Different Causes of Acute and Prolonged Febrile Illness in Military Fever Hospital in the Period between 1/1/2014 – 1/1/2015

Thesis

Submitted for partial fulfillment of requirement for Master Degree in Tropical Medicine

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2016


وأنزل الله عليك
الكتاب والحكمة
وعلَّمَكَ مَا لَمْ تَكُنْ
تَعْلَمُ وكَانَ فَضْلُ
اللَّهِ عَلَيْكَ عَظِيماً
صدق الله العظيم
سورة النساء الآية (١١٣)

First thanks to **ALLAH** to whom I relate any success in achieving any work in my life.

I wish to express my deepest thanks, gratitude and appreciation to **Prof. Hassan Salah El-Din Hamdy,** Professor of Tropical Medicine, Faculty of Medicine,Ain ShamsUniversity, for his meticulous supervision, kind guidance, valuable instructions and generous help.

Special thanks are due **Brg.Dr. Amr Mohammed Elsayed Abd El-Motagly,** Military Medical Academy, MD Tropical Medicine, Cairo University for his sincere efforts and fruitful encouragement.

I am deeply thankful to **Dr.Mohamed Salaheldin Abd El-Hamid,** Lecturer of Tropical Medicine, Faculty of medicine, Ain Shams University, for his great help, outstanding support, active participation and guidance.

Also I would like to thank my **Family** and who stood behind me to finish this work and for their great support.

Loay Mohammed El-Metwaly Mohammed

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AFB..... Acid fast bacillus
AFI..... Acute febrile illness
AFP..... α-fetoprotein
AIDS..... Acquired immunodeficiency syndrome
ALT ..... Alanine aminotransferase
ANA ..... Antinuclear antibodies
ANCA ..... Anti-neutrophil cytoplasmic antibodies
anti-ds-DNA Ab Anti-double stranded DNA antibodies
anti-SMA..... Anti-smooth muscle antibodies
ASO ..... Anti-streptolysinO titer
AST..... Aspartate aminotransferase
AUF ..... Acute undifferentiated fever
BBB..... Blood-brain barrier
bpm..... Beats per minute
BUN ..... Serum blood urea nitrogen
CA19-9 ..... Carbohydrate antigen 19-9
CBC..... Complete blood picture
CEA ..... Carcinoembryonic antigen
CLD..... Chronic liver disease
CMV..... Cytomegalovirus
CNS ..... Central nervous system
COX-2..... Cyclo-oxygenase 2
CRP ..... C-reactive protein
CSF ..... Cerebro-spinal Fluid
CT ..... Computer tomography
DMH ..... Dorsimedial hypothalamus
EBV ..... Epstein-Barr virus
ELISA..... Enzyme linked immunosorbent assay
EP3 ..... Prostaglandin E receptor3

List of Abbreviations (Cont...)

ESR..... Erythrocyte sedimentation rate
FMF ..... Familial Mediterranean fever
FUO ..... Fever of Unknown Origin
GIT ..... Gastrointestinal tract
Hb% ..... Haemoglobin concentration
HCC..... Hepatocellular carcinoma
HIV ..... Human immunodeficiency virus
IHBRD ..... Intra-hepatic biliary radicals
IL-1 ..... Interleukins 1
IL-10 ..... Interleukins 10
IL-1β ..... Interleukins 1β
IL-6 ..... Interleukins 6
INF-α..... Interferon- α
LN ..... Lymph node
LPS ..... Lipopolysaccharide
MAT ..... Microagglutination test
MRCP ..... Magnetic resonance cholangiopancreatography
PCR ..... Polymerase chain reaction
PFI ..... Prolonged Febrile Illness
PGE-2 ..... Prostaglandin E2
PLA-2 ..... Phospholipase A2
POA..... Preoptic area
PSA ..... Prostate specific antigen
PVN ..... Paraventricular nucleus
RBCs ..... Red blood cells
RDTs ..... Rapid diagnostic tests
RF ..... Rheumatoid factor
rRPa ..... Rostral raphe pallidus nucleus
RT-PCR ..... Real time polymerase chain reaction

List of Abbreviations (Cont...)

SBP ..... Spontaneous bacterial peritonitis

SLE ..... Systemic lupus erythematosus

TB ..... Mycobacterium tuberculosis

TNF..... Tumor necrosis factor

TRH ..... Thyroid releasing hormone

TSH ..... Thyroid stimulating hormone

UTI ..... Urinary tract infection

UUF ..... Undiagnosed undifferentiated fevers

VDRL..... Venereal disease research laboratory

WBCs ..... White blood cells

INTRODUCTION

Definition of Fever:

Fever (also known as pyrexia or febrile response) is one of the most common medical signs and is characterized by an elevation of body temperature above the normal range (36.5–37.5 °C) due to an increase in the temperature regulatory set-point ***(Karakitsos and Karabinis, 2008)***.

Fever is diagnosed when temperature in the rectum (rectal) is at or over 38.3 °C. or Temperature in the mouth (oral) is at or over 37.7 °C. or Temperature under the arm (axillary) or in the ear (otic) is at or over 37.2 °C ***(Barone, 2009).***

Types of Fever:

- Continuous fever: Temperature remains above normal throughout the day and does not fluctuate more than 1 °C in 24 hours, *e.g.* lobar pneumonia and typhoid ***(Inayatullah, 2009).***
- Intermittent fever: The temperature elevation is present only for a certain period, later cycling back to normal, *e.g.* malaria, kala-azar, urinary tract infection or septicemia ***(Inayatullah, 2009).***
- Remittent fever: Temperature remains above normal throughout the day and fluctuates more than 1 °C in 24 hours, *e.g.*, infective endocarditis.
- Pel-Ebstein fever (undulant): A specific kind of fever associated with brucellosis, Hodgkin's lymphoma, being high for several days and then low for several days and so on ***(Loscalzo et al., 2008).***

Presentation of Fever:

- **Short Febrile illness:** Most febrile illnesses last for fewer than 3 to 5 days. During this time, either a specific cause is identified and treated or

the fever resolves spontaneously it includes common cold, sore throat, and upper respiratory tract infection ***(Avner and Baker, 2002).***

- **Acute Febrile illness:** is defined as acute onset of fever (elevation of body temperature > 38 °C lasting for less than 2 weeks) and no cause found after full history and physical examination ***(Kashinkunti et al., 2010).***
- **Prolonged Febrile illness:** described as increased body temperature more than 38.3°C for three weeks or longer that did not have an established etiology despite a one-week inpatient evaluation ***(Gaeta et al., 2006).***

Military fever hospital has its unique character as it introduces its medical service mainly to soldiers, so we can't be popularized the results on another fever hospitals.

Acute undifferentiated febrile illness is a common clinical syndrome among patients seeking hospital care in Egypt. The main causes and patterns of acute febrile illness (AFI) are not well characterized and many patients with AFI are empirically diagnosed as having typhoid fever, one of the most frequently reported communicable diseases in Egypt. Although not routinely diagnosed, brucellosis is reported in all domestic animals in the Near East region, including Egypt ***(Refai, 2002)***.

The cause of acute undifferentiated fever (AUF) is driven by the regional disease burden, seasonality of infectious diseases, spectrum and severity of disease, availability of diagnostics and access to health care facilities ***(Mueller et al., 2014)***.

Some fever syndromes have a more clear localization to skin and soft tissue (abscess or cellulitis), meninges or neural tissue (headache, neck-

stiffness, altered sensorium with or without focal neurological signs), respiratory tract (cough, breathlessness), or urinary tract (dysuria, hematuria). These syndromes have better developed guidelines for their management. On the other hand, AUF-syndromes (such as fever-rash, fever-myalgia, fever arthralgia, fever-hemorrhage, and fever-jaundice) have overlapping etiologies, which makes their diagnosis and management even more challenging ***(Crump, 2014)***.

Fever of unknown origin remain one of the most common and difficult diagnostic problems faced daily by clinicians ***(Petersdorf and Beeson, 1961)***.

The prevalence of FUO among adult hospitalized patients is reported to be 2.9% ***(Tabak et al., 2003)***. The spectrum of FUO etiology may include more than 200 diseases ***(Gaeta et al., 2006)***.

The causes of FUO have traditionally been grouped into four categories: infectious, malignant, inflammatory and undetermined ***(Kazanjian, 1992) & (Agarwal and Gogia, 2004).***

The etiologies of prolonged febrile illness (FUO) have changed over time because of shifting disease patterns and new diagnostic techniques. There are more than 200 diseases in the differential diagnosis ***(Bleeker-Rovers et al., 2009)***.

In multiple case series, however, the etiology of FUO is turned out to be an atypical presentation of a common disease ***(Varghese et al., 2010)***.

In developed countries, the noninfectious inflammatory diseases and undiagnosed groups comprise a higher proportion of FUO cases ***(Goto et al., 2007)***.

Underdeveloped countries have higher rates of infection and neoplasm ***(Zenone et al., 2006)***. Drug fever is implicated in 1% to 3% of FUO cases ***(de Kleijn, 1997)***.

After the initial evaluation is complete and if there is no diagnosis, the patient is considered to have FUO, and a secondary evaluation should be considered. Several diagnostic algorithms have been suggested for FUO, but few are supported by evidence from prospective studies ***(Knockaert et al., 2003)***. Region specific serologic tests, more advanced radiologic studies and more invasive diagnostic procedures can be guided by potentially diagnostic clues. One review found that noninvasive procedures led to most of the diagnoses, whereas of the invasive procedures, biopsies had the highest diagnostic yield ***(Gaeta et al., 2006)***.

Aim of the study

To evaluate the current common causes of acute and prolonged febrile illness in Military Fever Hospital for proper diagnosis and perfect treatment of the diseases causing fever.

Objectives:

- To determine different common causes of acute and prolonged febrile illness in Military Fever Hospital.
- To determine the incidence of different causes of acute and prolonged febrile illness in Military Fever Hospital.
- To prioritize possible causes of acute and prolonged febrile illness in Military Fever Hospital.