# Cytomegalovirus Complement Fixing Antibody in Children with Congenital Abnormalities

## Thesis

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*Clinical and Chemical Pathology*

By

MONA ZAKI ZAGHLOUL

Supervised by

Prof. ISLAH HASSAN EL FALAKY
Prof. of Clinical Pathology
Ain Shams University

Dr. IBRAHIM KHALIL ALI
Assist. Prof. of Clinical Pathology
Ain Shams University

FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY

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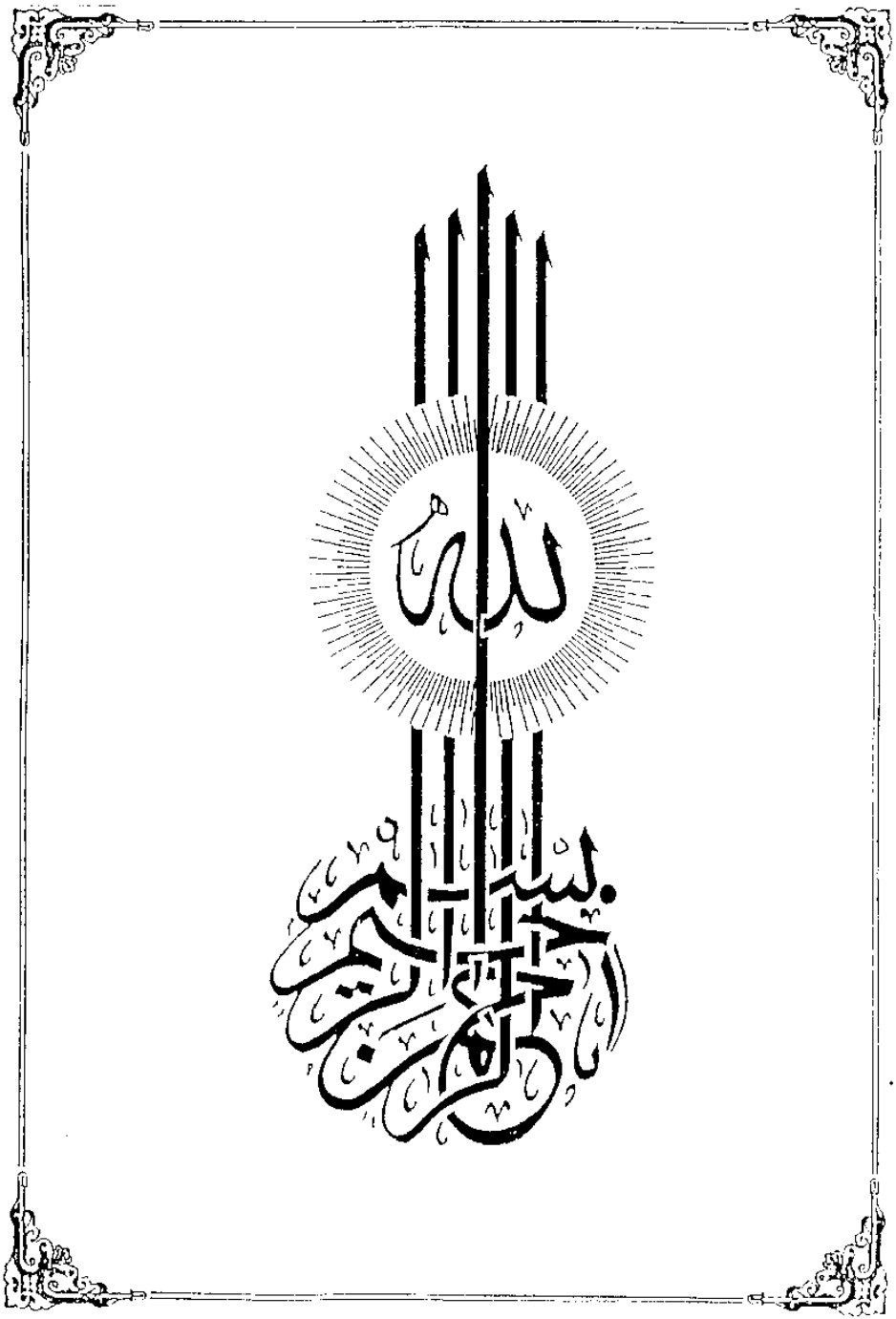
To My Parents
and My Husband Atef Khazbak



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# Contents

# INTRODUCTION

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In the late nineteenth century, several investigators described unusual cells in various tissues obtained from still born infants. Ribbert in 1881 was the first to note large "protozoan like" cells in the kidney of still born infant, the illness associated with their presence was referred to as protozoan cell disease. Subsequent reports have referred to the disease as the syndrome of (unknown etiology), salivary gland virus disease (Rowe et al., 1956) and most recently as cytomegalic inclusion disease (CID). Its viral etiology was first suggested by Jackson (1920), and thereafter the virus was isolated in tissue culture in several laboratories (Smith, 1959; Weller et al., 1957; Rowe et al., 1956).

Human cytomegalovirus (CMV) produces infections with a high incidence in the population all over the world (Horacek et al., 1977).

Infection may be congenital or acquired and may exist in symptomatic or subclinical forms. It is responsible for many clinical syndromes with jaundice, chorioretinitis, hepato-splenomegaly (Jamison et al., 1978), CMV mononucleosis (Luby et al., 1974), neurological manifestations as microcephaly and mental retardation (Hayward et al., 1984). Recently there is an increasing interest especially in CMV infections in infants and children.

## AIM OF THE WORK

This work is aimed to demonstrate the cytomegalovirus infection by detection of complement fixing antibodies in children with congenital abnormalities by using the microtitration of complement fixation test and comparing the antibody titres in these children with those in a group of apparently healthy controls.

# REVIEW OF LITERATURE

## MORPHOLOGY OF CYTOMEGALOVIRUS

CMV is considered a member of the herpes family (Weller, 1977). The viral capsid is icosahedral in shape, contains 162 capsomeres and is surrounded by one or more oval membranes. The viral genome of the CMV is DNA, its size is ranging from 100-200 nm . Analysis of human CMV by Na dodecyl sulphate polyacrylamide gel electrophoresis revealed the presence of 32 polypeptides with molecular weight ranging from 13500-235000 (Gupta et al., 1976).

The virus is ether sensitive, heat labile and has a low degree of infectivity (Smith et al., 1963). The virus has been isolated and propagated in tissue cultures in several laboratories (Smith 1959; Weller et al., 1957). CMV has the property of being specific for human fibroblasts and serial passage is required for adaptation to tissue culture. Several days are required for the inoculated cultures to show the cytopathic effects (Smith et al., 1963). Comparison between herpes virus and CMV showed that herpes simplex virus (HSV) replicates and released within 8 hrs. after infection whereas CMV required 4 days due to long eclipse phase (Duyckinck et al., 1973).

Smith, et al., 1962 had described a method for staining virus particles from fluid suspension so as to enhance contrast for electron microscopy and yet maintains good structural detail using:

**I. 0.25-50% potassium phosphotungstate (pH (7.0)**

CMV particles are negatively stained with potassium phosphotungstate.

**II. 0.25-50% uranyl acetate**

Stains the cores of several deoxyribonucleic acid (DNA) of the animal viruses. The average diameter of CMV and HSV after uranylacetate treatment were almost identical, averaging 108nm. Also there was structural similarity between the two viruses (Smith et al., 1963).

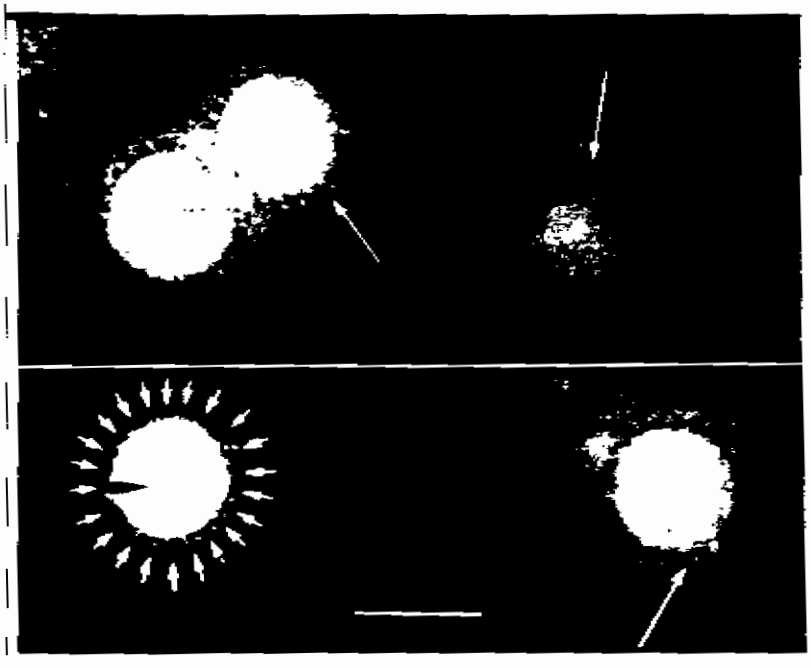

Fig. (1): Phosphotungstate negative stain of CMV showing core penetration of all particles. White arrows indicate capsomere like structure around less densely stained periphery of particles, black arrow indicates inner ring like structure. Micron marker is 100 mμ in all figures *(Smith et al., 1963)*.

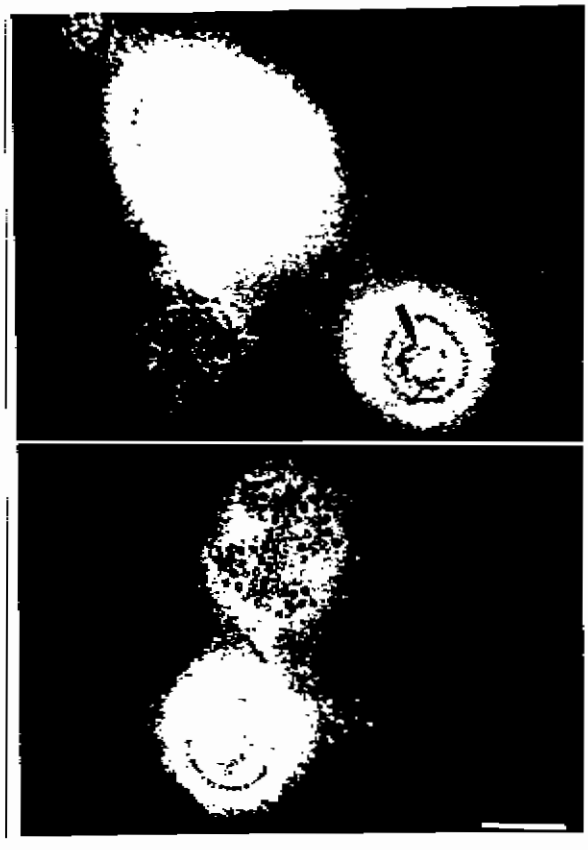

Fig. (2): Phosphotungstate negative stain of herpes simplex virus typical of that obtained 9 hr post infection, showing core penetration of most particles. Black arrow indicates ring like structure *(Smith et al., 1963)*.

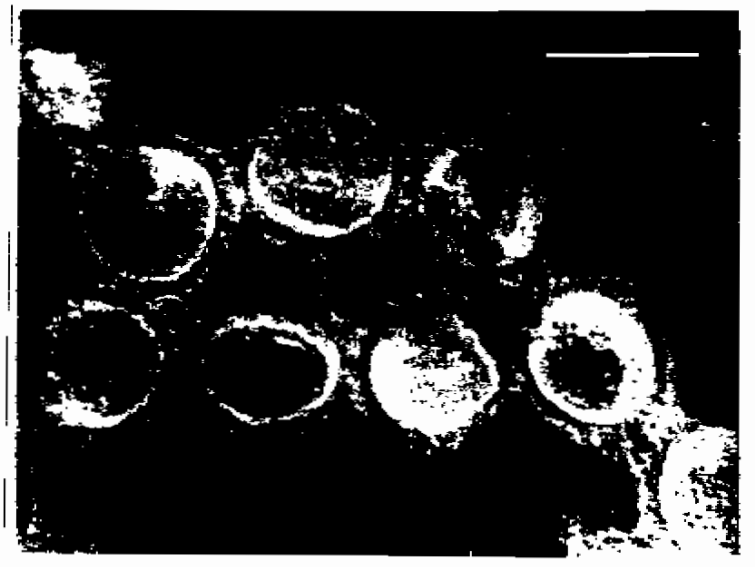

Fig. (3): Uranylacetate stain of CMV showing incomplete staining of cores *(Smith et al., 1963)*.

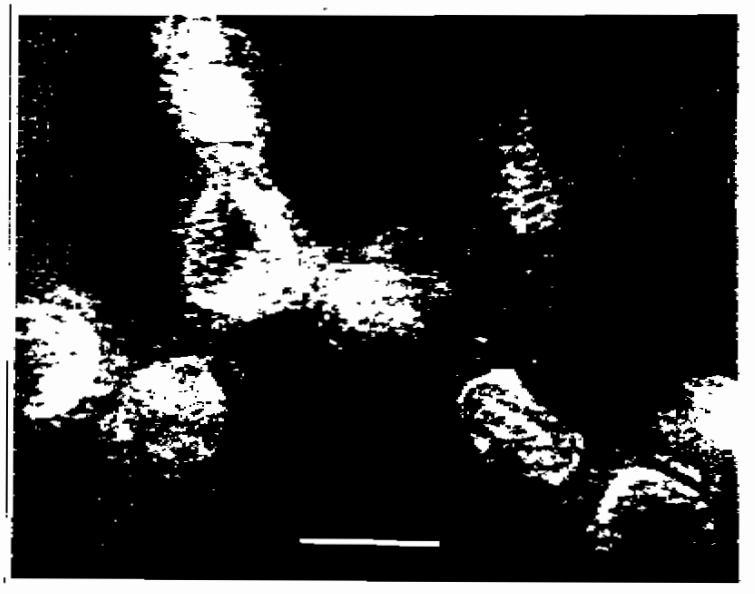

Fig. (4): Uranylacetate stain of 9 hr herpes simplex virus showing incomplete staining of the core *(Smith et al., 1963)*.

## EPIDEMIOLOGY OF CMV

Infection with CMV may be either congenital or acquired.

### Congenital CMV Infection

Intrauterine CMV infection may cause fatal or severe disease affecting several organs.

The characteristic features are hepatosplenomegaly, hepatitis, jaundice, petichiae, purpura, thrombocytopenia, chorioretinitis and other neurological manifestations as micro cephaly, cerebral calcification and mental retardation (Kathleen Hayes et al., 1971).

### Transplacental Transmission of CMV

Congenitally acquired CMV infections are acquired transplacentally as a result of viremia associated with primary maternal infection. So the next pregnancy should be protected from viral invasion by the presence of persistent maternal antibodies (Stagno et al., 1973).

Congenital cytomegalovirus infection in more than one Sibling may be rare due presence of antibodies which prevent viremia with its risk of transmission of virus across the placental barrier (Embil et al., 1970).

### Acquired CMV Infection

The risk of acquired infection begins at the moment of birth when the foetus passes through an infected birth canal.