

ORIGINAL ARTICLES

IDENTIFICATION OF TORCH PATHOGENS IN CONGENITAL CATARACT PATIENTS VISITING ARMED FORCES INSTITUTE OF OPHTHALMOLOGY

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ABSTRACT

Objective: To assess the rate of positivity of *Toxoplasma gondii*, *Rubella*, *Cytomegalovirus*, *Herpes simplex* (TORCH) pathogens in patients suffering from congenital cataract in Pakistan.

Study Design: Cross sectional comparative study.

Place and Duration of Study: Armed Forces Institute of Ophthalmology, Rawalpindi, from Jun 2017 to Mar 2018.

Methodology: Cataract group included sixty children already diagnosed with congenital cataract and control group included 60 children not suffering from congenital cataract. Serum samples of all children were collected to test against IgG and IgM antibodies of *Toxoplasma gondii*, *Rubella*, *Cytomegalo*, *Herpes simplex* pathogens using enzyme linked immune assay (ELISA) technique. Data were analyzed observe in difference between unilateral and bilateral cataract and between cataract and control group.

Results: Out of 60 children in cataract group, 29 were tested positive for *Toxoplasma gondii*, *Rubella*, *Cytomegalo* (CMV), *Herpes simplex* infections. CMV IgG antibodies were identified in 21 (35%) children followed by Rubella IgG 13 (21.7%), Toxoplasmosis IgG 8 (13.3%), CMV IgM 7 (11.7%), HSV I IgG 5 (8.3%), HSV II IgG 2 (3.3%) and HSV I IgM 1 (1.7%) antibodies. None of the children was positive for *Toxoplasmosis*, *Rubella* and HSV II IgM antibodies. There was no statistical difference in rate of positivity of *Toxoplasma gondii*, *Rubella*, *Cytomegalovirus*, *Herpes simplex* pathogens between unilateral and bilateral cataracts and between cataract and control group.

Conclusion: *Toxoplasma gondii*, *Rubella*, *Cytomegalovirus*, *Herpes simplex* pathogens are an important cause of congenital cataract with *Cytomegalovirus* and *Rubella* virus being most common respectively. In order to prevent paediatric complications, we need to increase awareness among pregnant women and treating physicians.

Keywords: Congenital cataract, Congenital infections, *Cytomegalovirus*, *Herpes simplex virus*, *Rubella virus*, *Toxoplasma gondii*.

How to Cite This Article: Javaid M, Masud H, Rathore HS, Ali D, Javaid H. Identification of Torch Pathogens in Congenital Cataract Patients Visiting Armed Forces Institute of Ophthalmology. Pak Armed Forces Med J 2021; 71(5): 1515-1518. doi: <https://doi.org/10.51253/pafmj.v71i5.4320>

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INTRODUCTION

Opacification of lens at birth or during early childhood years is defined as congenital cataract¹. It is the most common cause of preventable blindness in childhood.¹ Congenital cataract alters the quality of light available to a child during important period of sensory development, thus leading to permanent visual loss.² Pathogenic factors responsible for congenital cataract are multiple and diverse. These include genetic, environmental, metabolic, infective and idiopathic causes.²

Infections acquired during pregnancy or immediately after birth by mother are an important cause of childhood morbidity in the perinatal period. Parasites viral infections are responsible for majority of congenital cataracts.³ This includes viral infections with *Toxoplasma virus* (TOX), *Rubella virus* (RV), *Cytomegalovirus*

(CMV) and *Herpes simplex virus* I and II (HSV I and HSVII) (TORCH).⁴ Changes in modern lifestyle with increased interaction with domestic animals and alteration in sexual behaviors has led to increase in infection rates of pregnant women with HSV and toxoplasma (TOX).⁵ The World Health Organization (WHO) estimates that world-wide annual incidence of congenital rubella syndrome is more than 100000 infants predominantly in developing countries.⁶ The stage of gestation of mother is also closely related to the amount of risk to the fetus. First,⁸ weeks have highest infection rate of about 50% followed by 9-12 weeks with 33%. Least infection rate is observed between weeks 13-24 of about 10%.⁷ Therefore, it is extremely important to timely diagnose these infections.

South Asia has highest sero-positivity of TORCH pathogens where estimate 20% cases of congenital cataract are positive.⁸ Vast varieties of diagnostic aids are available to confirm the presence of TORCH pathogens in children. After infection with TORCH patho-

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Received: 14 May 2020; revision received: 21 Jul 2020; accepted: 28 Jul 2020

gens a series of antibodies are produced by immune system of mother. These antibodies reach fetus after crossing placenta and remain there for a given time period even after birth.^{8,9} This study aimed to identify such antibodies mainly IgG and IgM antibodies in children with congenital cataracts using ELISA method.

METHODOLOGY

This study was conducted at Armed Forces Institute of Ophthalmology (AFIO) Rawalpindi from June 2017 to March 2018. It was a cross-sectional observational study which was approved by the Ethics Committee of the Institute (IERB approval no. Ethical/2017/06/1) and informed written consent was taken from all parents. Children were divided between two groups; first group consisted of children suffering from congenital cataract and second group included children not suffering from congenital cataract (control). All the congenital cataract patients (n=60) presenting to the AFIO Rawalpindi from June 2017 to March 2018, were included in the study. Universal sampling technique was used. Children under 10 years of age were included in the study.

Inclusion Criteria: Children were included irrespective of the gender, ethnicity and residence for both groups.

Exclusion Criteria: Cases with known history of familial cataracts, traumatic cataract and a known metabolic disorder were excluded from the study.

Sixty children already diagnosed with congenital cataract were enrolled in cataract group and 60 children not suffering from congenital cataract were enrolled in control group. A proforma was used to record patient profile, family history, delayed milestones, initial ocular examination including anterior and posterior segment examination and any systemic complaints. Age of children ranged from 8 days old to 10 years of age in both groups. Eighteen children had unilateral cataract and 42 children had bilateral cataract in cataract group.

A sample of 1-2 ml of peripheral venous blood was collected from each child. The samples were kept at room temperature to allow clot formation, after which sera were separated through centrifugation. Enzyme linked immune assay (ELISA) test was performed on each of these samples for qualitative assessment of IgM and IgG antibodies of *Toxoplasma gondii*, *Rubella virus*, *Cytomegalovirus* and *Herpes simplex virus I* and II. Calbiotech ELISA kits were used for IgG and IgM antibodies of *Rubella virus* and *Toxoplasma virus*

while Dialab ELISA kits were used for *Cytomegalovirus* and *Herpes simplex virus I* and II.

Rate of positivity of TORCH pathogens was compared between unilateral and bilateral cataracts as well as between cataract and control group. Data was analyzed using SPSS software 24. Chi Square test was applied for the data variables. The *p*-value ≤ 0.05 was considered statistically significant.

RESULTS

The ages of the children ranged from 8 days to 10 years with a mean of 3.49 ± 2.84 years for both groups. In cataract group, there were 41 (68.3%) male and 19 (31.7%) female children. Control group included 38 (63.3%) male and 22 (36.7%) female children.

In cataract group out of 60 children tested, 29 were positive for TORCH infections. CMV IgG antibodies were most frequent and were identified in 21 (35.0%) children with congenital cataract followed by Rubella IgG 13 (21.7%), Toxoplasmosis IgG 8 (13.3%), CMV IgM 7 (11.7%), HSV I IgG 5 (8.3%), HSV II IgG 2 (3.3%) and HSV I IgM 1 (1.7%) antibodies. None of the children was positive for *Toxoplasmosis*, *Rubella* and *HSV II* IgM antibodies as shown in table-I.

Table-I: TORCH Profile of patients in cataract group.

TORCH Profile	Studied Children n=60
Toxoplasmosis IgG	8 (13.3%)
Toxoplasmosis IgM	-
Rubella IgG	13 (21.7%)
Rubella IgM	-
CMV IgG	21 (35%)
CMV IgM	7 (11.7%)
HSV I IgG	5 (8.3%)
HSV I IgM	1 (1.7%)
HSV II IgG	2 (3.3%)
HSV II IgM	-

Thirty one (51.7%) children had negative TORCH profile, 15 (25%) children were positive for a single organism while 14 (23.3%) children were positive for multiple organisms as shown in Figure.

In cataract group, 18 (30%) children had unilateral cataract and 42 (70%) children had bilateral cataract. When stratified the data for unilateral and bilateral involvement, substantial differences were observed but none of them reached statistical significance as shown in Table-II.

In control group, out of 60 children tested, 18 (30%) tested positive for TORCH pathogens and 42 (70%) tested negative. Among these CMV IgG 8(13.3%) was most frequent followed by Rubella IgG 4 (6.7%), TOX IgG 2 (3.3%) and CMV IgM 2 (3.3%). HSV-I IgG

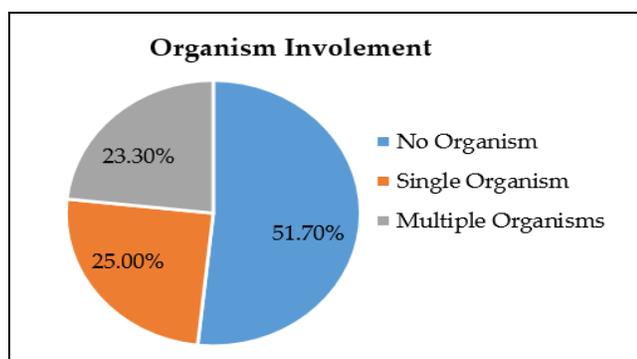


Figure: Distribution of Patients according to involvement of organism.

and HSV-II IgG had one case (1.7%) each. There were no positive cases observed for Rubella IgM, TOX IgM, HSV-I IgM and HSV-II IgM. When positivity rates of TORCH pathogens were compared between cataract and control group, substantial difference was observed but none of them reached statistical significance as shown in Table-III.

Table-II: TORCH profile for unilateral and bilateral cataract (n=60).

Torch Profile	Unilateral n=18	Bilateral n=42	p-value
Toxoplasmosis IgG	3 (16.7%)	5 (11.9%)	0.619
Rubella IgG	5 (27.8%)	8 (19%)	0.452
CMV IgG	8 (44.5%)	13 (30.6%)	0.315
CMV IgM	3 (16.6%)	4 (9.5%)	0.430
HSV I IgG	1 (5.6%)	4 (9.5%)	0.610
HSV I IgM	-	1 (2.4%)	0.509
HSV II IgG	-	2 (4.8%)	0.346

Chi-square test, Observed difference was statistically insignificant

Table-III: Rate of positivity of TORCH pathogen in cataract and control group (n=60).

Torch Profile	Cases n=60	Control n=60	p-value
Toxoplasmosis IgG	8 (13.3%)	2 (3.3%)	0.573
Rubella IgG	13 (21.7%)	4 (6.7%)	0.276
CMV IgG	21 (35%)	8 (13.3%)	0.524
CMV IgM	7 (11.7%)	2 (3.3%)	0.601
HSV I IgG	5 (8.3%)	1 (1.7%)	0.761
HSV II IgG	2 (3.3%)	1 (1.7%)	0.851

Chi-square test, Observed difference was statistically insignificant

DISCUSSION

Most common causes of congenital cataract include infection with TORCH pathogen. They mostly result from infections acquired by mother during maternity or immediate post op period. Therefore, it is pertinent to identify such cases to prevent the spread of infection to next offspring. In our study, we found high prevalence rate of TORCH pathogen positivity in children suffering from congenital cataract. Twenty-

nine out of sixty children tested were found to be positive for TORCH pathogens with IgG antibodies for CMV (n=21) and rubella virus (n=13) being most prevalent.

In order to diagnose TORCH infections a detailed review of maternal history is required. When this infection was acquired during pregnancy and any treatment received, should be documented.⁹ Screening serological tests are available for detecting TORCH pathogens. ELISA testing for IgM and IgG are by far the most common methods used. Presence of IgM antibodies shows current or recent infection whereas, presence of IgG antibodies signifies past infection. Hence, rate of IgM positivity is much less than IgG. Zhou *et al*, got similar low rates of IgM positivity as compared to IgG after screening 1194 children for TORCH infections.¹⁰

Among the TORCH pathogens, most common prevalent pathogens are CMV followed by Rubella virus. Biswas *et al*, showed in his study that the highest numbers of cases were of anti CMV IgM 19 (32.76%) and anti-rubella IgM 7 (12.07%) respectively. Anti HSV and Toxoplasma IgM were positive for equal cases, 3 (5.17%) each.¹¹ Similarly Dasgupta *et al*, reported IgG positivity was highest with CMV in 67.4% (31/46) children, whereas 43.4% (20/46) children were found non-immune to RV.¹²

Singh *et al*, conducted a study on 120 children suffering from congenital who were under the age of 6 years. He used PCR technique to diagnose Rubella (E1 gene), HSV-I (gpD gene) and toxoplasma (B1 gene). The positivity rate of IgM antibodies was 5.8% for Rubella Virus, 1.6% for HSV and 8.3% for Toxoplasma.¹³ In another study conducted by Saleem *et al*, on 68 children of congenital cataract in Pakistan, the positive rate for TORCH pathogens was 23.5%. Most common pathogen observed was CMV (n=8) followed by Rubella (n=2) and HSV (n=1).¹⁴ In our study rate of positivity for TORCH pathogen was 48.3%. CMV was the most common pathogen observed followed by Rubella.

Bin *et al*, conducted a study on 69 children suffering from congenital cataract and 59,¹⁴ children not suffering from congenital cataract. All children were screened for TORCH pathogens. They found higher positive rate for TORCH pathogens in cataract group. He also observed IgM positivity rate was lower than IgG.¹⁵ Similarly we also observed lower rate of IgM positivity as compared to IgG in our study. Mc Loone conducted a study on 30 patients suffering from non-

familial congenital cataract. He found that 9 of his patients tested positive for TORCH pathogens.¹⁶

Hamid *et al*, conducted a study on women with medical problems during pregnancy and congenital malformations in their children. He observed highest number of malformations in women infected from TORCH infections. Congenital anomalies were observed in 25% of women suffering from TORCH infections. Most common among them were CMV, TOX and RV infections.¹⁷ Leeper *et al*, discussed in utero and perinatal infections that can be vertically transmitted and cause birth defects. He found TORCH infections to be on the top of list.¹⁸

Other than cataract TORCH infections can also effect other ocular structure and systems. Congenital toxoplasmosis can cause abortion or even intra-uterine death, intrauterine growth restriction, hepato-splenomegaly and jaundice. Ocular or neurological involvement like hydrocephalus, intracranial calcifications or retino-choroiditis can also happen.¹⁹ Infection with Rubella virus has harmful effects on developing fetus leading to either abortion or result in sensori-neural hearing loss, cardiac defects or abortion.²⁰

Children with congenital CMV can have effects on brain, liver and spleen including intracranial calcifications, thrombocytopenia, hearing defects and delayed milestones.²¹ Herpes can cause primary infection followed by a latent period and reactivation resulting in encephalitis and congenital defects such as cardiovascular and neurodegenerative diseases.²²

TORCH infection can have hazardous consequences in the embryo leading to congenital abnormalities. Therefore, TORCH screening is must for all suspected mothers. Hamid *et al*, screened pregnant women for TORCH pathogens and observed the congenital mal-formations in their off spring. He reported that 35.71% of the infected cases had congenital defects. Most common pathogen observed was CMV followed by *Toxoplasma gondii* and *Rubella*. Congenital anomalies detected in these cases were intracranial calcification and cardiac anomalies, 20% each and microcephaly, hydrocephaly and strabismus 13.33% each. While cases of congenital cataract, anencephaly and meningocele/meningomyelocele were detected in 6.66%.²³ Hence, we need to screen both mother and baby timely for TORCH pathogens.

CONCLUSION

TORCH pathogens are an important cause of congenital cataract with cytomegalo virus and rubella virus being most common respectively. In order to prevent paediatric

complications we need to increase awareness among pregnant women and treating physicians

Conflict of Interest: None.

Authors' Contribution

MJ: Conception and design acquisition of data, analysis and interpretation of data, drafting of article, HM: final approval of article, HSR: concept and design, DA: concept and design, HJ: critical analysis.

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