Role of Respiratory Syncytial Virus as a Cause of Lower Respiratory Tract Infection Among Egyptian Children

Thesis Submitted for Partial Fulfillment of M.D. degree in Clinical Pathology

By

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Abstract

Respiratory syncytial virus (RSV) is one of the major respiratory tract viral pathogens throughout the world, causing acute lower respiratory infections among infants and young children. The present study was undertaken to compare between nested RT-PCR and viral culture methods for the detection of RSV infection in infants. This study included 107 pediatric patients admitted to Cairo University Children Hospitals with lower respiratory tract infections. RSV was isolated in 81 nasopharyngeal aspirates by viral cultures and identified in 88 samples by nested RT-PCR. In 7 samples RSV was identified by nested RT-PCR alone. In conclusion PCR appears to be more sensitive than viral cultures for detection of RSV in clinical samples.

Key words :

RSV – Viral culture – nested RT – PCR – Pneumonia .

إن فيروس الإندماج الخلوى التنفسى يعد من أهم أسباب عدوى الجهاز التنفسى السفلى فى الأطفال و الرضع فى جميع أنحاء العالم. تم إجراء الدراسة الحالية للمقارنة بين طريقتى "تفاعل البلمرة المتسلسل الانعكاسي المتداخل" و المزارع الفيروسية لتشخيص فيروس الإندماج الخلوى التنفسى فى الأطفال. إشتملت هذه الدراسة على 107 طفلا مريضا لديهم أعراض إلتهاب الجهاز التنفسى السفلى تم إختيارهم في مستشفيات الأطفال بجامعة القاهرة. تم تشخيص الفيروس فى 81 عينة بواسطة كلا من المزارع الفيروسية وبطريقة "تفاعل البلمرة المتسلسل الانعكاسي المتداخل"، بينما تم تشخيصه فى 7 عينات بطريقة "تفاعل البلمرة المتسلسل الانعكاسي المتداخل" فقط. نستخلص من هذا أن طريقة "تفاعل البلمرة المتسلسل الانعكاسي المتداخل" أكثر حساسية من المزارع الفيروسية فى تشخيص فيروس الإندماج الخلوى التنفسى فى الأطفال.

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Chapter 3: Laboratory Diagnosis of Respiratory Syncytial Virus

List of Tables

List of Figures

Abbreviations

ABGs	:	Arterial Blood Gases
ALI	:	Acute lung injury
AOM	:	Acute otitis media.
ARDS	:	Acute respiratory distress syndrome.
ARI	:	Acute respiratory infections.
ARTI	:	Acute respiratory tract infection.
BAL	:	Bronchoalveolar lavage.
BMT	:	Bone marrow transplantation.
CAP	:	Community-acquired pneumonia.
COPD	:	Chronic obstructive pulmonary disease.
CoV	:	Coronavirus.
CPE	:	Viral cytopathic effect.
CT	:	Computerized tomography
CTL	:	Cytotoxic T cells.
CXRs	:	Chest X-rays.
DCs	:	Dendritic cells.
DFA	:	Direct fluorescent assay.
EIA	:	Enzyme immunoassay.
FOB	:	Fibreoptic bronchoscopy.
HAI	:	Hemagglutination inhibition test.
HAP	:	Hospital acquired pneumonia.
HCT	:	Haematopoietic cell transplantation.
HSV	:	Herpes simplex virus.
hMPV	:	Human Metapneumo virus.
ICU	:	Intensive care unit.
LRTI	:	Lower respiratory tract infection.

LTCF	:	Long-term care facilities = Senior daycare.
MAbs	:	Monoclonal antibodies.
MRI	:	Magnetic resonance imaging.
NAATs	:	Nucleic acid amplification tests.
NASBA	:	Nucleic-acid-sequence-based amplification.
NPA	:	Nasopharyngeal aspirate.
NPS	:	Nasopharyngeal swab.
PCR	:	Polymerase Chain Reaction.
PIV	:	parainfluenza virus.
PSBs	:	Protected specimen brushes.
RSV	:	Respiratory Syncytial virus.
RT-PCR	:	Reverse transcriptase–polymerase chain reaction.
RVs	:	Respiratory viruses.
SARS	:	Severe acute respiratory syndrome
SOT	:	Solid organ transplantation.
SVC	:	Shell vial culture.
TCID50	:	50% tissue culture infective doses.
URTI	:	Upper respiratory tract infection.
VAP	:	Ventilator-associated pneumonia.
VZV	:	Varicella Zoster virus.

Introduction:

Acute respiratory infections are a major worldwide health problem because of associated high morbidity and mortality rates ***(Avendano et al., 2003).***

Human respiratory syncytial virus (RSV) is the most important viral agent causing serious pediatric respiratory disease worldwide. It is an enveloped, non segmented, negative-sense RNA virus classified in the subfamily *Pneumovirinae* of the family *Paramyxoviridae* ***(Falsey et al., 2003)***.

RSV infection causes common-cold-like symptoms that progress to lower respiratory tract disease in 25 to 40% of infected infants and results in hospitalization for 0.1 to 1.0% of those infected. Almost everyone has been infected by RSV by 2 years of age. The immunity induced by RSV infection typically is incomplete, and reinfection is common, although subsequent infections are partially restricted and the disease severity is reduced ***(Zhang et al., 2002).***

Numerous studies have described a strong association between respiratory syncytial virus (RSV) infection in infancy and the development of recurrent wheezing and airway hyperresponsiveness ***(Mejías et al., 2004).***

In addition, a study has uncovered that RSV is a serious problem among the institutionalized elderly, causing severe lower respiratory tract disease and high rates of mortality ***(Falsey and Walsh, 2000).***

More studies have shown that those at risk for developing serious disease following RSV infection also include the elderly, adults with underlying cardiopulmonary disease, and the severely immunocompromised. Compared with pneumonias caused by other respiratory viruses, RSV pneumonias are associated with the highest mortality rates in bone marrow transplant recipients and leukemia patients ***(van Elden et al.,2003).***

Reinfections due to RSV occur throughout life, reflecting incomplete immunity to the virus ***(Maitreyi et al., 2003).***

For appropriate treatment of RSV infection, it is crucial to have an accurate and timely diagnostic method for detection of the virus. A number of techniques are available for detection and identification of RSV, including cell culture, enzyme immunoassay (EIA), immunofluorescence (IF), and conventional reverse transcription (RT)-PCR (***Falsey et al, 2002).***

The effect of viral diagnostics on hospital length of stay and treatment costs has been assessed in single studies of adult and pediatric populations ***(Barenfanger et al., 2000)***. Likewise, data regarding the effects of viral diagnostics on antibiotic prescribing practices for hospitalized children are limited ***(Noyola and Demmler, 2000*** and ***Byington et al., 2002).***

Aim of the work:

- Detection of pneumonia cases caused by Respiratory Syncytial Virus.

- To compare between nested RT-PCR method and viral culture method for diagnosis of Respiratory Syncytial Virus infection in children and Infants.

(Chapter 1)

Lower Respiratory Tract Infections

(Chapter 1)
Lower Respiratory Tract Infections

INTRODUCTION

Paediatric respiratory disease remains an important cause of morbidity in both the developing and the developed world. In the UK respiratory illness is the most common reason parents cite for taking their children to see the general practitioner, and for attendance to the emergency department with a paediatric medical problem ***(British Thoracic Society of Standards of Care Committee, 2002).***

Respiratory viral infection is a major cause of morbidity and mortality. Infancy, in particular, is a time of increased disease susceptibility and severity. Early-life viral infection causes acute illness and can be associated with the development of wheezing and asthma in later life ***(Tregoning and Schwarze, 2010)***.

Respiratory syncytial virus (RSV), influenza virus types A (FluA) and B (FluB), and parainfluenza viruses (PIVs) are the most commonly detected viruses and the leading causes of viral lower respiratory tract infections in children ***(LeGoff et al., 2008).***

The World Health Organization estimates that approximately 14 million people die each year from infections that are transmitted via the respiratory tract, most of which occur in childhood. Viral infections of the respiratory tract are particularly serious during infancy, and viral pneumonia is the most common cause of infantile hospitalization in the developed world **(*Shay et al, 1999*)**.

Lower respiratory tract infections (LRTI) are among the most common infectious diseases of humans worldwide. In the United States alone, pneumonia and influenza rank as the sixth leading cause of death ***(Pinner et al., 1996).*** Changes in the characteristics of the population as it ages and the swelling numbers of patients with immunocompromising conditions have increased the number of individuals at risk. An expanded variety of emerging pathogens likewise provides challenges for the microbiology laboratory. Overtreatment of acute uncomplicated bronchitis, which is largely due to viruses, has led to unparalleled levels of multidrug resistance among invasive pathogens such as *Streptococcous pneumoniae*. Practice guidelines for a rational approach to the evaluation and treatment of patients with acute bronchitis have recently been published in an effort to decrease the overuse of antibiotics and as an attempt to prevent further increases in rates of resistance ***(Gonzales et al., 2001).***

(I) Bronchitis

Bronchitis refers to nonspecific bronchial inflammation and is associated with a number of childhood conditions. *Acute bronchitis* is a syndrome, usually viral in origin, with cough as a prominent feature. Even though acute bronchitis is clearly one of the most common diagnoses made in adult clinical practice, a precise definition does not exist. A cough that lasts 1 to 3 weeks, with or without sputum production, and that is associated with upper respiratory tract and constitutional symptoms is the typical presentation. Symptoms result from inflammation and hyper-responsiveness of the bronchial tree ***(Carroll, 2002)***.