

LIST OF Abbreviations

ACTH	Adrenocorticotrophic hormone
AIDS	Acquired Immune Deficiency Syndrome
ANC	Absolute neutrophil count
AUC	Area under the curve
AVP	Arginine vasopressin
BBB	Blood-brain barrier
BC	Before Christ
BCG	Bacilli of Calmette and Guerin
°C	Celsius
CBC	Complete blood count
CIS	Clinical infection score
CMV	Cytomegalovirus
CNS	Central nervous system
COX	Cyclooxygenase enzyme
CPE	Cytopathic effect
CRP	C - reactive protein
CSF	Cerebrospinal fluid
CT	Computerized tomography
CVOS	Circumventricular organ system
DTaP	Diphtheria, Tetanus and acellular Pertussis
E coli	Escherichia coli
EBV	Epstein-Barr virus
ECG	Electrocardiogram
EIA	Enzyme immunoassay
EnP	Endogenous pyrogens
ESR	Erythrocyte sedimentation rate
ExP	Exogenous pyrogens
FMF	Familial Mediterranean Fever
GCS	Glasgow Coma Scale
GFR	Glomerular filtration rate
HBsAg	Hepatitis B surface antigen
Hep A	Hepatitis A

LIST OF Abbreviations (Cont.)

Hep B	Hepatitis B
Hib	Haemophilus influenzae type b
HIV	Human Immunodeficiency virus
HPV	Human papillomavirus
HS	Highly significant
HSV	Herpes simplex virus
ICH	Intracranial hemorrhage
IFA	Immunofluorescent-antibody
Ig	Immunoglobulin
IL	Interleukin
INF	Interferon
IPV	Inactivated Poliovirus
IQR	Interquartile ranges
LA	Latex agglutination
LPS	Lipopolysaccharide
MCV	Meningococcal conjugate vaccine
MMR	Measles, Mumps, Rubella
MPV	Meningococcal polysaccharide vaccine
MRI	Magnetic resonance imaging
NS	Non significant
NSAID	Non-steroidal anti-inflammatory drugs
OPV	Oral polio vaccine
P	Probability
P vivax	Plasmodium vivax
PCR	Polymerase chain reaction
PCV	Pneumococcal conjugate vaccine
PGE	Prostaglandin E
PMN	Polymorphonuclear
POA	Preoptic-anterior hypothalamic area
PPD	Purified protein derivative
PPV	Pneumococcal polysaccharide vaccine
PCT	Procalcitonin

LIST OF Abbreviations (Cont.)

RA	Rheumatoid arthritis
RF	Rheumatic fever
ROC Curve	Receiver operating characteristic curve
RSV	Respiratory syncytial virus
S	Significant
S. aureus	Staphylococcus aureus
S.pneumoniae	Streptococcus pneumoniae
SBI	Serious Bacterial Infection
SD	Standard deviation
SLE	Systemic lupus erythematosus
Tc	Core temperature
TLC	Total leukocytic count
TNF	Tumor necrosis factor
UK	United Kingdom
USA	United States of America
US	Ultrasound
VC	Vasoconstriction
VD	Vasodilatation
WBC	White blood cells count.
χ^2	Chi-square test
YOS	Yale Observational Scale

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Study of clinical observation scales to identify serious illness in febrile children

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INTRODUCTION

Fever is one of the most common symptoms that bring a child for medical attention. Fever results from centrally mediated elevation of body temperature in response to stresses such as infection. Rectal temperature above 38 °C, oral temperature above 37.6 °C and axillary temperature above 37.2 °C are considered abnormal (**EL-Radhi and Carrol, 1994**).

Fever is a common manifestation of infectious diseases, but not predictive of severity. Young infants demonstrate limited signs of infection often making it difficult to distinguish clinically between serious bacterial infections and self limited viral illnesses (**Powell, 2008**).

Toxemia is characterized by signs of sepsis (lethargy, poor perfusion, marked hypoventilation or hyperventilation or cyanosis). The quality of cry, reaction to parents, color, state of hydration, response to social overtures, affect, respiratory status and effort and peripheral perfusion should be assessed (**Scruggs and Johnson, 2004**).

While WBC count $\geq 15000/\text{mm}^3$ was useful in identifying those patients at greatest risk for bacteraemia (**McCarthy et al., 1997**). However, clinical impression is more reliable than laboratory value (**Procop et al., 1997**).

Serious infections need hospitalization and parenteral drug therapy (**El-Nagggar, 2007**). One out of three of children referred with fever has a serious disease. Many studies found that degree of temperature and WBC count are poor predictors of serious disease. Interestingly, poor feeding and restlessness were more sensitive predictors, suggesting that high fever and WBC count cannot replace clinical assessment of the child with fever (**Nademi et al., 2001**).

Aim of the Work

The aim of this study is to evaluate certain clinical observation items and laboratory investigations that can identify, rapidly and reliably, serious diseases in febrile children.

Chapter I

Fever

Historical points:

Among the many symptoms and signs of diseases, fever has received most attention throughout medical history (*El-Radhi et al., 2009*).

Egyptian Medicine:

Egyptian medicine is known to us mainly from medical texts written on papyrus 1700 years before Christ (BC). These papyri contain a description of various infectious diseases such as erysipelas, hepatitis, bilharziasis, ankylostomiasis, gonorrhea and trachoma. Egyptians recognized that local inflammation was responsible for fever (*Dawson, 1967*).

Palpation was used to compare high and mild fever. Cold and warm compresses were prescribed for local inflammation as well as willow leaves which were the earliest known example of external application of salicylic acid (*Breasted, 1930*).

Sumerian Medicine (3000- 500 B.C.):

Early Sumerian writings (2500–3000 B.C.) indicate that fever as a clinical entity was clearly distinguished from local inflammation (*Majino, 1975*). These writings underwent a progressive transformation from about 2500 to 500 B.C. They contain lists of medicine ingredients, diagnoses, and prognoses of various febrile illnesses (*Major, 1954*).

Chinese Medicine:

The Chinese scholars believed that the soul possessed two antagonistic elements; good and evil, and that health and disease depended upon their balance (*Major, 1954*).

Chang-Chung-Ching was known as the Hippocrates of China. In the second century Anno Domini (AD), he wrote an Essay on Typhoid, which was a treatise on various forms of fever. Treatment of fever by antipyretic drugs and the use of cold applications were also described (**Hume, 1940**).

Hindu Medicine:

During the earliest period of Indian civilization, medicine was also characterized by belief in magic and demons (**Major, 1975**).

One of the greatest exponents was **Susruta**, who wrote “the Physiology of Susruta”. Like the Greek scholars (it remains debatable which culture influenced the other), he believed that the human body contained three humors: bile, air, and phlegm. Diseases were thought to be due to the disturbance within these humors (**Jones, 1946**).

Greek Medicine:

Greek scholars believed that the body was composed of four humors (or fluids): phlegm, blood, yellow bile, and black bile. Health was maintained when these humors were in equilibrium, while diseases- especially fevers- were caused by a disturbance of the four humors (**Jones, 1946**).

The Hippocratic writings characterize many febrile illnesses with such accuracy that diagnosis can be made from the descriptions. The Hippocratic writings contain evidence that fever was thought to be beneficial to the infected host and it cured it (**Hippocrates, 1950**).

Galen (A.D. 130–200) retained the Hippocratic humoral theory. Fever, according to **Galen**, could result from either excess of yellow bile, black bile, or phlegm, or from an excess of blood, a plethora. To restore a healthy balance, **Galen** advocated bloodletting (**Majino, 1975**).

Medicine in the Middle Ages (400–1400 A.D.):

Anatomical studies began at 1150 A.D. Physiology and pathology were still based upon the four humors (blood, phlegm, yellow bile, and black bile). All diseases were characterized as hot, cold, moist, or dry. Hot diseases were treated by cooling and moist diseases by drying. Bloodletting was widely practiced in febrile illnesses. The wrath of fever was still attributed to demonic possession and therefore it required exorcism to expel it (**Sarton, 1962**).

Arabic Medicine in the Middle Ages:

Arabic medicine reached its golden age in the ninth and tenth centuries. Two scholars were outstanding in this period. The first was **Abu Ali Husayn ibn Abdulla ibn Sina** (A.D. 980–1037) (**Sarton, 1962**). The 2nd great scholar was **Abu Bakr Muhammad Zakariya Al-Razi** (A.D. 864 - 923) who was the first scholar to differentiate measles from smallpox and that fever in tuberculosis is mild and blunt. He was probably the first scholar to distinguish between the two terms, fever and hyperthermia in the form of heat stroke (**Ar-Razi, 1963**).

European Medicine (1500-1948):

The concepts of fever in European medicine have gradually evolved over several centuries:

Toward the end of the sixteenth century, **Galileo** (1564–1642) reinvented the thermoscope. The first thermoscope had been invented by Heron of Alexandria in the second century B.C (**Woodhead and Jones, 1916**).

During the seventeenth century, fevers were classified as continued, intermittent, or eruptive (**Bollet, 1981**).

In the nineteenth century, the science of bacteriology was discovered, which was able to reveal the etiology of many