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EVALUATION OF PCR IN DIAGNOSIS OF MENINGOCOCCAL MENINGITIS

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By

Faten Mohammed Mohammed El-Abd
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SUPERVISORS

Prof. Dr.
Abd El-Raheem Gharib Ads
Head of Microbiology department
Faculty of Medicine
Tanta University

Dr. Raghda Zaki Talaat
Assistant Prof. of Microbiology
Faculty of Medicine
Tanta University

Dr. Hassan Ahmed Abdel-Salam
Assistant Prof. of Microbiology
Faculty of pharmacy
Zagazig University

Department Of Microbiology
Faculty Of Medicine
Tanta University
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List of abbreviations

AIDS	:Acquired immune deficiency syndrome.
CFU	:Colony forming unit.
CIF	:Counter immunoelectrophoresis.
CN	:Cryptococcus neoformans.
CNS	:Central nervous system.
CSF	:Cerebrospinal fluid.
DNA	:Deoxyribonucleic acid.
ELISA	:Enzyme – linked immunosorbent assay
H. influenzae	:*Haemophilus influenzae.*
H.I	:*Haemophilus influenzae.*
Hib	:*Haemophilus influenzae* type b.
HIV	:Human immunodeficiency virus.
ICP	:Intracranial pressure.
IL	:Interleukin.
LA	:Latex agglutination.
LCM	:Lymphocytic choriomeningitis.
LOS	:Lipo-oligosaccharide.
LPS	:Lipopolysaccharide.
mM	:Millimolar.
N. meningitidis	:*Neisseria meningitidis.*
N.M	:*Neisseria meningitidis.*
NAD	:Nicotinamide adenine dinucleotide.

PCR	:Polymerase chain reaction.
PMN	:Polymorpho nuclear leucocytes.
PRP	:Polyribosylribitol phosphate.
PS	:Polysaccharides.
RNA	:Ribonucleic acid.
RNAse	:Ribonuclease.
S. agalactiae	:*Streptococcus agalactiae*.
S. pneumoniae	:*Streptococcus pneumoniae*.
S.P	:*Streptococcus pneumoniae*.
SAS	:Sub-arachnoid space.
T. WBCs	:Total white blood cells.
TGFβ	:Transforming growth factor B.
TNFα	:Tumor necrosis factor alpha.
UV	:Ultraviolet rays.

Contents

Introduction

Meningitis is a serious medical disease which affects all ages of both Sexes **(Swartz 1985)**. It is common in tropical and subtropical areas, endemic in Egypt and sporadic cases occur all over the year **(Girgis *et al.*, 1983)**. A great proportion of the meningitic diseases are caused by bacteria. Acute bacterial meninigitis is a rapidly progressing, potentially lethal condition **(Berman *et al.*, 1976)**. Common causative agents of acute bacterial meningitis are *Neisseria meningitidis, Haemophilus influenza, Streptococcus pneumoniae* **(Greenwood *et al.*, 1971)**. Meningococcal disease may within hours from the early symptoms of fever and sore throat develop into meningitis or septicaemia, leading to disseminated intravascular coagulation, septic shock and death **(Bawler *et al.*, 1994)**.

The diagnosis of bacterial meningitis is suspected on the basis of clinical presentation and the finding of purulence in the cerebrospinal fluid **(Greisen *et al.*, 1994)**. The laboratory diagnosis of acute bacterial meningitis is based on direct microscopy, which is quick but non-specific and has a low sensitivity. Culture of CSF or blood culture, however, takes at least 12 to 24 hours and may shows negative results due to antibiotic treatment prior to sampling. Therefore various laboratory investigations of CSF have been developed for rapid and specific diagnosis of acute bacterial meningitis, mainly through detection of bacterial antigens by immunological methods **(Salih *et al.*, 1989)**.

The microscopic detection and cultures may also remain negative, if the disease is caused by a fastidious microorganism such as *Neisseria meningitidis* or a slowly growing microorganism such as *Mycobacterium tuberculosis*. Therefore, rapid and accurate diagnosis followed by early and adequate treatment is essential **(Meyer., 1998)**.

In recent years, diagnosis is based on molecular techniques, such as PCR, have constituted the most substantial technical advances in the field of rapid detection of bacteria in different types of samples **(Pickup, 1991)**. PCR not only useful in the diagnosis of the causative agents but also used in the identification and serogroup prediction of *Neisseria meningitidis* **(Taha, 2000)**.

Aim of the work

The aim of this study is to evaluate polymerase chain reaction (PCR) in the microbiological diagnosis of meningococcal meningitis as compared with other conventional methods.

Review of literature

Meningitis:

Meningitis is an inflammation of the arachnoid, the pia matter, and the intervening cerebrospinal fluid. Since the subarachnoid space is continuous through the brain, spinal cord and optic nerves, infection in this space extends throughout the cerebrospinal axis unless there is obstruction of the subarachnoid space (**Scheld, 1994**).

Causes of meningitis:

1- Bacterial meningitis:

It can be caused by any bacterium gaining entery to the subarachnoid space, but the most common organisms involved are *Neisseria meningitidis*, *Haemophilus influenzae* type b, and *Strepotococcus pneumoniae* (**Tunkel et al., 1990**).

2- Viral meningitis:

Viruses constitute the majority of the numerous infective agents that produce aspetic meningitis (**Beghi et al., 1984**). In outline, the clinical syndrome of aspetic meningitis consists of fever, headache and other signs of meningeal irritation, and predominantly lymphocytic pleocytosis with normal CSF glucose (**Adams and Victor, 1989**).

The majority of cases are due to viral infections of which the most common are enteroviruses such as Echovirus and Coxsackie virus. Mumps is the next most common, followed by herpes simplex (type 2), lymphocytic choriomeningitis (LCM) and adenovirus infections (**Johnson, 1982**). The California virus, which is an arthropod borne virus (Arbovirus), is responsible for a small number of cases (**Beghi et al., 1984**).

All these viral infections, together with leptospirosis, comprise about 95% of cases of aseptic meningitis (**Adams and Victor 1989**).

Rarely, the icteric phase of infectious hepatitis is preceded by mild meningitis. Infectious mononucleosis and *Mycoplasma pneumoniae* rarely causes meningitis **(Johnson, 1982).**

The infection with human immunodeficiency virus (HIV) may presents as acute, self-limited aseptic meningitis with an infectious mononucleosis-like picture. HIV has been recovered from the CSF in the acute phase **(Gray et al., 1988).** Herpes Simplex virus type I has been also isolated from the CSF of a patient **(Steele el al, 1982)**

3- Fungal Meningitis

Cryptococcosis caused by the capsulated yeast *Cryptococcus neoformans* (C.N) which is present in the excreta of wild and domestic birds most frequentiy presents as a disease of the central nervous system although the primary site of infection is the lungs. Cryptococcosis occurs sporadically throughout the world but recently most often seen in patient with AIDS. Infection follows inhalation of the mature cells of C.N, which are small enough to enter deep to the lung **(Evans, 1992).** Pulmonary infection has a tendency towards spontaneous resolution and is frequently asymptomatic but silent hematogenous spread to the brain leads to clusters of cryptococci in the perivascular areas of cortical gray matter, basal ganglia and other areas of the CNS giving the picture of meningoencephalitis which is fatal without appropriate therapy **(Bennett, 1987).**

4– Carcinomatous Meningitis

It is a common form of CNS invasion in malignancy that does not cause a myelopathy unless there is extensive sub-pial infiltration from adjacent roots causing nodules with secondary compression or infiltration of the cord **(Ropper and Martin, 1994).** Leukemias and lymphomas are the most common source of meningeal reactions in meningeal carcinomatosis. Great numbers of neoplastic cells may extend through the leptomeninges involving cranial and spinal nerve roots, and produce a picture of meningitis with normal or low CSF glucose levels **(Beghi et al., 1984).**