

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

Thesis

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وَأَنْزَلَ اللَّهُ عَلَيْكَ
الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ تَكُنْ
تَعْلَمُ وَكَانَ فَضْلُ
اللَّهِ عَلَيْكَ عَظِيمًا

□ صِرَاحُ اللَّهِ الْعَظِيمِ

□ سُورَةُ النِّسَاءِ (الآيَةُ ١١٢)



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List of Abbreviations

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	Dorsomedial 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 1 β
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 $> 38^{\circ}\text{C}$ 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.