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A Study to Determine the Clinico-Epidemiological Profile of CMV Seropositive Infants Admitted in a Tertiary Care Hospital

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ABSTRACT

Background: *Cytomegalovirus (CMV) infection is a common viral infection in new born and infants the clinical presentation of which is very variable. The objective was to study the clinical and epidemiological profile of CMV seropositive infants admitted in a teaching hospital of Western Rajasthan.*

Methods: *A prospective study was done in 30 infants who were diagnosed seropositive out of 85 clinically suspected cases of congenital/ acquired CMV infection. The epidemiological, biochemical and hematological profile of these patients was studied and their clinical presentation and associated morbidity was observed.*

Results: *Males (80.00%) outnumbered females (20.00%) and 90% of infants were from rural background. (76.92%) of the mothers were educated up to 8th standard or less, which was statistically significant (x2=12.03 p<0.001) 10% infants had a length for age < 2SD which was statistically significant when compared to length appropriate for age (n=21. x2=24.03 p<0.05). Pneumonia was the most common (53.33%) morbidity but accounted only for 3.33% mortality and the case fatality was 6.25% which was less than septicemia (33.33%).*

Conclusion: *CMV is a virus of paradoxes and can be a potential killer or a silent companion and is more prevalent in rural community. The linear growth is compromised the most and lung involvement in form of pneumonia is most frequent morbidity and though liver involved is with raised liver enzymes the synthetic functions of liver is not affected .*

Keywords: *cytomegalovirus, pneumonia.*

INTRODUCTION

Prevalence of CMV infection is very high in South East Asia region, and some clinicians believe it to be as high as 90% in India.[1] The prevalence varies within country, and epidemiol-ogical factors associated with this infection are also heterogeneous. The clinical presentation of the infection can be asymptomatic or with a variable spectrum of some common and some rare manifestations. Only limited study of the clinical spectrum of CMV infection has been done in Western Rajasthan. We conducted this study to determine the clinico-epidemiological profile of CMV seropositive infants of our region so as to

delineate the features that are more relevant to this geographical area.

METHODS

The study was a clinic - epidemiological observational study and the duration of study was one year from January 2014 to December 2015. Working diagnosis of CMV infection was done serologically and the study was conducted in the Department of Pediatrics, Umaid Hospital for Women and Children, Dr S.N Medical College, Jodhpur in admitted patients (infants) with positive serology and having symptoms or stigma of cytomegalovirus infection. 30 infants who tested positive for CMV serology out of the total 85 suspected cases were studied. Written informed consent was taken from parents and ethical clearance was taken from college ethical committee.

Patients Age less than 12 months who presented with stigma of congenital CMV infection and had significant titers in serology were enrolled. And were evaluated for various factors Hematological, Hemoglobin gm/dl ,Platelet/mm3 ,WBC/mm3; biochemical, Bilirubin total mg/dl SGPT SGOT IU/dl IU/dl ALP IU/dl Serum albumin gm/dl ophthalmological and neuroimaging findings, Clinico- epidemiological factors, anthropometry and other associated morbidities were also studied And those infants with Metabolic liver disorders. Congenital /acquired immuno deficiency, rash of a known skin disorder/systemic illness, thrombocytopenia due to IEM, chromosomal disorders and congenital thrombocytopenia, Hepatosplenomegaly due to known causes like malaria, liver disease, haemolytic disease or surgical causes were excluded from study.

Definitions

CMV infection was defined in an infant having IgM value more than 0.391 IU/L or one with lower value but with IgG more than 0.500 IU/L and avidity less than 30 percent CMV-associated pneumonia was defined as a positive serology, vide supra, with pneumonia.

RESULTS

Out of total 30 infants included, 24 had only IgM positive, 1 had only IgG positive and 5 had both IgM and IgG positive. Total 22 mothers of these babies had positive serology; majority 17/22 had only IgG positive followed by IgM positivity in 4/22, and both IgG and IgM were positive in 2/22. Majority of the patients (63.33%) were in the age group 1-6 months. Almost half (46%) of the infants had weight less than expected (13.33% <-1SD and 33.33%<-2SD). Forty percent had microcephaly. Length was not affected in majority, 70% being normal (Table 1). Males (80.00%) outnumbered females (20.00%) with male to female ratio of 4:1. Ninety percent patients were from rural background and 10.00% were from urban background. Hindu: Muslim ratio was 9:1. Majority (76.92%)of the women were educated upto 8th standard or less and only 27.07% of mother had educational qualification of more than 8th standard. Also multigravida (56.66%) outnumbered primigravida (43.33%). Most of the mothers (63.33%) belonged to middle socioeconomic class

Fever was the most common presentation (66.66%), followed by difficult breathing (46.66%) (Table 2). pneumonia was the most common morbidity 16 (53.33%) followed by septicemia, hepatitis, and convulsions (Table 3). Majority of the infant 17(56.66%) had a hemoglobin in normal range >10gm/dl and 9(30%) infants had moderate anemia and 4(13.33%) had severe anemia. Mean hemoglobin of the group was 10.71 ± 3.28. Also 17(56.66%) infants had WBC counts more than 10,000 and the average mean of the study group was 15360 ± 2965.46 Majority of the infants 22(73.33%) had normal platelet count and 1 in every 10 infants had severe thrombocytopenia (<50,000.) the mean platelet count of our study group was 165340 ± 85682. Most 12(40%) of the infants had bilirubin levels between 1-4 mg/dl and 1/3rd of the patients had bilirubin level more than 4 mg/dl. Half of the patients had an abnormal SGPT and ¾th had raised SGOT. 60% of patients (n=18) had normal serum

albumin and 23.33 % (n=7) had severe hypoalbuminemia (serum albumin <2.5gm/dl) (Table 4). Hematological and biochemical parameters comparable between survived and expired babies (table 5).

Table 1: clinical and demographic characteristics

Parameter	Number of infants	Number of infants	Number of infants	Mean SD
Age	<1month (8)	1 to 6months (19)	More than 6months (3)	2.64±2.54
Weight for length kg	Normal (16)	<-1SD (4)	<-2SD (10)	3.76±1.29
Length for age cm	Normal (21)	<-1SD (5)	<-2SD (4)	57.56±4.97
Head circumference cm	Normal (18)	<-3SD (12)		37.6±3.87

Table 2: Clinical presentation of seropositive infants

Symptoms	**No of cases**	**Percentage %**
Fever	20	66.66
Difficulty in breathing	14	46.66
Jaundice	03	10.00
Convulsion	02	6.66
Feeding difficulty	04	13.33
Bleeding from natural orifices	02	6.66
Abdominal Distension	02	6.66
Not gaining weight	01	3.33
Pallor	13	43.33
Icterus	10	33.33
Lymphadenopathy	00	00.00
Hepatomegaly	20	66.66
Splenomegaly	8	26.66

Table 3: Morbidity in seropositive infants

Morbidity	**n=**	**Percentage**
Pneumonia	16	53.33%
Septicemia	6	20.00%
Hepatitis	5	16.66%
Convulsions	3	10.00%
Ascites	2	06.66%
Hemorrhagic disease of newborn	2	06.66%
Intra cranial hemorrhage	1	03.33%
Osteomyelitis	1	03.33%

Table 4: Hematological and biochemical parameters of infants

Parameter				Mean SD
Hb gm/dl	<7gm/dl 4	7-10gm/dl 9	>10gm/dl 17	10.71 ± 3.28
TLC/mm3	<4000 (2)	4000-10,000 (11)	>10,000 (17)	15360 ± 2965.46
Platelets/mm3	<50,000 (03)	50,000-100,000 (03)	>100,000 (24)	165340 ± 85682.
Bilirubin total mg/dl	0-1 (04)	1-4 (12)	>4 (10)	4.41±5.19
SGPT IU/dl	<40 (15)	40-100 (11)	>100 (04)	78.03±123.84
SGOT IU/dl	<40 (07)	40-100 (19)	>100 (04)	64.56±119.79
ALP IU/dl	>130 (00)	130-350 (17)	>350 (13)	359.8±195.08
Serum albumin gm/dl	>2.5 (07)	2.5-3.5 (18)	3.5 (05)	3.07±0.47

Table: 5 Hematological and biochemical parameters in survived vs expired

Parameter		survived n=26(%)	Expired n=4(%)	p
Hemoglobin gm/dl		10.71±3.77	9.07±2.27	0.408
Platelet/mm^3		203807±126145	190250±148607	0.846
WBC/mm^3		12090.57±7477.7	15772±7837	0.369
BSL (mg/dl)		106.69±69.19	60±7.34	0.193
Bilirubin Total (mg/dl)		4.77±5.45	1.98±2.19	0.326
Bil Direct (mg/dl)		1.19±1.35	0.65±0.70	0.444
SGOT (IU/L		82.57±132.72	42.5±10.59	0.554
SGPT (IU/L		67.19±128.43	35.75±29.07	0.634
Albumin (gm/dl)		3.09±0.46	3.12±0.45	0.904
ALP IU/L)		365.5±196.72	574.25±369.03	0.090

DISCUSSION

CMV is common viral cause of congenital infections but up to 90% of newborns with congenital CMV infections have no clinical evidence of disease at birth and only 5% have disease involving the neurologic, hematopoietic, respiratory, gastrointestinal and other organ systems causing high mortality and long-term sequelae .The most common clinical manifest-ation of symptomatic congenital CMV infection is liver dysfunction in small for gestational age and premature infants [2].The incidence of congenital CMV infection is far greater than better-known childhood disorders, such as Down syndrome [3]

In our study 76.66% mothers were aged less than 25 years; the lower maternal age is associated with higher rate of congenital CMV infection. There is possibility that primary infection occurring in a young mother infects the fetus more than a secondary infection and greater chance of primary exposure to virus in this age group [4] or due to age related biological effect on CMV replication. [5] Regional distribution is highly variable, 90% of our patients were from rural background which is in contrast to the observation of Mohamad et al who reported 86.3% *women* cases from urban community.[6]

We found that 1 in every 10 mothers had a previous history of abortion. There are limited reports available on the association between CMV infection and recurrent pregnancy loss and results have often been controversial [7] Roya Sherkat et al from Iran also reported similar findings. They showed that previous exposure to CMV detected by a positive IgG antibody is significantly higher in recurrent pregnancy loss but it should be noted that CMV infection in infant is more common in mothers with recent infection /primary infection and IgM positive. In our study (76.92%)of the women were educated up to 8th standard or less. S.Khairi et al[8] from Sudan observed no significant association between maternal educat-ion status and CMV infection in the infant.

Multigravida (56.66%) utnumbered primigravida (43.33%) and IgG positivity in G1,G2,G3 was 30.76%,23.07% and 43.33% respectively. Hence multiparty may be an independent factor that contributes to transmission of infection to baby. IgM prevalence in mothers of infected infants was 13.33. % (4/30) and that in infected infants was 80.00% suggesting that it is not always an acute infection in mother that is transmitted to baby.

Yeager AS et al have shown that 13.5% of infants transfused with CMV positive blood developed CMV infection of whom 50% were symptomatic [10].In our group out of thirty only three patients had history of blood transfusion hence we conclude that blood transfusion was not a major cause of CMV infection in our study group.

Infection was more common in breastfed infants as (63.33%) were exclusively breast fed at least for the first 4 months of life as compared to top fed (36.66%) or mixed fed. Dworsky M et al, reported that CMV infection may be acquired perinatally through a CMV positive mother or through breast milk[11] ,but in our study most of

the mothers were sero negative and hence breast milk transmission of CMV infection should not be stressed on particularly in developing country like ours.

In our study respiratory system involvement was most frequent and though pneumonia was the most common (53.33%) morbidity, the mortality was only 3.33% and the case fatality was 6.25% which was less than that of septicemia (33.33%). Zampoli et al found that CMV- associated pneumonia was present in 47/170 (28%) children [12]. There were no differences in age, clinical presentation, and nutritional status in children with and without CMV associated pneumonia .In our study bilateral lung involvement was more frequent (68.75%).

Respiratory system was the most commonly affected system in clinical presentation. In our study half of the patients had an abnormal CXR. We found that in these infants with abnormal CXR about 68.75% had bilateral diffuse infiltrates and the remaining either had unilateral or hilar involvement. Smith. C et al reported that diffuse interstitial pneumonitis involving all five lobes of the lung tissues is common to CMV infection[13] they also found that most of the x-ray evidence of pneumonia resolved in less than 8 weeks, however few (4)patients had persistent changes.

We 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. Fifty percent of the patients had an abnormal SGPT but 75% had raised SGOT. Seven (23.33 %) infants had severe hypoalbuminemia (serum albumin <2.5gm/dl). Jaundice and cholestatis is most common in CMV infected infants[14] but in our study it was pneumonia that was the commonest morbidity

Majority of the infant [17(56.66%)] had hemoglobin in normal range >10 gm/dl and 9 (30%) infants had moderate anemia and 4 (13.33%) had severe anemia. Mean hemoglobin of the group was 10.71 ± 3.28gm/dl. Also 17(56.66%) infants had WBC counts more than 10,000 and the average mean of the study group was 15360 ± 2965.46 Majority of the infants [22(73.33%)] had normal platelet count and 1 in every 10 infants had severe thrombocytopenia (<50,000.) Only 3 infants had a platelet level <50,000, the mean platelet count of our study group was 165340 ± 85682/mm^3.

The platelet level in most of the infants (73.33%) was > 1.5 lac. Hanshaw JB, Dudgeon et al [15,16] from their study concluded that the generalized petechial rash of CMV is caused by thrombocytopenia. Platelet counts vary widely but usually range from 20 000 to 60 000 /mm^3. It is suggested that the suppression of haematopoiesis that is associated with CMV infection may be due to direct inhibition by the virus of progenitor haematopoietic cell growth, as well as to stromal cell dysfunction, or to effects of inhibitory cytokines produced by CMV infected leukocytes. Miyahara M et al [17] attributed the presence of some specific antibodies [18], and of other immunological abnormalities, in CMV-infected patients with haemolysis or myelodysplasia indicate a probable immune-mediated mechanism responsible for these manifestations.

In our study abnormal neuroimaging (cranial sonography) was present in three infants (10.00 %) Only one patient had the characteristic intracranial linear calcification that was confirmed by CT scan. CMV retinitis is a significant cause of ocular morbidity both with respect to its location within the retina and its progression and it may be different in infants compared to adults. We found that 11.53 % of our patients had an abnormal ophthalmological finding. One patient had salt pepper appearance and another non specific retinitis. More ever retinitis can be a delayed presentation and some studies mention that retinitis resolves on its own without the need of antiviral[19] Coors LE et al reported a case study where the child did not receive treatment with ganciclovir during hospitalization after birth despite severe manifestations of CMV infection and the location of retinitis was in the periphery of the retina of both eyes. The retinitis resolved during a period of 3 months[20].

CONCLUSION

CMV infection in infants is more common in those born to young multigravida mother having a lower educational qualification and belonging to rural area. Most infants are male in age group of 1-6 months, who are exclusive breast fed. Compromised growth in form of underweight for age is frequently seen. Respiratory system involvement with bilateral lung involvement is a common presentation. Hematological and biochemical derangements do not affect the outcome.

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