Needs for new diagnostic modalities in management of acute febrile infections in Egypt

Essay submitted for fulfillment of M.Sc. in clinical pathology and chemistry

BY

Sahar Mohamed Kamal

M.B.B.Ch.

Supervisors

Dr. Nevine Gamal-El-Dine El Racheedi

Professor of clinical pathology

Dr. Mervat G. Abd El Wahab

Ass. Professor of clinical pathology

Dr. Iman M. Abd El-Rahman Mousa

Ass. prof. of clinical pathology

Faculty of Medicine

Cairo University

2008

Abstract

More sensitive and rapid tests for diagnosis of typhoid fever include dip-S-tick and typhidot tests. PCR of blood samples is also a sensitive method for its diagnosis. Also, ELISA or dip-S-tick or BrucellaCapt tests are useful rapid and sensitive tests for dignosis of Brucella. PCR appears to be useful in diagnosis of acute brucellosis. The use of dip-S-tick and ELISA tests for diagnosis of Leptospira was found to be specific, fast and easy. PCR has a clear advantage in its diagnosis. IFA test is the most widely used in diagnosis of coxiella burnetti also PCR is a rapid and sensitive method. Chronic Q fever endocarditis is also diagnosed by IFA with IgG titer >1/800 in Egypt.

Keywords: Laboratory diagnosis- acute febrile infections- Egypt

الله

AKNOWLEDGEMENT

I WOULD LIKE TO EXPRESS MY DEEP THANKS AND GRATITUDE TO Professor Dr. **Nevine Gamal-El-Dine El Racheedi___Professor of clinical pathology, Faculty of Medicine, Cairo University** for the care, her generous help and support of the work. Grateful thanks for her good guidance and constant supervision of this work giving me the benefit of her advice.

I am much obliged and deeply indebted to DR. **Mervat G. Abd El Wahab Ass. Professor of clinical pathology, Faculty of Medicine, Cairo University** for her support and sincere help wherever seeked. Grateful thanks for her great efforts, valuable criticism and kind attention to represent this essay.

I am especially deeply indebted and grateful to DR. **Iman M. Abd El-Rahman Mousa Ass. Professor of clinical pathology, Faculty of Medicine, Cairo University** for her instructions, sincere help and suggestions. I would like to thank her for the interest in the subject of the essay and continuous encouragement.

List of Abbreviation

Abbreviation	Full name
AFIs	Acute febrile infections
Anti TH	Anti flagellar
Anti TO	Anti lipolysaccharide
ARDS	Acute respiratory distress syndrome
B. abortus	*Brucella abortus*
B. melitensis	Brucella *melitensis*
B.abortus	Brucella abortus
Brucella S-LPS	Brucella smooth liposaccharide
BCNE	Blood Culture Negative Endocarditis
BSC	Biological safety cabinet
C. burnetii	Coxiella burnetii
CDC	Centre for disease control and prevention
CFT	Complement Fixation Test
CFU	Colony forming unit
DFM	Dark field microscopy
DST	IgM dot-ELISA dip-S-tick test
E.coli	Echerichia coli
ELISA	Enzyme-linked immunosorbant assay
EMJH medium	*E*llinghausen, *M*cCullough, *J*ohnson, and *H*arris medium
FISH	Fluorescent In-situ Hybridization
HSA	Human serum albumin
IFA	Indirect Immunofluorescent assay
IHA	Indirect hemagglutination assay
IgA	*Immunoglobulin A*
IgG	Immunoglobulin G
IgM	Immunoglobulin M
LAT	Latex Agglutination Test
LDS	IgM dip-S-tick assay
MAT	Microscopic agglutination test
MAT	Microscopic agglutination test
MOHP	Ministry of health and population
PCR	Polymerase chain Reaction
PUO	Pyrexia of unknown origin
S. paratyphi	Salmonella paratyphi
S.typhi	Salmonella typhi
SAT	Standard tube agglutination test
TMP-SXT	Trimethoprim-sulfamethoxazole
Abbreviation	**Full name**
Vi antigen	virulance antigen
WHO	World Health Organization

Table of Contents

List of Tables

List of Figures

Cont'd: List of Figures

Acute febrile illness is a common clinical syndrome among patients seeking hospital care in different nations **(Montasser *et al*., 1991).** The main causes and patterns of acute febrile infection (AFI) are not well characterized and many patients with AFI are empirically treated **(WHO, 2008)**.

Brucella, Salmonella enterica serogroup Typhi Leptospira and coxiella burnettii are the common agents of AFI in Egypt**.** The occurance of coinfection with multiple pathogens has been reported **(Parker *et al*, 2007).** Defining the etiologies of AFI is imperative in guiding proper disease treatment, prevention, and control strategies in Egypt **(Afifi *et al*.,2005).**

Brucellosis has increasingly become recognized as a public health problem in Egypt. Because brucellosis and typhoid fever have similar signs and symptoms, brucellosis frequently was misdiagnosed as typhoid fever, resulting in provision of inadequate antimicrobial therapy. (**Crump *et al*., 2003**).

Because of limited resources and few number of trained personnel, most laboratories have the problem of identifying these pathogens. The endemicity of brucellosis and typhoid fever in our country necessitates isolation of the organism for confirmation of high serolgical positive titers. In addition serology for leptosirosis and rickettsia is not routinely done and diagnosis is made only in reference laboratory **.(Ministry of health, Egypt, 2000).**

As for other fastidious pathogens, molecular detection by PCR offers an alternative way of diagnosis **(Archibald and Reller., 2001).**

Aim of the work:

The aim of this work is:

- To understand the epidemiology of AFI in Egypt,
- To highlight the problems in laboratory diagnosis of common AFI in laboratories of Egypt.
- To try to install the proper and new diagnostic modalities of AFI pathogens.

Acute Febrile Infections

Definition

An acute febrile infection [AFI] is a clinically evident disease resulting from the presence of pathogenic microbial agents, including viruses, bacteria, fungi, protozoa, multicellular parasites whose duration is ≤ one week. Infectious pathologies are usually qualified as contagious diseases (also called communicable diseases) due to their potentiality of transmission from one person or species to another. Transmission of an infectious disease may occur through one or more of diverse pathways including physical contact with infected individuals. These infecting agents may also be transmitted through liquids, food, body fluids, contaminated objects, airborne inhalation, or through vector-borne spread **(Dorland, 2004).**

Incidence

The World Health Organization [WHO] (2003 a) collects information on global incidence of AFIs. They caused 0.3% deaths in 2002 (estimated) compared to 9% in 1993.

Causes and Mode of transmission

An infectious disease is transmitted from some source. Defining the means of transmission plays an important part in understanding the biology of an infectious agent, and in addressing the disease it causes. **(Kenneth *et al*., 2004).** Brucella, Salmonella enterica sero group Typhi, Leptospira and coxiella burnettii are the common agents of acute febrile

infections (AFI) in Egypt **(Wasfy *et al*., 2002).** They present urgent diagnostic problems that require experience and clinical judgment to make early evidence-based management decisions. Rapid diagnostic technology needs to be developed in Egypt to prevent significant delay in starting appropriate therapy, reduce hospital expenses, and even save lives **(Wasfy *et al*.,2002).**

Generally, AFIs in Egypt show a considerable rate of mortality and morbidity. Blood culture is the gold standard test for proving bacteraemia, and for identifying bacteria and their antibiotic sensitivities. **(Wasfy *et al*.,2002).**

Some of AFIs are considered to be zoonotic that is transmittable from animals to humans through contaminated milk, raw milk products as brucellosis or direct contact with infected animals as Leptospirosis. Although such infections in domestic animals have been controlled in most developed countries, it remains an important public and animal health problem in Egypt **(El Sherbini *et al*., 2000).**

Clinical picture

Signs and symptoms of typhoid and paratyphoid fever

Signs and symptoms are more likely to develop gradually — often appearing one to three weeks after exposure to the disease. The incubation period for paratyphoid fever is shorter — usually one to 10 days.

First stage is characterized by:

- Fever, (39 or 40 C).
- Headache.
- Weakness and fatigue.
- A sore throat.
- Abdominal pain.
- Diarrhea or constipation. Children are more likely to have diarrhea whereas adults may become severely constipated.

During the second week, a rash of small, flat, rose-colored spots appears on patient's lower chest or upper abdomen. The rash is temporary, usually disappearing in three or four days **(Parry *et al*., 2002)**

.**Second stage**

If no treatment is given for typhoid fever, a second stage develops during which patient becomes very ill. His fever will remain high, and he may develop either diarrhea or severe constipation. He may lose considerable weight during this phase, and his abdomen may become extremely distended **(Kawano *et al*., 2007).**

The typhoid state

By the third week, the patient may become delirious, lying motionless and exhausted with his eyes half-closed in what's known as the typhoid state. Life-threatening complications often develop at this time **(Kawano *et al*., 2007).**

Complications:

The bacteria move from the bloodstream into certain tissues of the body, including the gallbladder and lymph tissue of the intestine (called Peyer's patches). The tissue's response to this invasion causes symptoms ranging from inflammation of the gallbladder (cholecystitis) to intestinal bleeding to actual perforation of the intestine. Perforation of the intestine refers to an actual hole occurring in the wall of the intestine, with leakage of intestinal contents into the abdominal cavity. This leakage causes severe irritation and inflammation of the lining of the abdominal cavity, which is called peritonitis. Peritonitis is a frequent cause of death from typhoid fever. Other complications of typhoid fever include liver and spleen enlargement, sometimes so great that the spleen ruptures or bursts; anemia, or low red blood cell count due to blood loss from the intestinal bleeding; joint infections, which are especially common in patients with sickle cell anemia and immune system disorders; heart infections; and meningitis and infections of the brain, which cause mental confusion and even coma. It may take a patient several months to recover fully from untreated typhoid fever **(Olsen *et al*., 2004).**

Improvement

Improvement may come slowly during the fourth week. The fever is likely to decrease gradually until temperature returns to normal in another week to 10 days. But signs and symptoms can return up to two weeks after his fever has subsided Paratyphoid fever causes signs and symptoms similar to those of typhoid fever, but in a milder form. Complications aren't as severe, and patient generally recovers more quickly **(Olsen *et al*., 2004)..**