Genotyping of Mannose-Binding Lectin variant alleles in Egyptian infants with acute respiratory tract infections

Thesis

Submitted for partial fulfillment of master degree in Pediatrics

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DEDICATION

- To my lovely mother and father.

- To my helpful wife & my son Eyad.

- To babies parents who helped me to achieve my work

- To my prof Dr: Rabah Mohamed Shawky ,prof Dr:Sherine Abd-Elfattah & Dr Tarek kamal.

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Mohamed Ahmed El-saieed

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LIST OF ABBREVIATIONS

MBL: Mannose binding lectin.

PAMP: Pathogen associated molecular patterns.

DAMP: Damage-associated molecular patterns.

PRP: Pattern recognition receptors.

TOL: Toll-like receptors.

CLR: C-type lectin receptor.

NOD: Nucleotide oligomerization domain.

NLR: Nucleotide oligomerization domain like receptors.

RIG: Retinoic acid-inducible gene.

RIR: Retinoic acid-inducible gene like receptors.

NFκB: Nuclear factor kappa B.

NK cells: Natural killer cells.

MHC: Major histocompatibility.

DC: Dendritic cells.

APCs: Antigen presenting cells.

TCR: T cell receptors.

γδ T: Gamma delta T cells.

IgM: Immunglobulin M.

IgA: Immunglobulin A.

IgG: Immunglobulin G.

IgD: Immunglobulin D.

VLR: Variable lymphocyte receptor.

MBP: Mannan binding protein.

SP-A: Surfactant proteins A.

SP-D: Surfactant proteins D.

MASP: Mannose-associated serine proteases.

GlcNAc: N-acetyl-D-glucosamine.

Allo-HSCT: Allogeneic hematopoietic stem cell transplantation.

COP: Coat protein complex.

CRP: C reactive protein.

SBP: Spontaneous bacterial perotinitis.

Lea-Leb: Lewis A and Lewis B.

LTA: Lipoteichoic acid.

LBP: Lipopolysacharide binding protein.

C: Complement.

MAC: Mycobacterium avium complex.

BAL: Bronchoalveolar lavage.

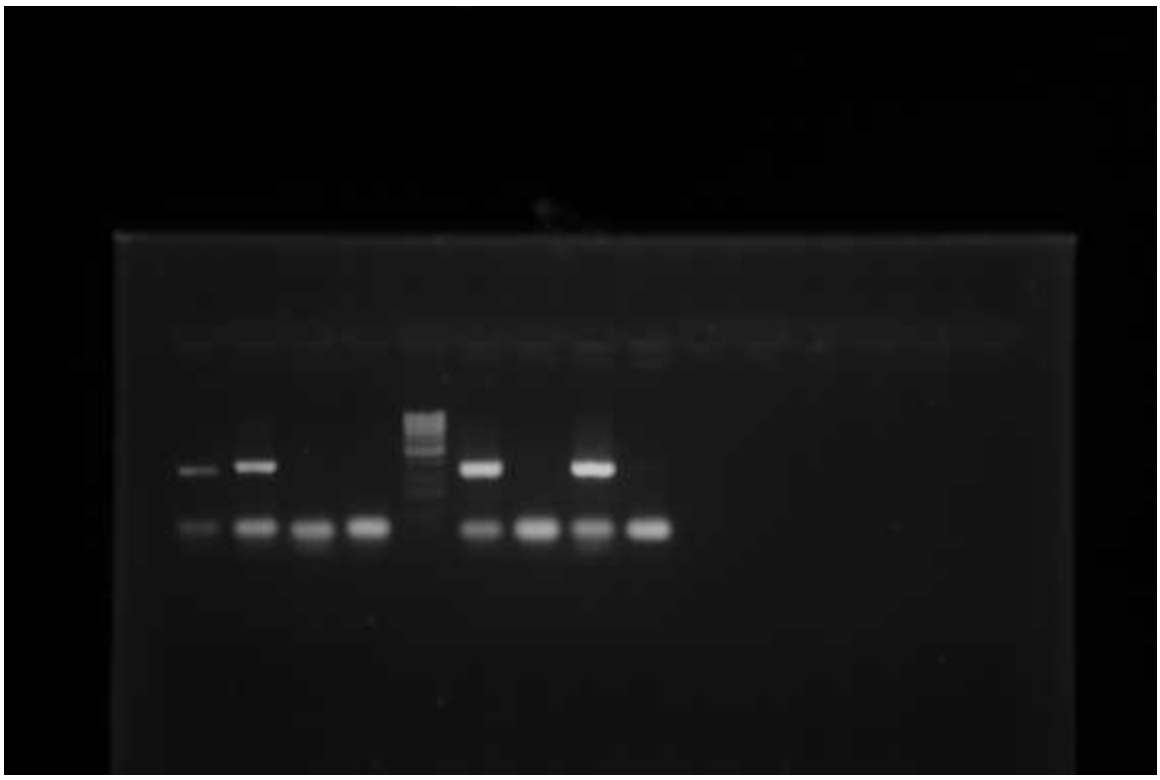
COPD: Choronic obstructive pulmonary disease.

CF: Cystic Fibrosis.

SSI: Statens serum institute.

CRC-VT: Co-operative Research Centre for Vaccine Technology

Figure ٢٩:



Lane no. ١: mutant allele CD ٥٤ (٣٢٩ bp)

Lane no. ٢: Positive variant allele LX in the promoter of mbl٢ gene.

Lanes no. ٣ and ٤: Negative HY and LY variant alleles in the promoter of mbl٢ gene.

Lane no. ٥: Molecular weight marker (٥٠ bp).

Lane no. ٦: Positive for HY variant allele in the promoter of mbl٢ gene.

Lane no. ٧: Negative LX variant allele in the promoter of mbl٢ gene.

Lane no. ٨: Wild type ٥٤ allele (٢٤٥ and ٨٤ bp).

Lane no. ٩: Negative LY variant allele in the promoter of mbl٢ gene.

Figure ٣٠:

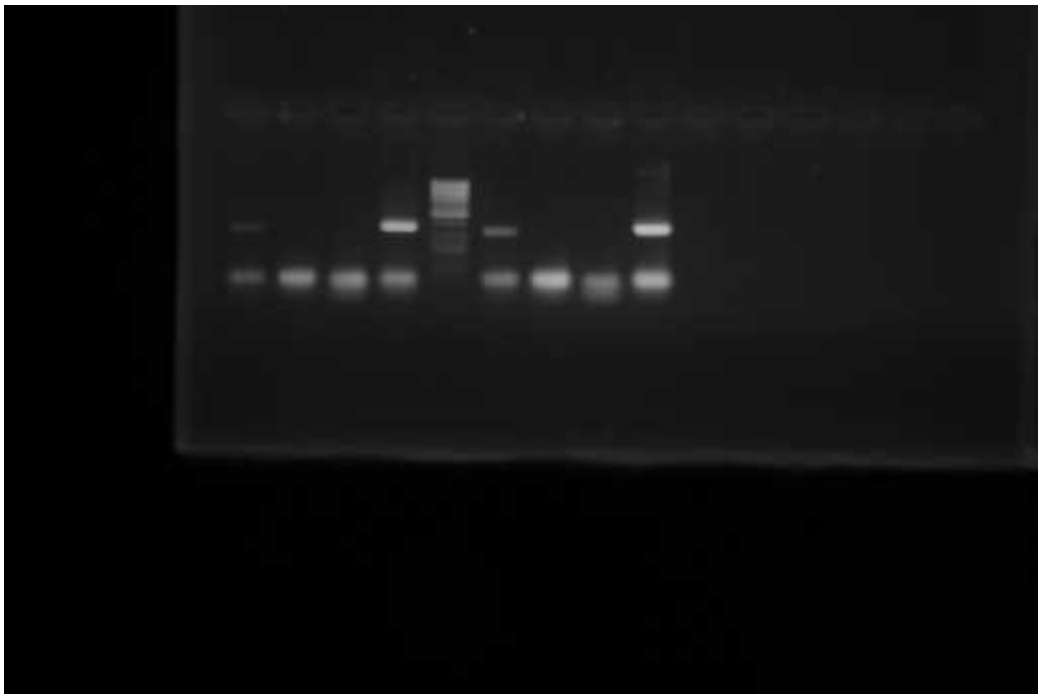


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Figure ٣١:

Introduction

Acute respiratory tract infections are among the most prevalent infections in childhood worldwide, with the highest incidence among children younger than ٢ years (Graham, ١٩٩٠).

Many risk factors have been identified to contribute to occurrence of respiratory tract infections; however, it is also possible that innate characteristics of the individuals such as genetic factors could play a role, and various attempts have been made to analyze the human genetic composition in relation to both infection susceptibility and development of clinical manifestations (Choi et. *al*., ٢٠٠٣).

Mannose-Binding Lectin (MBL) is a serum protein (Turner, ١٩٩٦) and believed to be particularly important in the early stages of primary infections in infants during the decay of maternal antibodies (Super et. *al*., ١٩٨٩). The MBL is known to be an important component of innate immunity toward microbes by activating complement and augmenting opsonization and phagocytosis (Garred et. *al*., ٢٠٠٦). MBL is known to play a role in enhancing attachment, ingestion and killing of opsonized pathogens by phagocytes (Kuhlman et. *al.*, ١٩٨٩) and activation of complement system through the MBL-associates serine protease (Matsushita et. *al.*, ١٩٩٢). There is evidence that the risk of developing bacteremia might be genetically modulated (Adewoye et. *al.*, ٢٠٠٦). The susceptibility to *W. bancrofti* infection also appears to be significantly affected by the MBL expression genotype of the host (Dan et. al., ٢٠١٠).Trans-racial studies have looked at the association between the status of MBL protein production, the MBL genotype and the clinical phenotype (Mombo et. *al*., ٢٠٠٣). A single gene, *MBL*٢ located at chromosome ١٠, codes for human MBL and exerts its action through binding to high mannose and N-acetyl glucosamine oligosaccharides present on various microorganisms (Thiel et. *al.*, ١٩٩٧).

Aim of the work

The present study aimed at:

١-Characterization of the structural alleles of *MBL*٢ gene located on chromosome ١٠ (high- and low-MBL expression genotypes).

٢- Trying to make a correlation between genotyping of *MBL*٢ alleles and occurrence of acute respiratory tract infections in Egyptian infants.

٣- Trying to find out the most prevalent *MBL*٢ variant alleles among the Egyptian samples in study.