbidity 16 (53.33%) followed by septicemia, hepatitis, and convulsions. Shen Z et al18found Hepatitis, thrombocytopenic, purpura, pneumonia as 33.07%, 13.49%, 6.35% respectively. In terms of antenatal history and postnatal history majority of them is nonsignificant.

In terms of hematological parameters Majority of infant 21 (50%) had hemoglobin range 7 to 10 gm/dl, 14 (33.33%) had hemoglobin range more than 10 gm/dl. Mean of hemoglobin was 9.09±2.76 gm/dl. In a Similar Distéfano et al19 found that anemia was one of the main clinical manifestations among the patients. Min CY et al20 also observed anemia as one of the important findings among similar patients.

Total leucocyte count 29 (69.05%) infants had >11x103 /dl, while 12 (28.57%) of infants had TLC level between 4 to 11x103 /dl, and 1 (2.38%) of infant had TLC level 1.5 lac. Hasosah MY et al21 observed thrombocytopenia among 22% of patients. Evaluating the biochemical parameters We found that 13 (30.95%) of the infants had bilirubin level in range of less than 5 mg/dl and 29 patients had level more that 5 mg/dl. Similar in Pradeep Singh et al found that 12 (40%) of the infants had bilirubin levels in range of 1-4 mg/dl and 33.33% of the patients had level more than 4 mg/dl. In a similar study, Min CY et al37observed peak total bilirubin in serum ranged from 0.11–21.97 mg/dL. 90.48% of the patients had an abnormal SGOT, 78.57% of patients had an abnormal SGPT. Kylat RI et al22 reported elevated transaminases in 50% patients.

Albumin levels in Most of the infants 27 (64.29%) with CMV was between 2.6 – 3.5 g/dl, while 12 (28.57%) infants had serum albumin level ≥3.5 g/dl. 3 (7.14%) infants had serum albumin level less than 2.6 g/dl. And serum albumin level mean±SD Discussion 55 was 3.36±0.98. In contrast to our study Hasosah MY et al72 observed hypoalbuminemia among 55% of patients.

Most common USG finding among infant with CMV was Hepatosplenomegaly 16 (38.10%), as followed by Hepatomegaly 10 (23.81%), Ascites 5 (11.90%), Splenomegaly, Lymphadenopathy were present in 2 each (4.76%). Almost similarly hepatosplenomegaly was observed among 44% of patients with CMV by Hasosah MY et al

On assessing various factors associated with mortality, the mean Hemoglobin level was lower among patients who died (7.39 g/dl) as compared to those who survived (9.62 g/dl), the difference was however found to be statistically significant (p=0.0236). The mean platelet count was lower among patients who died (1.66 lakh/dl) as

compared to those who survived (3.67 lakh/dl), and this difference was found to be statistically significant (p=0.0123). Most of the LFT were worse in those who died as compared to those who survived, the difference was however not found to be statistically significant.

CONCLUSION

Infants born to young, multi-gravida mothers belonging to rural area have CMV infection. Most of them are males with less than 6 months age, and underweight for age is common leading to poor development. Jaundice was the most common clinical feature followed by abdominal distension and fever Derangements in haematological parameters do affect the outcome of disease however biochemistry have no impact on the outcome. Most infants with CMV infection had self-limiting disease with favourable outcome, still mortality occurred in a significant number of infants and timely diagnosis and treatment can reduce morbidity and mortality and also reduce complications among survivors.

REFERENCES

1. International journal of infectious diseases, Birth prevalence and characteristics of congenital CMV infection in an urban birth cohort, Jakarta Indonesia.
2. Journal de Paediatrics, The prevalence of congenital CMV infection in newborn infants at Intensive Care unit.
3. T Lazzaratto et al , Perinatal Indicators Of Congenital CMV Infection
4. Harrison GJ. Cytomegalovirus. In: Feigin and Cherry's Textbook of Pediatric Infectious Diseases, 7th ed, Cherry JD, Harrison GJ, Kaplan SL, et al (Eds), Elsevier Saunders, Philadelphia 2014. p.1969
5. Britt W. Cytomegalovirus. In: Remington JS, Klein JO, Wilson CB, Baker CJ, eds. Infectious diseases of the fetus and newborn infant. 7th ed. Philadelphia: W.B. Saunders Company, 2011:704–53
6. Pass RF, Anderson B. Mother-to-Child Transmission of Cytomegalovirus and Prevention of Congenital Infection. J Pediatric Infect Dis Soc. 2014 Sep;3 Supply (Suppl 1):S2-6. doi: 10.1093/jpids/piu069. PMID: 25232473; PMCID: PMC4164178.
7. Viral Infections In Stillbirths, Journal of Perinatal Medicine 2022.
8. Dollars SC, Grosse SD, Ross DS. New estimates of the prevalence of neurological and sensory sequelae and mortality associated with congenital cytomegalovirus infection. Rev Med Virol 2007; 17: 355– 363 Kenneson A, Cannon MJ. Review and meta-analysis of the epidemiology of congenital cytomegalovirus (CMV) infection. Rev Med Virol 2007; 17: 253–276.
9. Kenneson A, Cannon MJ. Review and meta-analysis of the epidemiology of congenital cytomegalovirus (CMV) infection. Rev Med Virol 2007; 17: 253– 276.
10. Enders G, Daiminger A, Bader U, et al. The value of CMV IgG avidity and immunoblot for timing the onset of primary CMV infection in pregnancy. J Clin Virol 2013; 56: 102–107
11. Lazzarotto T, Varani S, Spezzacatena P, et al. Maternal IgG avidity and IgM detected by blot as diagnostic tools to identify pregnant women at risk of transmitting cytomegalovirus. Viral Immunol 2000; 13: 137–141.
12. Boppana SB, Ross SA, Shimamura M, et al. Saliva polymerasechain-reaction assay for cytomegalovirus screening in newborns. N Engl J Med 2011; 364
13. Mohammad et al2007 Study of some immunological and Cytogenetics Aspects in patients infected with CMV.
14. Stango S. cytomegalovirus. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF. Nelson Textbook Of Pediatrics 18th ed. philadelphia .WB saunders .Co.2007;
15. Distéfano et al Distéfano AL, Alonso A, Martin F, Pardon F. Human cytomegalovirus: detection of congenital and perinatal infection in Argentina. BMC Pediatr. 2004 Jun 23;4:11. doi: 10.1186/1471-2431-4-11. PMID: 15214967; PMCID: PMC449715.
16. Khairi S. I., Intisar K. S .2, Enan K .H., Ishag M Y, Baraa A.M. 2 and Ali Y. H. 2 Seroprevalence of cytomegalovirus infection among pregnant women at Omdurman Maternity Hospital, Sudan. Vol.4(4) Oct 2013.
17. Pradeep S and R K Bishnoi,et al . clinicoepidemiological profile of CMV seropositive infants. Journal of medical science and clinical research. 2017
18. Shen Z, Shang SQ, Zou CC, Zheng JY, Yu ZS. The detection and clinical features of human cytomegalovirus infection in infants. Fetal and Pediatric Pathology. 2010; 29(6):393-400.
19. Stagno 5, Cloud 0, Pass RF, et at. Factors associated with primary cytomegalovirus infection during pregnancy. J Med Virol 1984: 13: 347
20. Min CY, Song JY, Jeong SJ. Characteristics and prognosis of hepatic cytomegalovirus infection in children: 10 years of experience at a university hospital in Korea. Korean J Pediatr. 2017 Aug;60(8):261- 265. doi: 10.3345/kjp.2017.60.8.261. Epub 2017 Aug 14. PMID: 29042868; PMCID: PMC5638724. 38.
21. Hasosah MY, Kutbi SY, Al-Amri AW, Alsahafi AF, Sukkar GA, Alghamdi KJ, Jacobson K. Perinatal cytomegalovirus hepatitis in Saudi infants: a case series. Saudi J Gastroenterol. 2012 May-Jun;18(3):208-13. doi: 10.4103/1319- 3767.96461. PMID: 22626801; PMCID: PMC3371424.
22. Kylat RI, Kelly EN, Ford-Jones EL. Clinical findings and adverse outcome in neonates with symptomatic congenital cytomegalovirus (SCCMV) infection. Eur J Pediatr. 2006 Nov;165(11):773-8. doi: 10.1007/s00431-006-0172-6. Epub 2006 Jul 12. PMID: 16835757.