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#### **Research Article**

# Barriers of Attendance Clinical Follow-Up of Congenital Cytomegalovirus Infection in a Low-Income Population, Brazil

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- Congenital infection
- Clinical follow-up
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#### Abstract

The clinical follow-up for congenital Cytomegalovirus (CMV) infection has been pointed as a main barrier for low-income populations. Here, we addressed factors related to the lack of attendance to clinical follow-up for congenital CMV infection in a low-income population from South Bahia, Brazil. A total of 25 newborns with positive diagnosis for congenital CMV infection were enrolled in this study. Only one patient was symptomatic and died due to CMV infection. Half of the families attended a medical follow-up visit during newborn's first years of life and 8.3% presented hearing changes, the main late symptoms associated with CMV infection. Individuals presenting late symptoms did not return brainstem-evoked response audiometry. The reported barriers to the absence of clinical follow-up were urban mobility, negligence, and lack of resources. Our results suggest that congenital CMV infection and irreversible outcomes such as mental retardation and hearing loss could be neglected in low-income populations due to barriers and low-adherence to the clinical follow up. We believe that increasing efforts promoting public health and education goals could improve the population awareness and commitment to clinical follow up.

# **INTRODUCTION**

Human Cytomegalovirus (CMV) is a widespread pathogen and frequently associated with intrauterine infections, with a prevalence rate up to 70% [1]. CMV has also been implicated as an opportunistic infection to immunocompromised individuals. CMV is usually transmitted through body fluids such as blood, saliva, urine, cervical secretions, and breast milk [2]. After a primary infection, pregnant women are able to transmit the virus to the fetus in approximately 40% of cases, in which 10–15% are symptomatic at birth [1].

CMV is mostly asymptomatic (85-90% of cases) or mildly symptomatic in infants, children, and adults. In newborns, CMV infection results in long-term neurodevelopment morbidity of all the perinatally acquired viral infections, which can be progressive and irreversible during early childhood [3]. Severe neurological and systemic sequelae such as sensorineural hearing loss (SNHL) (the most frequent and impactful sequel) and neurological impairment in children are reported [3]. Congenital CMV infection presents a significant impact on newborns quality of life, evidencing the importance confirmatory diagnosis aiming to minimize the effect of related sequences [4].

Prenatal screening is recommended for infectious diseases in order to avoid future complications for pregnant women and

expected babies [2,5]. The early detection of infections can help with the implementation of preventive healthcare measures, and consequently reducing the burden of congenital infections and associated outcomes [2,5]. However, besides improvements in medical care, assessing barriers related to individual and community levels are important factors to be considered when planning for infectious diseases screening and prevention [6]. The lack of adherence of prenatal care has been associated with some factors such as low educational level, low income, urban planning, and transportation logistics [6].

Here, we aimed to describe the lack of adherence of pregnant women to the clinical follow-up of congenital Cytomegalovirus infection in a low-income population in South Bahia State, Brazil. This study also brings an opportunity to discuss the impact related to the lack of attendance clinical follow-up among families with newborns that had a confirmed diagnostic for congenital CMV infection, as well as the barriers associated.

# **MATERIAL AND METHODS**

This study was carried out in a reference Pregnancy Care Center at Ilhéus city, South Bahia State (14º 47' 20" S, 39º 02' 58" W), during 2010–2012. According to data provided by the Brazilian Institute of Geography and Statistics (IBGE), Ilhéus city has an estimated population of 176.341 inhabitants, distributed

in an area of  $1.584,693 \, \mathrm{km^2}$ . Only 23.1% of the urban area is paved and 65.9% has adequate sanitary conditions [7,8]. The Maternity Santa Helena is a hospital serves several other neighboring cities and districts, as well as a large rural area, a large part of the socioeconomic status of the population (only 19.9% of the population) and 12.5% of the population, aged 15 or over, are illiterate [9]. The wide range of municipalities served, as well as the extensive rural area of the municipality are important factors that hamper clinical follow-up of medium and long term [9,10].

The study was approved by the Research Ethics Committee of Universidade Estadual de Santa Cruz under the registration protocol 209/08. An informed consent about the risks of participation in the study was provided to all participants. In case of minors, consent was signed by parents or guardians.

### **RESULTS**

A total of 25 newborns with confirmed diagnosis of congenital CMV infection were studied [10,11]. Quarterly medical visits were planned up to the second year of life for all patients. The visits also included clinical and complementary laboratory exams such as hemogram, hepatic function, total bilirubin and fractions, and audiometry evaluation. A total of 12 newborns (48.0%) attended to the clinical follow-up aiming to evaluate and reduce the development of late sequelae caused by CMV infection. Two of these children (16.7%) presented changes in the hearing status, which is one of the main late symptoms caused by congenital CMV infection. The remaining 10 patients (83.3%) were asymptomatic. Only one newborn was symptomatic at birth and evolved to death due to CMV infection at the first week of life. After 21 months of follow-up, only 4 children (16.7%) returned to the physician for continuing evaluation. Unfortunately, we lost the patients who presented hearing changes due to the nonattendance of BERA. The main reported reason for non-attending BERA was due to moving of the families to other regions in Bahia State. As already mentioned in previous studies, the high urban mobility observed in the South of Bahia State is one of the factors that make difficult the long-term clinical follow-up [12]. Although we detected only two children with changes in the hearing status due to CMV infection, our findings suggest that the number of children with late-onset symptoms and sequels due to congenital CMV infection may be even higher, underestimate the reality, since we had low adherence and loss during follow-up.

### **DISCUSSION**

Neonatal screening for the early detection of infectious diseases is important and recommended. In fact, the early detection congenital CMV infection and the follow-up of infected children, since there is a possibility of interventions with antiviral therapies to avoid the progression of the disease, which is progressive. Furthermore, alternatives such as speech therapy, hearing implants, and specialized education and physiotherapy for cognitive and motor development can be implemented and improve quality of life of affected children [10,13,14]. In addition, prolonged CMV detection in the blood can lead to progressive sequelae such as SNHL if not properly treated [1,15].

As already mentioned, only half of families attended to postnatal consultation scheduled periodically until the

second year of life. In attempting to make feasible the samples collection and to reinforce the importance of medical follow-up (reducing the circumvention of children in the study), we proposed to additional home visits and clinical follow-up free of charge. Furthermore, we provided some educational resources to enhance about the importance of medical follow-up and complementary laboratory exams.

The most common factors related to the low adherence to clinical follow-up were change in contact (cellphone number has changed), changing place of residence, lack of financial conditions for transportation, lack of commitment of family members, and lack of knowledge regarding congenital CMV infection.

It has been already demonstrated that screening for congenital CMV infection during pregnancy is essential in order to prevent primary infection, clinical consequences and its sequelae prevented [9,15,16]. It is also important to emphasize that regular monitoring for progressive and late-onset deficits permits early rehabilitation [17,18]. Regular monitoring of all congenitally infected newborns including regular neurological, developmental, auditory, and visual assessments at least until school age in symptomatic newborns are recommended [16].

Furthermore, the low adherence to the medical returns can contribute to progression of CMV disease, due to the lack of adequate treatment in early infection. This issue highlights the importance of education programs to better inform the population about infections and prevention and treatment.

#### CONCLUSION

In conclusion, our findings could help with better strategies to increase the attendance of low-income populations in areas of high incidence of congenital CMV infection. Our data can also guide clinicians, decision makers, and public health authorities to better assist affected families. Congenital CMV infections continue to be a burden to public health, neglected in most developing countries such as Brazil. Providing resources such as transportation and home medical visits at affordable conditions or free of charge could help guarantee the follow-up of affected newborns as alternatives.

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