

## Torch Positivity Amongst Children Presenting With Congenital Hydrocephalus In Bangladesh.

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ToRCH is an acronym for four congenital infections that are sometimes difficult to distinguish: Toxoplasmosis, Rubella, Cytomegalovirus, and Herpes Simplex Virus. This group of organisms produces serious CNS and other infections, which are potentially preventable and treatable. Methods: Neonates and infants with hydrocephalus (N=65) identified via the outpatient department of the National Institute of Neurosciences and Hospital (NINS&H), were prospectively screened for ToRCH antibodies. Patients with hydrocephalus secondary to tumor, trauma, hemorrhage, arachnoid cyst, and Dandy Walker Malformation were excluded from this study.

Results: Evidence of 75.38% of patients was positive for ToRCH antibodies. *T. Gondii* IgG 18.5%, CMV IgM 9.2 %, CMV Ig G 47.7%, Rubella, and Herpesvirus 1& 2 antibodies were also identified.

Conclusion: The vast majority of cases of idiopathic neonatal hydrocephalus at one institution were post-infectious in etiology and related to ToRCH infections. Many of these cases could have been prevented with improved maternal education, screening and treatment. While this single institution study may not be representative of the entire population, further study and implementation of a standardized screening protocol would likely benefit this population.

Key Words: Congenital Infection, ToRCH, Hydrocephalus, Prevention, CMV, Toxoplasmosis.

### Manuscript:

**Introduction:** Post-infectious hydrocephalus caused by congenital ToRCH infections is a significant source of morbidity and mortality, and its prevalence is known to vary by region. Transplacental spread is the usual route of infection in

neonates. This study was done to assess the status of ToRCH infection in congenital hydrocephalus (HCP). Early diagnosis and treatment of congenital ToRCH infections leads to improved outcomes. In an Indian study in Hyderabad *T. Gondii* was present in 28% and CMV in 92% of the population among pregnant woman.<sup>1</sup> Post-infectious hydrocephalus has been shown to be more prevalent in low- and middle- income countries compared with high income countries. Congenital toxoplasmosis may lead to a wide range of ocular and neurologic sequelae, including hydrocephalus, although avoiding exposure to cats and uncooked meat can aid prevention. *Toxoplasma* tachyzoites are secreted into milk in various farm animals.<sup>2</sup> Hydrocephalus has been estimated to affect approximately 4% of infants with congenital toxoplasmosis and is a significant cause of morbidity and mortality in this disease, however treatment during pregnancy appears to dramatically reduce the incidence of hydrocephalus.<sup>3</sup> The incidence of congenital rubella syndrome was significantly reduced over the last century due to vaccination.<sup>4</sup> CMV is the most common cause (10-20%) of congenital infection in the United States<sup>5, 6</sup> with a mortality rate of 12% by six months of age.<sup>7</sup> Global prevalence of CMV infection in developed countries (45%) and developing countries (100%).<sup>8</sup> Herpes simplex is most often acquired during delivery rather than during gestation, it is more preventable and treatable compared with CMV or Rubella.<sup>9</sup> Little is known about the role of ToRCH infections in the development of neonatal hydrocephalus in Bangladesh.

**Material and Method:** This was a prospective observational study in a consecutive cohort. Study was conducted in Pediatric Neurosurgery department of National Institute of Neurosciences and Hospital (NINS&H). Dhaka, Bangladesh. Sixty five patients were recruited between November 2017 to

October 2018. Inclusion criteria were neonatal HCP who had ToRCH positive result in serological exam [ELISA, ERBA®, USA<sup>10</sup>] Exclusion criteria included HCP associated with tumor, trauma, hemorrhage, arachnoid cyst, and Dandy Walker Malformation. Literature review regarding ToRCH related hydrocephalus, including screening and treatment protocols was also performed. Data were analyzed for association between Neonatal HCP and Congenital ToRCH infection using SPSS17. Categorical Data was analyzed using one sample t test where p Value <0.5 was considered statistically significant. We followed standard ethical guidelines as per institutional review board (IRB).

### Results:

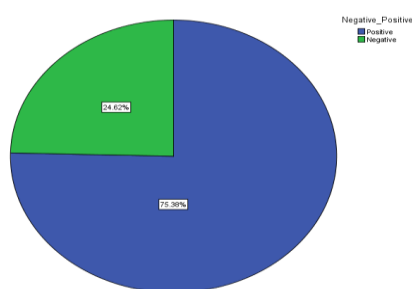


Fig 1: Pie Chart of ToRCH positive patient.

A total 65 cases of Congenital HCP with ToRCH positive serology were recruited according to selection criteria. Among the 65 cases 75.38 % cases were ToRCH Positive. Most of the patients came from rural areas, 56.9 % were male.

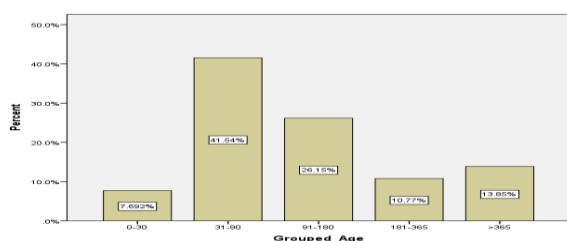


Fig 2: Bar Chart for Age Distribution of ToRCH positive Patients.

The commonest age group was 31-90 days (41.5 %). The total age range was 26 days to 6 years. All three patients with concurrent encephalocele and all eight patients with concurrent myelomeningoceles were also found to have congenital ToRCH infections. *T. Gondii* IgM antibody was absent but 18.5% were

*T. Gondii* IgG positive. Among the 12 cases of toxoplasma positivity, 6 (50%) had known contact with cat during pregnancy. Rubella IgM & IgG Antibody was present in 1.5% and 38.5 % respectively. As 86% of population under coverage of vaccination, so, antibody against Rubella may not important.<sup>11</sup>

	Frequency	Percent
<i>T. Gondii</i> IgG	12	18.5
CMV IgM	6	9.2
CMV IgG	31	47.7
Herpes-1 IgM	3	4.6
Herpes-1 IgG	17	26.2
Herpes-2 IgG	6	9.2

Table 1: Distribution of *T. Gondii* IgG, CMV IgM and IgG Antibody.

CMV IgM & IgG Antibody was present in 9.2% and 47.7% respectively. Herpes 1 IgM and IgG Antibody were present in 4.6% and 26.2% respectively. Herpes 2 IgM Antibody was absent but 9.2% patients were Herpes 2 IgG Positive.

Discussion: During the past 20 years, a number of scientific and sociological changes have altered the scenario of ToRCH infections. The incidence of these diseases has changed significantly because there are better preventive measures. The potentially significant relation between ToRCH infections and CNS anomalies including HCP and also NTDs is now an important subject of investigation. Few previous articles address this issue, although maternal ToRCH infection is common in Bangladesh, India, Malaysia and Thailand.<sup>12</sup>

Our data, derived from a prospective cohort of children with congenital hydrocephalus, show that 75% of cases were serologically positive for ToRCH antibodies. Although this study is based on association rather than establishing a causal link between infection and hydrocephalus, and although there is no control or comparator group, the data strongly suggests that actively screening for and treating these infections in utero, and improving maternal education about simple steps to avoid risk of infection, is critically important.

In a future study, we will include a control group (such as babies with hydrocephalus due to another known aetiology, such as a brain tumour or periventricular haemorrhage) and compare the incidence of seropositivity in the two groups.

Toxoplasma infection commonly causes cerebral calcification and generalized periventricular inflammation (asymmetrical dilatation of the lateral ventricles).<sup>13</sup> Treatment for toxoplasmosis in utero and during the first year of life has been shown to significantly improve outcomes.

Rubella is a benign, self-limited viral illness. Since the availability of mass immunization, the reported incidence of rubella has dropped significantly.<sup>14</sup> Hydrocephalus may be due to leptomenigitis and is a very rare presentation in congenital rubella syndrome with very few cases been reported in literature.<sup>15</sup>

A meta-analysis of fetal ultrasound findings indicates an association between CMV congenital infection and hydrocephalus in 4.7% of pregnancies.<sup>16</sup> CNS anomalies induced by congenital CMV infection are likely to result from a direct effect of viral replication in the brain and in the placenta. HCP in CMV as a result of ventriculitis and inflammatory infiltrate of T lymphocytes in the ependyma, which can be detected in antenatal Ultrasound (USG).<sup>17</sup> In our study we found 9.2 % of HCP due to recent CMV infection and 47.7 % HCP had IgG Antibody of CMV indicate maternal infection at least 3 months before. Transmission of the CMV virus requires direct contact with body fluids. Thorough hand washing and other preventive hygienic measures can decrease spread in daycare centers and at home.<sup>18</sup>

Known complications of intrauterine HSV infection include seizures, bulging fontanelle, chorioretinitis, microcephaly, and hydranencephaly, though occurring of infection is less frequent than might be expected.<sup>19, 20</sup> In our Study HSV-1 IgM positive in 3%, IgG positive in 26.2%. HSV-2 IgM not found in any case. Whereas HSV-2 IgG present in 9.2%. So, HSV-1 IgG present significantly ( $P < .05$ ). Literature review indicates relation between congenital HCP and Herpes infection is very weak.

**Limitation:** This study used serology as a diagnostic tool however PCR is more sensitive and specific. Other limitations were that the birth and recruitment interval was not fixed. History regarding immunization of baby, seropositivity of mother and contact with disease person was not recorded. On the basis of serology alone, it is impossible to assert whether hydrocephalus is given by possible infection or other causes, because it is not possible to distinguish a previous maternal infection from one that occurred during pregnancy, regarding this limitation we want to identify the mothers previous infection ground and do Molecular examination.

**Proposal:** Results of this study is a primary notice, as we face this profound problem we need to focus on this issue by further study. Then we can advice routine maternal and newborn screening as well as enhance preventive activity in high risk people.

**Conclusion:** Congenital TORCH infection and CNS involvement especially HCP is a severe problem for new born babies which produces serious socio-economic burden. This is an urgent issue to prevent, treat and do further research on this disease.

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