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Frequency and Clinical characteristics of congenital cytomegalovirus infection among low-birth-weight newborn in a tertiary care hospital, Dhaka, Bangladesh

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Abstract
Background: Cytomegalovirus (CMV) infection is currently the leading cause of congenital infections. Despite being asymptomatic in 90% of cases at birth, it can affect myriad organs including the nervous system. Congenital CMV infection has a common association with low birth weight specially IUGR. But in most of the cases, it remains undetected.
Objective: To evaluate the frequency & clinical characteristics of Congenital Cytomegalovirus infection in low birth weight (LBW) newborns.
Methodology: This prospective observational study was conducted in the Department of Neonatology, BSMMU over a one and half years from March 2022 to August 2023. Urine was collected within three weeks of birth from the admitted low birth weight (LBW) newborn and was sent for urinary CMV DNA analysis. Newborn with Positive urinary CMV DNA was labeled as CMV infected. All LBW newborns were followed up during the hospital stay for any features of congenital CMV infection. Statistical analyses were performed using SPSS version 25.
Results: Among 58 LBW newborns, 3 (5.2%) were found to have congenital CMV infection (cCMV). Hepatomegaly (100%) & direct hyperbilirubinemia (100%) were the most common clinical characteristics followed by hepatosplenomegaly (66.7%), microcephaly (66.7%), petechiae/purpura (66.7%) & thrombocytopenia (66.7%). Hearing impairment was found significantly higher on hearing screening in CMV infected compared with CMV non-infected newborns (66.7% vs 9.4%, p= 0.047). No abnormality was found in ophthalmological evaluation.
Conclusion: Frequency of CMV infection in LBW newborns is 5.2% in this study. Mostly detected clinical characteristics are hepatomegaly and direct hyperbilirubinemia. There is association of hearing impairment with CMV infection. There is no effect of CMV infection on vision in this study.

Keywords: Congenital Cytomegalovirus Infection, Low Birth Weight New

Introduction

Birth weight has been a key predictor of neonatal mortality and morbidity. Epidemiological observations reflect that low birth weight (LBW) newborns have a 20 times higher risk of dying than normal-weighted ones. Despite a declining neonatal mortality rate globally, marked disparities in neonatal mortality exist across the countries. Regionally, neonatal mortality was highest in Sub-Saharan Africa (i.e., the combination of the West and Central Africa and Eastern and Southern Africa regions) and South Asia, with the neonatal mortality rate estimated at 27 and 23 per 1,000 live births, respectively, in 2021. A newborn born in South Asia was nine times more likely to die in the first month than a newborn in a high-income country [1]. Among these LBW contributes to 40-60% of neonatal mortality [2]. The global prevalence of low birth weight is estimated to be 15% to 20% of all births representing over 20 million births in a year [3]. In Bangladesh, the prevalence of low birth weight is around 22% [4]. According to the Bangladesh health and demographic survey, 2022, the under-5 mortality rate was 31 per 1,000 live births and the neonatal mortality rate was 20 per 1,000 live births, among this prematurity and LBW contributed 32%. There has been a steady downward trend in childhood mortality in Bangladesh, with a 35% decline in neonatal mortality and a 28% decline in under-five mortality in the last 5 years.

To achieve the United Nations' Sustainable Development Goal (SDG) target 3.2 (i.e., Reduction of neonatal deaths to at least as low as 12 per 1,000 live births, whereas during this study period, the neonatal mortality rate was 20 per 1000 live birth), Bangladesh needs to reduce neonatal deaths by 40% [5]. A goal of the 4th Health, Population, and Nutrition Sector Program (4th HPNSP) is to reduce under-5 mortality to 34 deaths per 1,000 live births by 2023, and this has been achieved. Another goal is to reduce neonatal mortality to 18 deaths per 1,000 live births by 2023, and meeting this goal is within close reach. The most common causes of neonatal mortality are prematurity (29.7%), birth asphyxia & birth trauma (22.9%), sepsis (19.9%), congenital anomalies (12.7%) & others [6]. Congenital cytomegalovirus (cCMV) infection is one of the familiar causes of prematurity & congenital anomalies that is responsible for not only neonatal mortality but also morbidity. Newborns can acquire it from their mothers both during the antepartum and intrapartum periods. It is one of the risk factors for low birth weight especially intrauterine growth restriction (IUGR) and small for gestational age (SGA) [7]. The worldwide prevalence of cCMV is 0.67% with significant variation**,** whereas in developing countries it varies from 0.6% to 6.1% [8, 9]. In India, the prevalence i**s** 0.40% whereas in China 0.69%, and in Indonesia 5.84% [10-12]. However, there is no available data found in Bangladesh.

Although we have a lack of national data, Cytomegalovirus (CMV) is one of the most identifiable cause**s** of congenital infection worldwide. Around 80 to 90% of congenital cytomegalovirus infection remain subclinical, despite being asymptomatic can lead to permanent sequelae in 15% to 18% of cases including death in 1%, neurocognitive sequelae in 5% to 15% and hearing loss in 12% of individuals [8, 13, 14]. Approximately 10% of these newborns have apparent clinical signs of infection at birth (referred to as symptomatic congenital CMV infection) [14]. The typical clinical characteristics of congenital CMV infection that are found in infected neonates include intrauterine growth retardation, microcephaly, hepatosplenomegaly, jaundice, chorioretinitis, thrombocytopenic purpura [15, 16]. Congenital CMV infection is highly prevalent in the human population, with seroprevalence ranging from 45% to 100% [12]. It has a common association with low birth weight but in most cases, it remains undetected. Accurate diagnosis [17] of congenital CMV infection is possible if only within the first 3 weeks of life virus is isolated from blood, urine, saliva, buffy coat, cerebrospinal fluid, bronchial lavages, or tissue samples were taken at biopsy [17]. This can be done by cell culture, shell vial assays, or DNA amplification by Polymerase Chain Reaction (PCR). Serological tests include anti-CMV IgM and anti-CMV IgG antibodies. Beyond 3 weeks virologic and serological tests can no longer clearly distinguish between congenital and acquired infection [18]. Early diagnosis of congenital CMV infection is essential to start treatment and reduce permanent sequelae. Al-Dasoky (2012) in his study found an 80% improvement in thrombocytopenia after 6 weeks of treatment, regression of hepato-splenomegaly (70%) after one year, 55% improvement of chorioretinitis and 66% improvement in SNHL [19]. A study published in Bangladesh by Mahbub, Azam and Khan revealed a significant improvement in hearing among treated children compared to untreated controls [20]. This study aims to observe the frequency and clinical characteristics of Congenital Cytomegalovirus infection in admitted low birth weight newborns.

Materials and Methods

Study design: Prospective comparative study.

Place of Study: Department of Neonatology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, Bangladesh.

Time of Study: March 2022 to August 2023.

Study population: Low Birth Weight (LBW) newborns admitted within three weeks of postnatal age (age 1 to 21 days) were included in this study.

Exclusion criteria: Parents of infants who refused to give consent, baby's postnatal age beyond three weeks, babies whose birth weight was unknown or was not measured just after birth, and mothers having inadequate medical records regarding the gestational age of her delivery were excluded from this study.

Sample size: 58

Study Procedure: This prospective observational study was conducted for eighteen months in the Department of Neonatology, BSMMU, Dhaka after approval from the Institutional Review Board (IRB). Low birth weight (LBW) newborns were identified as per their birth weight. The birth weight of inborn babies was taken without clothing soon after birth on an electronic scale with a precision of ±5 g [Model KINLEE EBST-20]. In the case of outborn babies, birth weight was taken from their medical records. The length was taken by infantometer & OFC was measured by flexible non-stretchable measuring tape, expressed in centimeters (cm). Informed written consent was taken from the parents/legal guardians of eligible newborns and face-to-face interview was conducted. The mother's medical records were also reviewed and recorded in a data collection form. Newborn's gestational age was calculated based on the mother's first day of last menstrual period (LMP) or first-trimester antenatal ultrasonography or New Ballard scoring of newborns soon after birth.

Five ml urine was collected by pediatric urine collection bag within 3 weeks of age of admitted low birth weight newborn during this study period, transferred into a sterile test tube, and then sent to the department of Virology of BSMMU as soon as possible within 24 hours of collection for detection of Congenital Cytomegalovirus by Real-Time Polymerase Chain Reaction Analysis (RT PCR) of urine.

Urine was analyzed in the Applied Biosystems™ 7500 Real-Time PCR system, USA by using Fast-track Diagnostics Real-Time PCR Kits (FTD) Cytomegalovirus, Luxembourg kit. The limit of detection of FTD Cytomegalovirus was at 100 IU/ml in 95% of tested specimens. The quantitative result of Cytomegalovirus (CMV) DNA was reported as International Units (IU) /ml. The linear range of the FTD Cytomegalovirus Quantification kit was determined by analyzing a dilution series of HCMV quantification standards ranging from 5x 10^3 IU/ml to 5x10^6 IU/ml per run in a 25uI reaction. These quantification standards were correlated with the 1st WHO International standard for HCMV for Nucleic Acid Amplification Techniques NIBSC code: 09/162 (version

3.0, dated. 30/11/2010).
Infants with detected urinary CMV DNA were labeled as CMV infected and undetected urinary CMV DNA was labeled as CMV non-infected.
All enrolled LBW newborns were followed up during the hospital stay for any features of congenital CMV infection and recorded.
A complete blood count (CBC) was done in all enrolled newborns to assess thrombocytopenia. Neonates developed jaundice were assessed clinically and were confirmed by total and fractionated serum bilirubin.
Hearing screening was done by TEOAE (transient evoked otoacoustic emission) test (by GSI Corti™ OAE Instrument) in the NICU of BSMMU by the principal investigator during discharge as per our departmental protocol.
Ophthalmological evaluation of enrolled newborns was done by indirect ophthalmoscope in the ophthalmology department of BSMMU or NICU of BSMMU by two assigned expert ophthalmologists as per their departmental protocol. If the newborn was <30 weeks of gestation or birth weight < 1200g, screening was done at 20 days of age. Screening was done at 30 days if the newborn was ≥30 weeks of gestation or birth weight ≥ 1200g.
All confirmed CMV-infected newborns were isolated and consultation was taken from the pediatric neurology department and treated according to their management protocol. Newborns without congenital CMV infection were treated according to the departmental protocol.

Statistical analysis
After collecting the data, it was entered into a personal computer. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS), version 25. Quantitative variables were presented as mean ± SD. Qualitative variables were presented as mean and percentages. The Independent t-test was used for quantitative variables. The chi-square test or Fisher exact test was used for categorical variables. The result was considered statistically significant if values of- $p < 0.05$.

Results

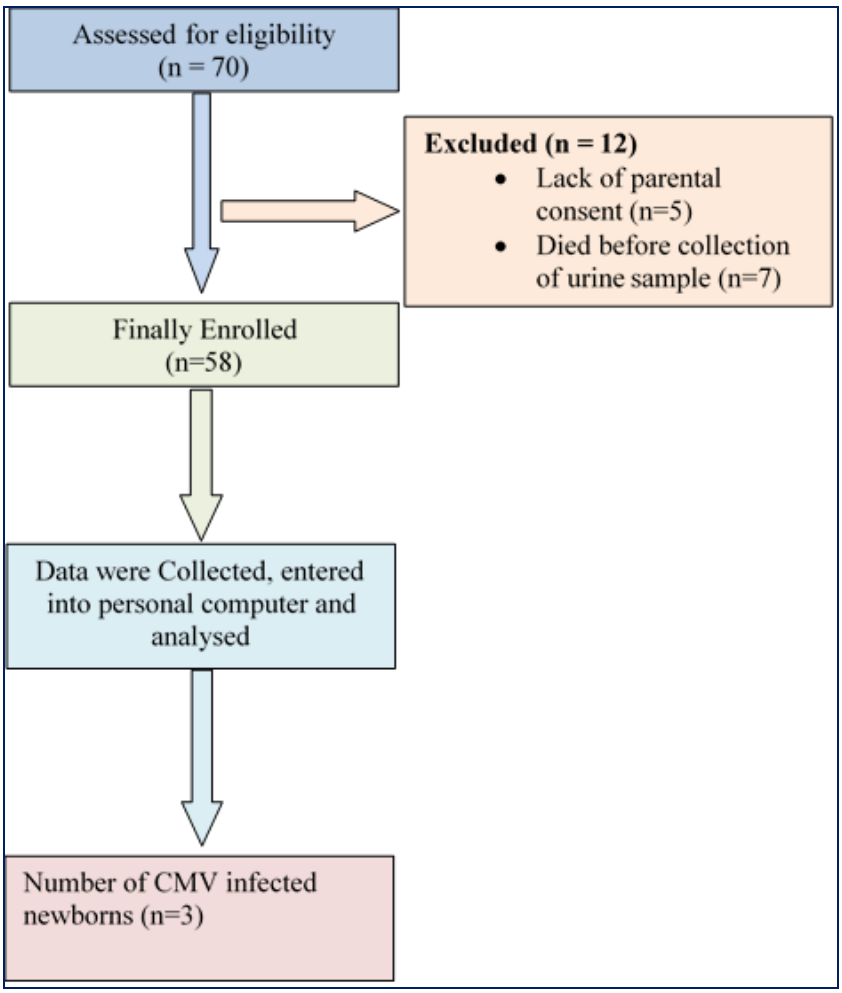

Fig 1: Flow chart of participants & results in the study

During the study period, 70 newborns were assessed for eligibility by consecutive sampling from admitted low birth weight (LBW) newborns. Among them 12 patients were excluded due to 5 newborns' parents did not give consent, and 7 patients died before the collection of urine samples. Finally, 58 newborns were enrolled in the study & 3 newborns were found CMV infected.

Table 1: Frequency of CMV infection in LBW newborns (N= 58)

LBW newborns	58
CMV-infected newborns *	3
Frequency	5.2%

Qualitative data are expressed as percentage (%), LBW: Low Birth Weight, CMV: Cytomegalovirus, *CMV DNA positive

The frequency of CMV infection in LBW newborns in BSMMU was 5.2% (Table 1).

Table 2: Baseline characteristics of enrolled newborns (N=58)

Characteristics	CMV infected newborns (n=3)	CMV non-infected newborns (n=55)	p-value
Gestational age in weeks (mean±SD)	35 ± 1	33.51± 3.24	0.434 ns
Birth weight in g (mean±SD)	1866.67±540.12	1554.87±438.68	0.240 ns
Length in cm (mean±SD)	43.33±3.79	40.15± 3.90	0.173 ns
OFC in cm (mean±SD)	30.33 ± 4.93	29.42± 2.92	0.611 ns
Mode of delivery			
LUCS, n (%)	2 (66.7%)	39 (70.9%)	0.875 ns
VD, n (%)	1 (33.3%)	16 (29.1%)	
Sex			
Male, n (%)	2(66.7%)	26(47.3%)	0.513 ns
Female, n (%)	1(33.3%)	29(52.7%)	

Numerical data are presented as mean±SD and categorical data as percentage (%)
NS: Not significant, S: Significant, Statistical test: Independent Sample t test and Chi square test, SD: Standard deviation, OFC: Occipitofrontal circumference, LUCS: Lower Uterine Cesarean section, VD: Vaginal delivery

Regarding the baseline characteristics of the studied newborns, mean gestational age, mean birth weight, mean length, mean OFC of CMV infected and CMV non-infected newborns were 35 weeks and 33.51±3.24weeks, 1866.67±540.12 g and 1554.87±438.68 g, 43.33±3.79 cm, and 40.15±3.90 cm, 30.33±4.93 cm and 29.42±2.92 cm respectively. More than two-third of CMV infected and CMV no-infected newborns were delivered by LUCS, 66.7% and 70.9% for respectively. Gender distribution reflects male predominance in CMV infected newborns than CMV no infected newborns. But there was no statistically significant difference (p- value > 0.05) between CMV infected newborns and CMV non-infected newborns in baseline characteristics (Table 2).

Among the three CMV infected newborns 1 (33.3%) and 2 (66.7%) belonged to (32-<34) weeks and (34-<37) weeks group respectively. Among the 55 CMV no infected newborns 15 (27.3%), 16 (29.1%), 12 (21.8%) and 12 (20.7%) were belonged to below 32 weeks, (32-<34) weeks, (34-<37) weeks and ≥37 weeks group respectively (Table 3).

Table 3: Distribution of gestational age among the enrolled newborns (N=58)

Gestational age categories	CMV infected, n (%)	CMV non-infected, n (%)	p- value
<32 weeks	0 (0)	15 (27.3)	0.277 ns
32-< 34 weeks	1 (33.3)	16 (29.1)	
34-<37 weeks	2 (66.7)	12 (21.8)	
≥ 37 weeks	0 (0)	12 (20.7)	

NS: Not significant
Statistical test: Fisher's exact test

About 1 (33.3%) of CMV infected LBW newborns were very low birth weight and 2 (66.7%) were low birth weight. Approximately 6 (10.9%) of CMV non-infected newborns were extremely low birth weight, 23 (41.8%) were very low birth weight and 26 (47.3%) were low birth weight (Table 4).

Table 4: Distribution of birth weight among the enrolled newborns (N=58)

Birth weight Category	CMV infected, n (%)	CMV non-infected, n (%)	p- value
< 1000 g	0 (0)	6 (10.9)	0.741 ns
1000- <1500 g	1 (33.3)	23 (41.8)	
1500- < 2500 g	2 (66.7)	26 (47.3)	

NS: Not significant
Statistical test: Fisher's exact test

Among 58 LBW newborns 30 (51.8%) were appropriate for gestational age (AGA). Whereas 28 (48.27%) were found intra uterine growth restriction (IUGR). About half of them 14 (50%) were asymmetrical IUGR and rest 14 (50%) were symmetrical IUGR**.**

Table 5: Types of IUGR among the enrolled newborns (N=28)

Types of IUGR	CMV infected (n=2)	CMV non-infected (n=26)	p-value
Symmetrical IUGR, n= (%)	2 (100)	12 (46.2)	0.481 ns
Asymmetrical IUGR, n= (%)	0 (0)	14 (53.8)	

NS: Not significant
Statistical test: Fisher's exact test

Among the 28 IUGR newborns 2 (66.7%) were CMV infected and 26 (47.3%) were CMV noninfected. Among the types of IUGR all the 2 CMV infected newborns were symmetrical IUGR. In case of CMV noninfected newborns

12 (46.2%) and 14 (53.8%) were symmetrical IUGR and asymmetrical IUGR respectively. In comparison between the CMV infected and CMV non-infected IUGR newborns p- value was not statistically significant (p-value 0.481) (Table 5).

Table 6: Clinical and laboratory features of enrolled newborns (N=58

Clinical characteristics	CMV infected newborns (n=3)	CMV non-infected newborns (n=55)	p-Value
Microcephaly, n (%)	2(66.7)	12(21.8)	0.077 ns
Hepatomegaly, n (%)	3(100)	21(38.2)	0.034 s
Hepatosplenomegaly, n (%)	2(66.7)	7(12.7)	0.042 s
Petechiae/Purpura, n (%)	2(66.7)	18(32.7)	0.228 ns
Jaundice Indirect hyperbilirubinemia*, n (%)	0(0)	39(70.9)	0.031s
Direct hyperbilirubinemia, n (%)	3(100)	10(18.2)	0.001s
Thrombocytopenia, n (%)	2(66.7)	28(50.9)	0.595ns

S: Significant
NS: Not significant

Statistical test: Chi square test and for * Fisher's exact test: Regarding clinical characteristics of congenital CMV infection, microcephaly, petechiae/ purpura and thrombocytopenia were found higher in CMV infected than CMV non-infected newborn but p-values were not statistically significant (p-value 0.077, 0.228, 0.595 respectively). Hepatomegaly, hepatosplenomegaly and direct hyperbilirubinemia were found significantly higher in CMV infected newborns than newborns having no CMV infection (p- value 0.034, 0.042, 0.001 respectively). Indirect hyperbilirubinemia was found significantly higher among CMV non-infected newborns compared with CMV infected newborns (p- value 0.031) (Table 6).

Table 7: Hearing screening of enrolled newborns in both ear (N= 35)

Hearing screening	CMV infected newborns (n=3)	CMV non-infected newborns (n=32)	p-value
Refer, n (%)	2 (66.7)	3 (9.4)	0.047s
Pass, n (%)	1 (33.3)	29 (90.6)	

S: Significant
Statistical test: Fisher's exact test

Among 58 newborns 23 were died. So, hearing screening could be performed in 35 newborns, 3 in CMV infected newborns and 32 in CMV non-infected newborns. Hearing screening was significantly found 'refer' in CMV infected newborn (p=0.047) (Table 7). So, hearing impairment was significantly higher in CMV infected than CMV non-infected newborns.

Ophthalmological features (Chorioretinitis, Pigmentary retinitis, Macular scarring, Optic atrophy) of CMV infection were not found among the enrolled newborns.

Discussion

Cytomegalovirus is the most common viral cause of congenital infections in newborns. This infection has a common association with low-birth-weight newborns especially in IUGR. But in most of the cases it remains undetected. The significance of CMV infection lies in its potential to cause long term neurological impairment. Therefore, an early identification of this infection is essential to take necessary intervention and for better outcome. This cross-sectional study was conducted with an objective to find out the frequency and clinical characteristics of congenital cytomegalovirus infection in low-birth-weight newborns.

In the current study the frequency of CMV infection was 5.2% among 58 enrolled LBW newborns. Putri *et al*., (2019) reported the prevalence of congenital cytomegalovirus infection 5.8% in Jakarta [12]. A systematic review conducted by Lanzieri *et al*., (2014) found the CMV birth prevalence varied from 0.6% to 6.1% in developing countries [9]. A large systematic review conducted by Ssentongo, Hehnly, Birungi, Mikayla A. Roach, *et al*., (2021) from 1960 to 2021, estimated that the overall prevalence of cCMV 0.67%. They also found that the pooled birth prevalence of cCMV was three-fold greater in low- and middle-income countries (1.42%) than high income countries (0.48%). These studies showed different prevalence rates of congenital CMV infection in different population. As this study was conducted in high-risk newborns (LBW newborns), the frequency was found to be higher than the other study conducted in common population [8].

Present study aimed to observe the clinical characteristics of congenital CMV infection. Though microcephaly was found more in CMV infected newborns compared to CMV non-infected newborns but was not statistically significant (66.7% vs 21.8%, p = 0.077) may be due to small sample size. However, a study in United states done by Messinger *et al*., (2020) reported that cCMV increases the prevalence of microcephaly at birth by at least 7-fold [21].

In this study hepatomegaly (100% vs 38.2%, p=0.042) and hepatosplenomegaly (66.7% vs 12.7%, p=0.042) were significantly higher in CMV infected newborns than newborns having no CMV infection. A study done by Gandhoke *et al*. (2009) in India revealed that among clinical manifestations in cCMV, hepatosplenomegaly was the most common feature [22]. Albanna *et al*., (2013) found hepato-splenomegaly (42%) in their study [23]. Vaudry, Lee and Rosychuk (2014) found splenomegaly (22.4%) and hepatomegaly (20.4%) in their study [24].

Regarding jaundice, direct hyperbilirubinemia (100% vs 18.2%, p=0.001) was found to be significantly higher among CMV infected newborns in current study. Indirect hyperbilirubinemia was not found in any CMV infected

newborns in this study and it was significantly higher in CMV non-infected in comparison to CMV infected newborns (p- value 0.031). However, Albanna *et al*. (2013) found jaundice (63%) in their study [23]. Whereas another study done by Gandhoke *et al*., (2006) revealed hepato-splenomegaly followed by neonatal cholestasis (direct hyperbilirubinemia), microcephaly were the most common clinical features in cCMV [25].

Though petechiae/purpura (66.7% vs 32.7%, P=0.228) and thrombocytopenia (66.7% vs 50.9%, P=0.595) were more frequently observed in CMV infected newborns but not statistically significant when compared with CMV non-infected newborns. However, a study in Canada by Wendy Vaudry found thrombocytopenia (53.1%) was the most common characteristics [24]. Purti *et al*., (2019) also found significantly higher frequency of thrombocytopenia (33% vs 9%, p < 0.001) in CMV-positive compared to CMV-negative neonates [12]. Whereas Albanna *et al*., (2013) and Mc Mullan *et al*., (2011) found thrombocytopenia in 21% and 33% patients respectively in their studies [23, 26].

The clinical manifestations of symptomatic CMV infection reported by de Vries, (2019) were low birth weight, jaundice, hepato-splenomegaly, thrombocytopenia, purpura and microcephaly. In the current study hepatomegaly, hepatosplenomegaly and direct hyperbilirubinemia were the most common clinical manifestations [7].

According to present study hearing impairment was found significant in 1st screening in CMV infected newborns compared to CMV non-infected newborns (p-value 0.047). 23 newborns died before hearing screening. So, this result might be differed if hearing screening could be done in all patients.

Manan and Manan (2021) mentioned that CMV-associated hearing impairment can be a finding not only detected at birth but also may be identified later in life. Up to 50% of sensorineural hearing loss (SNHL) due to cCMV was delayed-onset loss of hearing, and almost half of these patients experienced progressively deteriorating auditory function [27]. Lanzieri *et al*., (2017) also documented that approximately 5% of the asymptomatic patients may develop at least unilateral SNHL within 12 months of age [28]. Whereas Dahle et.al. (2000) mentioned in their study, late-onset hearing loss occurs throughout the first several years of life with the median age for late-onset hearing loss at 44 months of age indicating that children with congenital CMV infection should be evaluated for hearing function at least annually until 6 years of age [29]. Ophthalmological abnormality was not observed in any patient in this study. This may be due to small sample size and detection of these abnormalities requires long term.

Bhatt *et al*., (2018) performed serial eye examinations on children with congenital CMV infection up to college graduation of age. Severe visual impairment was found in 10 (13.0%) symptomatic patients, and was caused by optic nerve atrophy (6/10), chorioretinitis (6/10), cortical visual impairment (7/10), and chronic retinal detachment (1/10) among 237 infants and children. All abnormalities leading to severe visual impairment were diagnosed before the age of 18 years in both the symptomatic and asymptomatic groups. They also found non-ocular findings, including sensorineural hearing loss (SNHL), microcephaly, abnormal brain CT imaging, and intracranial calcifications were significantly higher in the symptomatic CMV group than in the asymptomatic CMV group. SNHL in particular was highly associated with the six leading ophthalmologic findings: optic nerve atrophy, nystagmus, cortical visual impairment, retinal scars, strabismus, and severe visual impairment [30]. So, long term follows up is necessary for detection of hearing impairment and ophthalmological abnormality.

Regarding demographic characteristics no significant difference was observed between CMV infected and CMV non-infected LBW newborns in this study. Mean gestational age of CMV infected newborns were 35 ±1 week. Among the 3 CMV infected newborns, two of them were preterm IUGR (66.7%) and remaining one was term appropriate for age (AGA) (33.3%). All the CMV infected IUGR were found symmetrical IUGR in this study.

Al-Khawaja *et al*., (2012) mentioned that preterm newborns tend to show higher susceptibility to postnatal and perinatal infections [31]. In the study done by El-Fouhil *et al*., (2006) the prevalence of congenital CMV infection was significantly higher among preterm newborns (12.2%) compared to full term newborns (5.6%) [32]. However, the frequency of CMV infection in the preterm newborns (16.7%) was similar to that observed in full term newborns (14.7%) in a study done in Hungary by Nagy *et al*., (2004) [33].

In the present study mean birth weight of CMV infected newborns was 1866.67 ± 540.12 g. About two third (66.7%) of them were low birth weight, one-third (33.3%) were very low birth weight. This finding was consistent with Morgan *et al*., (2003) who reported CMV infections are of more prevalence in premature and low birth weight neonates [34].

Males (66.7%) were more affected by CMV infection than females (33.3%) in this study. This is consistent with the findings of Munro *et al*., (2005) who found 54.3% males and 38.6% females in their study comprising of 62 patients [35]. Mc Mullan *et al*. (2011), El-Fouhil *et al*. (2006) and Mahbub, Azam and Khan (2011) also mentioned similar findings revealing that CMV infection had a male predominance [26, 32, 20].

In current study 66.7% of CMV infected newborns were delivered by LUCS and 33.3% were delivered by vaginal delivery. As BSMMU is a referral institution and in most of the cases mother had some complications like uncontrolled hypertension, premature rupture of membrane and severe oligohydramnios which contributed to this higher rate of Cesarean section.

Limitations of the study

As a number of patients died due to their other morbidities, hearing & ophthalmological screening could not be done in all enrolled patients in this study. This limitation could impact the completeness and generalizability of the study's findings. Another challenge in the study was that multiple ophthalmologists conducted ophthalmological evaluations, introducing variability in the assessment process due to differences in expertise and diagnostic criteria among these specialists. The study lacked a follow-up period to assess the long-term consequences of hearing and visual impairments in enrolled patients.

Conclusion

Frequency of Congenital cytomegalovirus infection among LBW newborns is 5.2% in this study. Congenital CMV infection is significantly higher in Symmetrical IUGR newborns. Hepatomegaly, hepatosplenomegaly and direct

hyperbilirubinemia are the most common clinical characteristics. Hearing impairment is found significantly higher in CMV infection but effect of CMV infection on vision was not found in this study.

Recommendations

Studies involving multicenter/ community can be recommended to make better comment on frequency and clinical characteristics of the congenital cytomegalovirus infection.

Author contribution: All authors contributed to the study conception and design. Material preparation, data collection and statistical analysis was performed by first author. The first draft of the manuscript was written by first author and respected other authors further reviewed and commented on the first and the following drafts, until the final version of the article. All authors commented on previous versions of the manuscript. All authors read the final manuscript.

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Conflict of interest: The authors declare that they have no conflict of interest.

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