Chapter One

Introduction

1.1 Background of the study

Fever defined as an elevated body temperature ≥ 37.5 °C is a physiologic response to illness[1]. It is a bothersome event to caregivers and parents as well as the commonest reason why parents/caregiver seek hospital care for the children [2,3]. The causes of febrile illness in children are of variable spectra either infectious or non-infectious etiology [4]**.** Although, infectious agent; parasitic, bacterial and viral etiologies are the leading causes of fever and the reasons for hospital presentation or admission among children under 5 years of age. These infectious agents are similar in symptomatology with fever the most common manifestation [5,6,7].

In sub-Saharan African continent where the burden of infectious diseases is highly prevalent, associated with appalling health indices of children is challenged with inadequate medical experts and laboratory capacity. This trend is similar in Nigeria a nation in west of the continent with enormous human and material resources. In addition, a high disproportionate number of its populace are impoverished with limited access and availability to quality health care clinical and laboratory services despite on-going advocacy for universal health care through the Primary Healthcare structures. The country has one of the highest abysmal child health indices globally with the leading causes of the childhood illnesses due to infectious agent such as malaria, gastroenteritis, respiratory tract infection [8].

Febrile illness presentation most time are alluded to malaria considering the endemicity profile of the nation with (out) diagnostic support [10,11]. This presumptive treatment of all fevers in children under five with antimalarial drugs is in concordance with World Health Organization (WHO) recommendation for endemic countries where the availability and use of laboratories are limited [12,13]. Although with the advent of the rapid diagnostic test (RDT), the policy was modified in 2010 to promote treatment of malaria only after confirmatory positive RDT[14]**.** However, challenges persist among health care workers and caregivers/parents when the RDT is negative, potentiating the risk of antimicrobial abuse/misuse. These assumptions blur the prompt management of other febrile illness of different infective etiology worsening the risk of antimicrobial resistance, and outcome of child health related morbidity and mortality. Therefore, the illness causing the fever needs to be determined and it is essential to distinguish between a child with fever at high risk and those at low risk to ensure adequate management [15].

In view of the challenges associated with the prompt diagnosis and management of febrile illness in the most needed setting in the country the management of febrile illness in the U-5 and beyond age is mostly through a syndromic approach [16]. To ensure prompt and quality treatment and curtail the abysmal health indices, in Nigeria and other developing country where dearth of medical and laboratory expert remains a bottleneck, the World Health Organization developed the Integrate Management of Childhood Illness (IMCI), Integrate Management of Adolescent and Adult Illness (IMAI) and Integrate Community Case Management (ICCM). The IMCI was instituted as an important tool for prompt management of common childhood illness with fever as common symptom in most cases[17]. The common childhood illness includes Malaria, Respiratory tract infection, diarrhea diseases among others [18].

Considering the current drive to reduce the appalling child health indices from common preventable infectious despite the existing IMCI guidelines, the need to fast-track the attainment of the Sustainable Development Goals, it is of significance to evaluate the management pattern of febrile illness in Primary Health Care Centre. Thus, this study proposed to evaluate the treatment guideline adopted by healthcare professionals at selected Primary Healthcare Centres in the management of febrile illnesses among children U-5 year in Ibadan, Oyo State Nigeria. It is hoped that the outcome of the study will help inform training, strengthen policy guidelines in the management of febrile illnesses among U-5years in PHC.

1.2 Statement of the Problem

In Nigeria, the majority of the primary healthcare facilities are located in remote (rural) locations with poor road systems, unstable power supplies, a shortage of qualified healthcare professionals, inadequate infrastructure, and limited access to pharmacies and testing facilities. Due to these reasons, clinicians managing non-malarial fevers have little guidance, which frequently leads to patients receiving incorrect diagnoses and treatments. To improve the quality of primary healthcare, it is necessary to study the methods of diagnosis for febrile illness management, to identify the workforce and professional qualifications, to identify availability and adherence to National guidelines for treatment, to identify the factors on how they evaluate, diagnose, and treat a child who presents to the hospital acutely ill with a fever.

1.3 Justification of the Study

Management of febrile illness in various PHCs which is based on clinical findings excluding laboratory investigation of some of the fever cases and non-adherence to treatment guidelines mitigate the provision of quality health services needed to address the issue.

1.4 Aim and Objectives of the study

The aim of this study is to evaluate the management of febrile illness cases among Under 5 years in selected Primary Healthcare Centres in Ibadan, Oyo State.

The objectives are to:

i) To assess the knowledge of febrile illness management guideline in selected Primary Healthcare Centres in Ibadan, Oyo State.

ii) To examine the adoption of national guideline for febrile illness management in selected Primary Healthcare Centres in Ibadan, Oyo State.

iii) To identify the factors influencing the adoption of national guideline for febrile illness management.

1.5 Research Questions

i) What is the knowledge of febrile illness management guideline in selected Primary Healthaare Centres in Ibadan, Oyo State?

ii) What is the adoption of national guideline for febrile illness managent in selected Primary Healthcare Centres in Ibadan, Oyo State?

iii) What are the factors influencing the adoption of national guideline for febrile illness management?

1.6 Significance of the Study

1. The study will provide the information on the treatment guideline in the management of febrile illness among children U-5 years
2. The study will help guide modalities needed to improve healthcare delivery at PHC in tandem with National Health Policy
3. Data generated from the study will be used to provide recommendation to the scientific knowledge of public health management of febrile cases

1.7 Scope of the Study

This research aims to assess management of febrile illness cases in selected primary healthcare Centres in Ibadan, Oyo state. This research is restricted to five (5) selected LGAs, in Ibadan.

1.8 Limitation of the Study

This study is limited by its small geographical area and moderate sample size.

1.9 Operational Definition of Terms

- **Treatment guidelines**: described as a methodically created statement intended to help practitioners and patients decide on the best course of treatment for particular clinical situations.
- **Primary Healthcare Centre**: encompasses the provision of accessible, complete, ongoing, coordinated, and person-centered care in the context of family and community, and is the first point of contact for individuals and families in a continuing healthcare process. Through health promotion,

disease prevention, disease management, and supportive care, it improves the population's health.

- **Febrile illness**: is any ailment that causes a fever, which is a body temperature that is higher than 38 °C.
- **Laboratory investigations**: are extensions of a physical examination in which patient samples of tissue, blood, urine, or other substances are collected and examined under a microscope, biochemically, microbiologically, or immunologically.
- **Clinical Diagnosis**: is a procedure for figuring out what kind of problem or illness there is. It is based on analyzing the symptom pattern and going over the medical data. Additionally, it entails the administration of several diagnostic tests to investigate background variables.

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Chapter Two

Literature Review

2.1 Conceptual Review

2.1.1 Definition of Febrile

Physiologically, fever is "a state of elevated core body temperature that is often, but not necessarily, part of the defensive response of multicellular organisms against invading living microbial or inanimate objects recognized by the host as pathogenic or foreign." is defined as Unfortunately, this physiologic definition has limited clinical use due to controversy over what is meant by "elevated core body temperature." Although attention has been paid to patient temperature for thousands of years, there is still no universally accepted temperature definition of fever [1]**.** Febrile diseases caused by various pathogens are the most common causes of morbidity and mortality in tropical and subtropical developing countries. Such diseases pose a public health challenge because empirical diagnosis is common and diagnostic facilities are scarce. Fever is a very common symptom in clinical practice. Fever has infectious causes (malaria, dengue fever, typhus, leptospirosis, enteric fever, acute viral hepatitis, sepsis, etc.) and non-infectious causes (connective tissue diseases, autoimmune diseases, malignant diseases, and many others). cause), and many other causes. A unified strategy for determining etiology is difficult because the epidemiology of fever changes over time. The term acute undifferentiated fever (AUF) is used to describe fever typically lasting no more than 14 days and lacking localized or organ-specific clinical features. AUF poses diagnostic and therapeutic challenges to healthcare professionals, especially in resource-constrained settings. Non-specific symptoms and signs and failure to obtain an accurate diagnosis not only test the clinical skills of smart physicians, but often lead to irrational use of antibiotics and antimalarial drugs. On the other hand, AUF syndromes (including febrile rash, febrile myalgia, febrile joint pain, febrile hemorrhage, and febrile jaundice) have overlapping causes, making diagnosis and treatment even more difficult [2].

2.1.2 Overview of Febrile Illness

Persistent febrile illness (PFI), defined as fever lasting more than 7 days, is a neglected area of clinical research in low- and middle-income countries (LMIC). Due to the lack of available diagnostic tools and laboratory resources, it is difficult to determine the differential diagnosis of his PFI in tropical rural areas, including Nepal. This leads to the inability to make a definitive diagnosis and poor clinical management of patients, including inappropriate use of antibiotics. This study, conducted as a nested study within the Neglected Infectious Diseases Diagnosis (NIDIAG) study, presents a systematic literature review on the causes of his PFI in Nepal, with a potential focus in eastern Nepal. We report the results of his NIDIAG research division conducted. Severe and treatable conditions in Nepal, Congo, Sudan, and Cambodia, and the extent and risk factors for pre- and post-hospital antibiotic use [3]. Febrile illness is a public health challenge, especially in developing countries, especially for medical professionals who often have to rely on empirical clinical diagnosis due to limited diagnostic capacity. However, empirical diagnosis can lead to poor patient management, disease recurrence, exacerbation, and even death. Importantly, inappropriate use of antibiotics can compromise the gut microbiota and promote the development of antimicrobial resistance. According to the Ethiopian Ministry of Health, respiratory and gastrointestinal infections were the leading causes of morbidity among Ethiopian children in 2014 and 2015. Children primarily suffered from malaria, skin and eye infections, and parasitic infections, as well as bloody/non-bloody diarrhea and upper/lower respiratory tract infections. organ infections, diarrhea, malaria, human immunodeficiency virus/AIDS, meningitis and measles, non-communicable perinatal complications (birth asphyxia, prematurity, neonatal sepsis), and severe malnutrition. The African Typhoid Surveillance Program (TSAP) evaluated the incidence and etiology of acute febrile illness in children ≤15 years of age recruited from January 2012 to January 2014 in pizzella, central and southern Ethiopia. Established in 2009, TSAP provides future standardized blood culture-based fever surveillance in 13 health facilities in 10 sub-Saharan African countries: Burkina Faso, Ethiopia, Ghana, Guinea-Bissau, Kenya, Madagascar, Senegal, Southern Africa, Sudan, Tanzania. The purpose of this program was to provide the evidence necessary to assist policy makers in introducing preventative measures, particularly safe and effective vaccines against typhoid fever and invasive non-typhoid salmonellosis. Pizzella blood culture positive rates were found to be low in contrast to other TSAP sites. Therefore, in addition to the analysis of prospectively collected surveillance data, we developed a retrospective case classification scheme consistent with unpublished country-specific charts and published literature, making optimal use of clinical and laboratory surveillance data [4].

Etiology Of Febrile

Acute febrile infections (AFI) continue to have a significant worldwide impact despite advancements in health care access and a decline in malaria transmission. According to recent research, non-malaria etiologies account for about 80% of cases of acute febrile illness (AFI), even those in areas where malaria is endemic.

Due to a lack of suitable diagnostic tests, viral infections such zika, dengue, and chikungunya can go undetected or be incorrectly diagnosed. Therefore, a lot of these AFI patients receive care based on their clinical presentation. The abuse of antibiotics as well as negative patient outcomes might result from relying solely on clinical presentation. This is especially true for the Zika virus, which, like many other AFI-causing agents, is hard to identify and can exhibit clinical symptoms similar to those of infections caused by Brucella spp., Listeria spp., and Salmonella spp [5].

Pathophysiology

A common neurological condition defined by neuronal hyper-excitability in children between the ages of 3 months and 5 years, febrile seizures are brought on by an elevated core body temperature during a fever that was brought on by an underlying systemic infection. These infections trigger the immune system to launch an inflammatory response, which causes macrophages to release cytokines. Interleukin-1 (IL-1), IL-6, and tumor necrosis factor (TNF) are cytokines that fight infection in the localized area before spreading into the bloodstream and causing high cytokine levels. The blood brain barrier (BBB) becomes "leaky" as a result of the interaction between the cytokines and pathogen-associated molecular patterns (PAMPs) expressed on pathogens, such as lipopolysaccharide (LPS), allowing cytokines and LPS entrance. The cytokines trigger the release of the microglia's own cytokines, particularly IL1. When IL- interacts with the brain endothelium, cyclooxygenase 2 is activated, catalyzing the synthesis of prostaglandin 2 (PGE2). PGE2 enters the hypothalamus and raises the body temperature. The pathophysiology of convulsions is mediated by abnormally elevated IL-1 levels, which also gradually enhance excitatory (glutamatergic) and reduce inhibitory (GABAergic) neurotransmission. Current treatments for febrile seizures have negative health side effects, which increases the need for an alternative, more cost-effective treatment with fewer negative side effects and 1 that is easily accessible, especially in low-income areas where febrile seizures are a growing health concern and are also affected by other underlying socio-economic factors [6].

2.1.4 Burden of Febrile Illnesses

Most people in South and Southeast Asia live in rural areas, which are often characterized by high poverty rates and limited access to healthcare[7]. Data on the etiology of these areas prioritizing interventions for scale-up are limited. Nonetheless, there is evidence that diseases of infectious etiology, often characterized by fever as a symptom and commonly referred to as 'febrile illnesses', are responsible for significant morbidity and mortality [8]. Malaria is a typical febrile disease. For decades, empirical antimalarials have been recommended for febrile patients, reflecting the burden associated with this deadly but treatable disease. In many parts of Asia, Village Health Workers (VHW) and/or Village Malaria Workers (VMW) are deployed to improve access to treatment as part of comprehensive malaria eradication programs. As a result, a rapid decline in malaria incidence has been observed [9]. As a result, fever is rarely transformed into malaria in these areas today, but the exact cause of the disease, optimal management, and the future of these individuals remain unclear [10]. The decline in malaria incidence highlights the inadequacies and weaknesses of this vertical approach to health care. VHW/VMW have access to limited training, support and coverage, and are often unable to offer patients further testing or treatment once malaria is ruled out. As a result, treatable bacterial infections are overlooked, and even when antibiotics become available, they are overused and untargeted. In addition, the current inability to treat non-malarial fever has a negative impact on the spread of malaria testing. If malaria were excluded in areas where malaria is already rare, 4,444 patients would be few and far between, but no other treatment for their disease would be offered [11]. This hampers eradication efforts and jeopardizes the resurgence of drug-resistant malaria. Encouragingly, it has been shown that the downward trend in patient care (and malaria testing) can be reversed by extending VHW mandates to other critical health care [913]. VHW training and skills vary widely, and even within the same country, there are different types of VHW funded by different actors and managed by different agencies. For example, in the Lao People's Republic, Village Health Volunteers (VHV) are her one category of her VHW administered by the Department of Health and Health Promotion and do not receive scholarships. She will complete a 10-day training course supporting health education, hygiene and hygiene programs, immunizations, maternal health care, nutrition, infectious disease prevention and control, and administration of revolving drug funds. In contrast, the VMW in Laos is tasked with diagnosing and treating uncomplicated malaria cases, referral of severe cases, distribution of bed nets, and provision of health education/promotion, but unlike VHV, it is usually receiving a monthly stipend funded by the Global Fund [12,13]. Brucellosis, listeriosis, typhoid and paratyphoid fevers, invasive non-typhoidal Salmonella infections, and typhoid fever are a few examples of such foodborne diseases that primarily manifest as febrile illnesses. Interventions aimed at improving food safety are probably capable of making a significant dent in the global incidence of febrile illness. Here, we outline some of the difficulties and potential remedies in measuring the burden of febrile illnesses, such as those brought on by tainted food [14].

2.1.5 Febrile Illness among Nigerian Nomads

The formal health system appears to be poorly suited to providing services to nomadic populations that are continuously on the move, and local authorities frequently ignore the presence of nomads when it comes to the provision of health care. For instance, guinea worm case detection scouts in Southwestern Nigeria "failed" to include trips to nomad camps and ivermectin distribution in the fight against onchocerciasis frequently neglected nomadic Fulani villages. Nomadic camps, which are situated on the outskirts of populated places, are frequently disregarded to the point where, in some regions, fewer than 3% of children under the age of two may benefit from full immunization services. Nomads are excluded from ongoing malaria management initiatives while being disproportionately more susceptible to infectious diseases like malaria. Malaria is to blame for up to 20% of maternal mortality in sub-Saharan health facilities, making up more than 10% of the continent's overall illness burden. Malaria continues to be the leading cause of pediatric morbidity and mortality in Nigeria. Malaria accounted for 63.4 percent of all diseases recorded in 2000, with 50% of the population experiencing at least one episode, which resulted in between 30 and 50% of inpatient admissions and 50% of outpatient visits to medical institutions. The headman, his wives, children, and dependents make up the traditional Fulani family. A wuro (camp) is formed when about 15 households congregate in one place, and there are many wuro comprise a gure. In their quest for health, Nomadic Fulani are widely known for their reliance on herbal remedies and private medical facilities. Even though the government is currently working to reduce the disease burden by distributing and promoting the use of insecticide-treated nets (ITNs), straightforward diagnostic tools, behavior change communication, appropriate chemotherapy, intermittent preventive treatment, and community management of febrile illnesses, the nomads still have difficulty accessing these services. Given that the idea of illness is influenced by cultural identity, one of the key health challenges in Africa is how beliefs about health and illness are used in the administration of healthcare. The way the Fulani accept illness, for instance, illustrates how they vary from other communities in this regard. Being Fulani requires tenacity and resilience, character, self-control, and showing others how to behave. Integration with the malaria control program is hampered by the lack of understanding of their cultural experiences with malaria. But even when the disease eventually declines to a level below public health importance among settled people, if the issue is not addressed, nomads will continue to represent an epidemiologically significant group. Prior to the creation of a suitable intervention program, a study on the malaria disease experiences of nomadic Fulani populations that camp in the valleys of rivers Benue and Gongola of Northeastern Nigeria during the dry season was conducted [15,16].

2.1.6 Effects of Febrile

An increase in senseless fluid loss, dehydration, metabolic demands, and a dysregulation of body temperature are only a few of the negative impacts of fever on the body. Fever is caused by endogenous or exogenous pyrogens that raise body temperature by resetting the hypothalamic set point. Hyperthermia, as opposed to fever, is described as an increase in body temperature brought on by the generation of heat that exceeds the body's capacity to efficiently expel heat. Vasodilation and sweating, two common bodily functions that help the body cool itself under heat stress, are not present when a person has a fever. The most typical condition that causes fever is infection. Fever is a multistep adaptive response to a range of circumstances. Pyrogens, which may be endogenous or external, start this adaptive reaction. Bacterial toxins, viral pathogens, bacterial cell wall components, and antigen-antibody complexes are examples of exogenous pyrogens. The endogenous pyrogens, which include interleukins, interferons, and other cytokines, are released when the exogenous pyrogens attach to macrophages and trigger the creation of prostaglandin E2. These chemicals interact with the preoptic area of the hypothalamus and raise the body's "set point" temperature [17]. This elevated set point temperature is maintained by thermoregulatory regulation until the initial threat or external stimulation has subsided. Rarely does the body temperature rise beyond 40°C when in a feverish state. Alpha-melanocyte stimulating hormone (ADH), corticotropin-releasing factor (CRF), and other naturally occurring antipyretic hormones generated by the body serve as negative feedback mechanisms that control the self-limiting process of fever. Fever is an acute phase response component that involves endocrine, biological, psychological, and autonomic systems. Adrenaline production rises, which boosts the body's metabolism, heart rate, and muscle tone. Every 1°C rise in body temperature results in a roughly 10% increase in metabolic rate. By promoting glycolysis and inducing peripheral vasoconstriction, adrenaline continues to contribute to raising body temperature. By reducing the quantity of free glucose in circulation and switching to a metabolism based on lipolysis and proteolysis, the immune system also makes the environment unfavorable for infections. Increased peripheral vascular resistance, which diverts blood away from the peripheral capillary beds and reduces heat loss through conduction, radiation, convection, and evaporative processes, contributes to raising the body temperature further. While benefiting the immune system, these drops in free glucose and peripheral blood flow, while boosting the immune system, this reduction in vital nutrients also benefits functioning muscles. Fever decreases antidiuretic hormone synthesis, which can exacerbate dehydration. Mammals try to control their body temperature during hyperthermia by using evaporative cooling. In order to conserve water at the expense of greater body temperatures, if they are also extremely dehydrated, their body reduces or blocks these methods of cooling. Selective hypothalamic cooling prevents heat loss by evaporation, preserving bodily water and supporting the body's need for both thermoregulation and osmoregulatory balance. Additionally, it was discovered that animals who were dehydrated had much higher daily body temperatures[18]. Exercise-induced hyperthermia and dehydration in human participants resulted in larger reductions in cardiac output and blood pressure than either condition alone. Hypohydration can lower heat stress tolerance and increase heat storage. Therefore, if athletes exercise while they have a fever, their bodies' natural temperature-regulating processes are disturbed and could lead to increases in body temperature that could be hazardous, especially if the febrile sickness also resulted in some degree of dehydration [18].

Thermoregulation disorders

The Intensive Care Unit frequently experiences fever as a symptom. A minimum of 50% of febrile episodes are brought on by an infection. Attention should be directed to abnormalities of the thermoregulatory center after excluding viral etiology and other non-infectious causes of fever, particularly in individuals with central nervous system (CNS) disorders. Central fever is most often brought on by subarachnoid hemorrhage, brain trauma, ischemic or hemorrhagic stroke, and other conditions. The ability to implement preventative measures against the damaging effects of hyperthermia on the CNS and to avoid the negative effects of ineffective therapy depends on an accurate, prompt identification of the fever's underlying cause. This review's objective is to examine recent recommendations for the management of central fever and discuss available choices for therapy. Due to the dearth of randomized clinical trials demonstrating the efficacy of such treatment, the recommendations of American and European groups are varied. The elimination of other causes is still used to make the diagnosis of central fever. Finding diagnostic markers or establishing diagnostic criteria for central fever is very crucial. It is also important to carry out additional randomized clinical trials to assess the hyperthermia therapy indications [19].

2.1.7 Burden of Disease from Nonmalarial Febrile Illness

Without localizing factors, no estimate of the global burden of disability and mortality from febrile illnesses has been made. As a result, this category of infections has not received much attention as a whole. Therefore, it is difficult to estimate the size of the effect of therapies for fevers. The World Health Organization (WHO) [20] and the Institute for Health Metrics and Evaluation evaluate disability-adjusted life years (DALYs), including fatalities from diarrhea and pneumonia, at the syndrome level before attributing them to specific causes (IHME). These sources do not, however, estimate the individual illness loads of other forms of fever, such as chikungunya, leptospirosis, and Q fever, such as malaria, dengue fever, and enteric fever [20].

As a result, academic, national, and international institutions of public health rarely include interdisciplinary knowledge treating fever across the spectrum of accountable pathogens Similar to this, research on the causes of fever has tended to concentrate on a small number of pathogens rather than a wide variety of factors [21]. The inadequate autopsy practices also contribute to the difficulties in calculating the global burden of death from febrile diseases. Malaria-related deaths can be hard to identify from other fever-causing diseases using verbal autopsy. In locations where malaria is endemic, verbal autopsy may identify fever deaths as malaria-related. By verbal autopsy, many causes of febrile sickness cannot be determined. On autopsy, deaths attributed to cerebral malaria may turn out to be the result of other causes even when a malaria diagnostic test is positive [22]. Full autopsy for diagnostic purposes is being researched as a way to lessen confusion surrounding causes of mortality in underdeveloped countries, but is not commonly available in low-resource settings[23].

2.1.8 Challenges in Acute Febrile Illness

Epidemiologic Challenges

For informing public health plans, allocating resources, and tracking the results of treatments, knowledge of the epidemiology of a region is essential. The lack of data from many LMICs is the main obstacle preventing the compilation of this knowledge, but there are other significant obstacles as well. Only 45 researches, done in 22 different locales, were found to be eligible in a systematic review of severe febrile illness in LMICs. No studies from southern or middle Africa, eastern Asia, oceania, Latin America, the Caribbean, or Europe were found to be eligible. But more than 120 trials that were carried out in outpatient settings were not included in that review. A significant percentage of cases could be missed since individuals may not regularly visit a hospital for care during a feverish illness causing the full burden to be underestimated. In one study, all fever patients were sent to a community clinic, but only 30% of them showed up for an evaluation, highlighting the limitations of passive surveillance. Another drawback is that many studies that assess febrile sickness are carried out over a short period of time rather than a full year. Therefore, despite the fact that their presence has been well-documented, these studies would not effectively take into account seasonal fluctuations in sickness and illness [24].

Febrile Pattern and Diseases

One of the oldest and most prevalent clinical indications of disease in the mammalian host, fever is also one of the main causes of medical consultations around the world. As a result of an infection, inflammation, or trauma, fever frequently develops. This view of fever, however, is simply an oversimplification given the mounting evidence that fever is an intricate adaptive response of the host to a variety of immunological stressors, whether infectious or not. Although a higher-than-normal body temperature is a necessary part of the febrile reaction, fever is not the same thing. Fever is typically defined as a controlled increase in body temperature above typical daily swings that takes place in conjunction with a raised thermoregulatory set point. To emphasize the flexible character of the febrile reaction, Fever is a state of elevated core temperature that is frequently—but not always—part of the defensive responses of multicellular organisms (host) to the invasion of live (microorganisms) or inanimate matter that is recognized by the host as pathogenic or alien. This definition was provided by the International Union of Physiological Sciences Commission for Thermal Physiology in 2001[25]. The multi-systemic consequences of the febrile response, which are coordinated by endocrine, neurological, immunological, and behavioral processes, may explain the intricacy of the response. Fever is accompanied by a controlled rise in body temperature as well as a variety of illness behaviors, modifications to the physiological and metabolic makeup of numerous body systems, and changes to immunological responses. Therefore, the febrile response continues to play a major role in the pathophysiology, clinical manifestation, and course of many illnesses and disorders. Consequently, Fever is a state of elevated core awareness of fever and febrile response is essential in the diagnosis, treatment, and follow-up of various ailments and diseases. Fever was defined as an elevated state of core awareness by the International Union of Physiological Sciences Commission for Thermal Physiology in 2001[26].

Pathophysiology of the febrile response

Fever is defined as an increased core body temperature by the International Union of Physiological Sciences Commission for Thermal Physiology in 2001. The typical thermoregulatory processes that occur after being exposed to cold temperatures are similar to how the febrile response develops. The thermoregulatory circuitry now perceives normal peripheral and central body temperatures as chilly temperature signals during fever because the thermal balancing point has been adjusted to a higher level [2–5]. Fever is therefore distinct from heat stroke and hyperthermia, conditions in which the body temperature rises without a commensurate rise in the thermal balancing point. According on the location, kind, and severity of the inflammation, many independent afferent and efferent processes may be used to produce fever, similar to how thermoregulation occurs biological compounds are mentioned [27].

Classification, types and patterns of febrile

Based on how long they last, fevers can be arbitrarily divided into acute, sub-acute, and chronic fevers. Chronic bacterial illnesses like tuberculosis, viral infections like HIV, malignancies, and connective tissue diseases are all known to cause acute fevers that last for two weeks. But if left untreated, any cause of acute fever might develop into a persistent or chronic condition. Fever can also be divided into low grade, moderate grade, high grade, and hyperpyrexia depending on the height of the body temperature. There may be some diagnostic and prognostic consequences of the peak body temperature. Although other research has demonstrated that children with high fevers are at an equal high risk for deadly bacterial infections and viral illnesses, several studies have linked high grade fevers in infants to serious bacterial infections. There may occasionally be a spike in fever as shown in experimental dengue virus infection, experimental shigellosis, and acute falciparum malaria, where the presence of hyperpyrexia signals a severe illness with a poor prognosis. The severity of the sickness is, however, more strongly predicted by the patient's general clinical condition than by the fever's peak. Sustained/continuous fever, intermittent fever, and remittent fever are three of the most common kinds of fever that have been identified. These main fever patterns are depicted in Figs. 2 and 3. A continuous or maintained fever is one that does not change more than roughly 1 degree Celsius (1.5 degrees Fahrenheit) throughout the course of a day, never reaching normal [28].

Continuous fevers

These characteristics include typhoid, acute bacterial meningitis, lobar and gram-negative pneumonia, urinary tract infection, among others. Typhoid fever is typically characterized by a high plateau and a steady incremental temperature rise.

However, in actual practice, this fever pattern is only observed in around 12 percent of cases, presumably because most feverish patients self-medicate with antibiotics and antipyretics before seeking medical attention. Untreated cases of typhoid, leishmaniasis, brucellosis, Legionnaire's disease, psittacosis, and Yellow Fever, among others, are characterized by fever coupled with relative bradycardia (also known as Temperature Pulse Dissociation or Faget's Sign).

Intermittent fever

This is characterized as a fever that only lasts for a few hours during the day. Malaria, pyogenic infections, tuberculosis (TB), schistosomiasis, lymphomas, leptospira, borrelia, kala-azar, and septicemia are among the illnesses that can cause this pattern of fever. Sources of persistent, sporadic, or transitory bacteraemia may result in persistent, sporadic, or transient fevers, accordingly. Fever in malaria can occur every 24 hours (quotidiandue to Plasmodium falciparum), every 48 hours (tertian — Plasmodium ovale and vivax), or every 72 hours (quartan — Plasmodium malariae). A low-grade intermittent fever known as Pel-disease Epstein's causes 3–10 days of fever followed by a 3–10-day febrile interval. It is believed to be a typical, albeit uncommon, Hodgkin's lymphoma presentation. Remittent fever is described as having a daily fever fluctuations more than 2 C, but never approaching normal. Recurrent fevers are frequently linked to infectious disorders such brucellosis, rickettsia infections, and infective endocarditis, among others. Relapsing fevers are defined as those that occur repeatedly and are separated by intervals of low fever or no fever. Malaria, lymphoma, borrelia, cyclic neutropenia, and rat-bite fever all cause periodic or relapsing fevers. Infectious conditions like TB, Nocardia, brucellosis, liver or lung abscesses, and subacute infective endocarditis have been linked to fever and night sweats, as have non-infectious conditions like polyarteritis nodosa and tumors like lymphomas [28].

Pathophysiology of the febrile response

The typical thermoregulatory processes that occur after being exposed to cold temperatures are similar to how the febrile response develops. The thermoregulatory circuitry now perceives normal peripheral and central body temperatures as cold temperature signals during fever because the thermal balance point has been adjusted to a higher level. Fever is therefore distinct from heat stroke and hyperthermia, conditions in which the body temperature rises without a commensurate rise in the thermal balancing point. According on the location, kind, and severity of the inflammation, many independent afferent and efferent processes may be used to produce fever, similar to how thermoregulation occurs. The next section discusses the many biological molecules involved in the production of the febrile response as well as the pathways connected to these reactions [29].

Fever: the role of pyrogens and cryogens

The pyrogenic and anti-pyretic properties of numerous exogenous and endogenous chemicals are necessary for the initiation, symptoms, and modulation of the fever response. Cryogens prevent excessive temperature rise, whereas pyrogens either directly or indirectly cause fever. The intensity and length of the febrile response to each immunological challenge depend on how well pyrogens and cyrogens interact with one another [30].

Pyrogens

Based on where they are created, pyrogens are divided into exogenous (made outside the host) and endogenous (produced within the host) pyrogens. Exogenous pyrogens are essentially entire or fragmented microorganisms or their byproducts, like poisons. Most of the existing information regarding the febrile response is based on studies utilizing the gram-negative cell wall component lipopolysaccharide (LPS) as the pyrogenic agent. LPS is still the most extensively studied exogenous pyrogen. Muramyl dipeptidase, a component of cell-walled microorganisms, and the enterotoxins of Staphylococcus aureus and group A and B Streptococcus, collectively known as superantigens, are further clinically relevant endogenous pyrogens. Interleukins (IL) 6, IL-1, interferon gamma (INF-), ciliary neurotropic factor (CNTF), and tumour necrosis factor (TNF) are among the pyrogenic cytokines that make up the majority of endogenous pyrogens. However, depending on the experimental circumstances, TNF exhibits both pyrogenic and antipyretic effects. In reaction to exposure to external pyrogens, immune cells such neutrophils, macrophages, and lymphocytes, as well as endothelial cells, astrocytes, and glial cells, create endogenous pyrogens. However, several naturally occurring compounds, such as antigen-antibody complexes, inflammatory bile acids, complements, and different molecules generated from lymphocytes, may act as pyrogens without being induced by external pyrogens [31].

Cyrogens

Cyrogens include hormones (such as -melanocyte stimulating hormone, corticotrophin, and corticotrophin releasing hormone), anti-inflammatory cytokines (like IL-10), and many other neuroendocrine substances, including cytochrome P-450 (P-450). They do this, among other things, by decreasing the production of pyrogenic cytokines (such as glucocorticoids), blocking the cytokine receptors (such as IL-1 receptor antagonist), and promoting heat loss by sharpening the sensitivity of warm-sensitive neurons (such as bombesin). These in-built antipyretic mechanisms shield the host from the negative effects of uncontrolled fever [32].

The fever pathways

Through two fundamental mechanisms, namely the humoral and brain pathways, fever signals carried by exogenous and endogenous pyrogens ultimately result in the reset of the thermoregulatory circuitry.

The humoral pathway

Pathogen associated molecular patterns (PAMPS), which are parts of microbial metabolites, or pyrogenic cytokines are responsible for carrying fever signals in this pathway. It is known that circulating PAMPS of microorganisms, such as gram-negative LPS, bind toll-like receptors 4 (TLR-4) on a variety of cells. They cause the release of prostaglandin E2 (PGE2) from the arachidonic acid pathway in cytoplasmic membranes by binding to and activating TLR-4 found on the fenestrated capillaries of the circumventricular organ in the blood brain barrier. In order to activate thermal neurons in the anterior hypothalamus and raise the thermal balance point, prostaglandin E2 binds to specific PGE2 receptors (EP3 receptor) in the preoptic area. Prostaglandin E2 is a tiny molecule that quickly diffuses through the blood brain barrier. Whether or not microbial products also lead to direct access to the brain by disruption of the BBS, which will raise the thermal balancing point. An early quick phase and a delayed late phase define the feverish response. According to research done in animal models with polyphasic LPS-induced fever, the first stage of this febrile response is thought to be dependent on PGE2 synthesized in the liver and lungs before migrating to the brain, whereas the latter stages are thought to be dependent on PGE2 synthesized centrally. Therefore, centrally produced PGE2 may play a major role in maintaining the febrile response, whereas peripherally synthesized PGE2 may act to induce it. Circulating pyrogenic cytokines control the second humoral pathway. Indirect and direct methods are used to provide fever signals to the thermoregulatory circuitry. By binding to and activating cytokine receptors on the fenestrated capillaries of the circumventricular organ, pyrogenic cytokines act outside the brain in the indirect pathway, causing the release of PGE2. Circulating cytokines can contact cytokine receptors located on vascular, glial, and neuronal components of the brain directly through the direct channel, which involves disrupting the blood brain barrier. These central receptors are activated, which encourages the brain to produce more cytokines or PGE2 on its own. Even though PGE2 is still a crucial component of the febrile response, other inflammatory mediators such as certain cytokines and many others can also cause the response to become active. The hyperpyrexia experienced in CNS infections and hemorrhages, both of which can cause direct PGE2-independent activation of the thermal neurons by cytokines, may be caused by these conditions, the latter of which is also known as central fever. Under these circumstances, the CNS's anti-pyretic functions are compromised, causing an uncontrolled rise in body temperature. Other inflammatory mediators, such as bradykinin, corticotropin-releasing hormone, nitric oxide, MIP-1, IL-6, and IL-8, preformed pyrogenic factors (PFPF), substance P, and endothelin-1, may also reset the thermal balance point independently of PGE2 [33].

The neural pathway

Through peripheral nerves like the vagus nerve and cutaneous sensory nerves, peripheral fever signals can interact with the central nervous system (CNS). Another mechanism by which fever is quickly initiated is thought to be brain circuit activation. It has been hypothesized that localized PGE2 production at areas of inflammation contributes to the production of fever by triggering cold-sensitive cutaneous nerves, which then send fever signals to the brain regions in charge of fever production. A more complicated method is followed by the vagus nerve to transmit fever signals. The liver's Kupffer cells are stimulated to create endogenous mediators, such as pyrogenic cytokines, by circulating pyrogens like LPS that activate complement and complement products. These cytokines cause the vagus nerve's hepatic branch to become active, which It sends fever signals to the nucleus of the tractus soleus, which is the central projection of the vagus nerve (NST). The ventral noradrenergic bundle carries the signal from the NST to the preoptic and hypothalamic regions, resulting in the release of norepinephrine into the intrapreoptic space. The vagal pathway is mediated by norepinephrine, which causes definite increases in core body temperature. While the second is alpha (2)-AR-mediated, delayed, and PGE2-dependent, the first is alpha (1)-adrenoceptor (AR)-mediated, quick in onset, and PGE2-independent. Experimental observations in rats supported the hypothesis that vagal afferents contribute to the development of fever by attenuating or completely eliminating febrile responses to pyrogenic signals. Recent research, however, has refuted this theory and blamed pyrogenic signals for the lack of a febrile reaction, malnutrition, one of the vagotomy side effects. Experimental investigations in rats reveal that total or partial vagotomy did not stop the febrile response to pyrogenic signals such intravenous PGE2 when such adverse effects of vagotomy are avoided [34].

Symptoms of fever

The above-mentioned humoral and neural fever signals cause the thermal balance point to be reset to a higher level, which starts a feedback loop that results in a series of clinical and behavioral manifestations that define the feverish response. Skin vasoconstriction (which causes goose bumps and the chills) and behavioral strategies like adopting the fetal position to reduce body surface area, donning thick clothes, and seeking out warmer locations all work together to prevent heat loss in order to reach the new equilibrium point. Then, a number of heat-gaining mechanisms, such as increased muscular contraction, are engaged (leading to rigors). The equilibrium point returns to normal with the activation of heat loss mechanisms like perspiration once the fever signal has left the CNS. So, fever is frequently marked by rigors, chills, an increase in body temperature, followed by sweating and a drop in body temperature. Fever may sometimes be accompanied by systemic symptoms as headache, lethargy, anorexia, and other sickness-related behaviors. An overview of the pathways leading to fever and related acute phase reactions is provided by the fact that these symptoms are brought on by the systemic effects of microbial products and pyrogenic cytokines, which cause a variety of acute phase reactions mediated through the neuroendocrine system. One of the largest pandemics in history, coronavirus disease 2019 (COVID-19) is a febrile respiratory ailment that has spread wildly over the world. In addition to the direct mortality effects of COVID-19, the diagnosis and treatment of acute febrile infections (AFI) are also greatly concerned. There is a significant delay in the diagnosis and treatment of AFI in patients with suspected COVID-19 because to overlap in presentation, shunting of available resources, and infection control measures. The difficulties in treating acute febrile sickness during the COVID pandemic are highlighted in this paper, along with potential remedies [35].

Current concepts among physicians

Pediatricians frequently have the misconception that fever is dangerous. Pediatricians frequently have the misconception that fever is hazardous. The majority of pediatricians in Massachusetts, USA (65%) think that fever itself could be harmful for a kid who has seizures; if the temperature is 40 °C or above, the most serious side effects of fever are death and brain damage. Although the majority of pediatricians concur that giving an antipyretic to a febrile child is primarily for the relief of fever symptoms, many still have a tendency to provide antipyretics to any child who has a fever. Pediatricians may be encouraging fever phobia by giving children antipyretics when they are only moderately feverish or by advising patients to alternate between paracetamol and ibuprofen. Biological significance of fever. Physicians disagree on the usefulness or danger of fever, which is why it is aggressively treated in an effort to avoid its repercussions. The accepted practice mandates steps to eradicate fever, even for mild cases, and considers the extensive use of antipyretics to be a necessary. Parents prefer using antipyretics to treat fevers, and over the past 20 years, this choice has increased from 67 percent to more than 90 percent (91 percent to 95 percent). Health specialists are concerned that parents frequently administer antipyretics at the wrong dose and frequency. Underdosing encourages alternating antipyretics to maintain a normal temperature and increases the need of medical services. The dangers of overdosing are possible. On pediatric patients, the use of alternating antipyretics has become commonplace and experts are unsure of the validity of this treatment and whether there are any negative effects as a result. Between 52 percent and 67 percent of parents reported engaging in this activity in 2007, up from 27 percent in 2001. Pediatricians who treat children in hospitals have learned to accept the fact that, with the sole indication of a fever, an antipyretic is frequently routinely recommended on the treatment sheet. Both a youngster with considerable fever-related discomfort and a febrile child who is playful on the ward are given antipyretics. It is probable that fever's unfavorable reputation has a long history. Fever was feared by common people for the majority of history as a punishment sign, a sign of malevolent spirits, or a warning sign. The eminent French scientist Claude Bernhard (1813–1878) understood that heat loss and production were balanced in healthy organisms to control body temperature. He showed that animals perished quickly when their body temperatures rose by 5 to 6 degrees Celsius, indicating that fever would be dangerous and that antipyretics, which were later developed, might be helpful. "The mankind has three adversaries, illness, famine, and war, but fever is by far the greatest,"wrote William Osler (1849-1919). The majority of pediatricians in Massachusetts, United States, (65%) [36].

Benefits of fever are found among ancient scholars

Evidence from the works of Hippocrates shows that fever was considered advantageous for the sick host and that it treated ophthalmia. Hippocrates gave little attention to fever therapy because he thought that fevers had benefits. When one of the four body humors was overproduced, the surplus humor was "boiled," divided, and expelled by the fever. A surgeon named Rufus of Ephesus, who practiced at the start of the second century AD, fervently supported the positive effects of fever. He was the first doctor to advocate "fever therapy," such as malarial fever, as a means of treating epilepsy. "Fever is a good cure for a person stricken with convulsions," he remarked. It would be pointless to look for any other treatment for an illness if a doctor had the ability to induce a fever. As seen by his statement that "fever is a great motor which nature throws into the earth to eliminate her adversaries," Thomas Sydenham (1624-1689) plainly saw fever as useful [37]. A key component of the malaria control approach is the efficient treatment of malaria episodes. In August 2001, Tanzania switched its first-line malaria medication from chloroquine (CQ) to sulphadoxine/pyrimethamine (SP) due to the emergence of CQ resistance. Health professionals received training on the new treatment guidelines during the SP policy's adoption, some of which were based on the integrated management of childhood diseases (IMCI) guidebook. The WHO's 1997 IMCI is a symptom-based approach for identifying and treating the most typical children’s ailments, such as malaria, in environments with minimal resources. According to the Tanzanian policy, which is based on the IMCI strategy, all fevers should be treated as malaria in settings without access to a microscopy. The first point of contact with formal health care services is made by medical staff such as clinical officers and prescription nurses who work in outlying dispensaries and health facilities. Poor health worker performance in terms of history taking, physical examinations, and consultation time at primary healthcare facilities has been documented in studies from Tanzania as well as other nations like Bangladesh and Burkina Faso (Krause et al. 1998; Nsimba et al. 2002; Arifeen et al. 2005). Inadequate clinical evaluation may result in inaccurate diagnosis and ineffective management of malaria episodes and other circumstances. Various techniques have been used to evaluate the quality of care. Most involve a quality indicator-based rating system of some form. A tool called the multi-country assessment (MCE) was created by the WHO to assess IMCI in various contexts (WHO 2001). This has been proposed as a standard for simpler comparisons between studies and has been utilized by a number of other researchers (Armstrong Schellenberg et al. 2004; Arifeen et al. 2005). (Rowe et al. 2005). The major findings of a study on malaria case management conducted in Kibaha District, Tanzania, prior to the national treatment policy change (Nsimba et al. 2002) were subpar performance in terms of brief consultation times, rarely physical examinations, and scant history taking. Cases without a confirmed malaria diagnosis were administered CQ and without eliciting past drug use. With CQ (the first-line antimalarial at the time), there was a high rate of self-medication, which led to high drug pressure in the general population and possibly toxic blood levels in kids who were prescribed the drug. In a rural district of Tanzania, two years after the national malaria treatment policy changed and in anticipation of a future change to artemisinin-based combination therapy, the current study evaluates home management of febrile illness and the quality of malaria case management in children under five at health facilities (ACT). The MAMOP project, a controlled community malaria intervention with a pre-post design, aims to improve the management of pediatric malaria by bridging the gap between mothers and health care professionals. The MAMOP study's overarching goal was to assess the viability and efficacy of an intervention targeted at enhancing case management of malaria in children under the age of five through primary caregivers in cooperation with local women's groups and preexisting health centers [38].

Management of Febrile Illness

Causes of Febrile Illness

In a febrile illness, the hypothalamus raises body temperature in reaction to stress. Although fevers can have infectious or non-infectious etiologies, they are frequently brought on by an infectious disease. The severity of the sickness does not always correlate with the body's temperature. Fever-related infectious causes: Infections caused by bacteria include typhoid, which can be contracted through contaminated food or water, meningococcus, staphylococcus, and streptococcus (which causes strep throat) (meningitis of brain), virus infection - Common viruses include the measles, mumps, rubella, dengue fever, coronavirus, and influenza. Giardiasis (contaminated water), Lyme disease (tick bite), Malaria (mosquito bite), and Candida (yeast), Cryptococcus (meningitis), and Pneumocystis (fungal infection) are all examples of parasitic infections (pneumonia) Etiologies of acute febrile fever that are not infectious: Malignant cancer, autoimmune illness, heat exhaustion or heat stroke, malignant malignancy, Prescription drugs and vaccinations Finding the underlying cause of the fever is the first step in treating a febrile disease when it presents to a medical professional [39,40]. In low-resource tropical countries, fever is one of the most often reported symptoms by people seeking medical attention. It may occur alone or in conjunction with other widespread symptoms like cough or diarrhea; Prasad, Sharples, and others 2015. Health care professionals and healthcare systems face particular difficulties when treating fever without localizing symptoms because it can be brought on by a variety of bacterial, fungal, parasitic, viral, and bacterial infections as well as noninfectious conditions. Clinical evaluation is not always accurate in determining the probable etiology of a condition or in identifying patients who will eventually develop a serious or fatal illness. Adding to the shortcomings of clinical evaluation is the lack of epidemiologic information on prevalent causes of fever that is readily available as well as the paucity of clinical laboratory services in many places [41]. Malaria has long been the frequent default diagnosis for fever without localizing symptoms in the tropics due to its ubiquity and severity. In regions where malaria has historically been endemic, vertical strategies are used to manage and control fever. However, an increasing number of research on the causes of fever and a greater use of malaria diagnostic tests have helped to reveal the issue of overdiagnosis of malaria in patients who are febrile in many regions [42]. Since 2004 there have been documented decreases in malaria and Health care professionals are dealing with an increasing number of patients who have fever but a negative malaria diagnostic test as a result of the rise of nonmalarial illnesses like dengue and the widespread use of diagnostic testing for malaria. This increase is alarming since people who visit hospitals with fever that is not related to malaria are just as likely to pass away as those who do. Additionally, febrile infections other than malaria are rarely treated with vertical programs. One of the most difficult diagnoses in clinical medicine is that of individuals who present with an acute febrile illness [43]. Fever has long been mistakenly treated as malaria in Africa and other tropical areas. The improvement in the creation and usage of fast diagnostics for malaria but it resulted in unacceptable levels of assuming that patients with negative results from a quick test for malaria should take antibiotics. This unanticipated effect has major implications for antibiotic conservation for future generations since it increases antimicrobial resistance. Yukari C. Manabe and colleagues demonstrated in their article published in The Lancet Infectious Diseases that highly accurate multiplex molecular tests for identifying some of the causes of fever are now available outside of laboratory settings, requiring only 2-3 minutes of hands-on time and yielding results in under an hour. These multiplex molecular assays that can be run on-demand are yet another significant step towards resolving the conundrum of acute febrile illness differential diagnosis, and they have increased utility as a public health tool for investigations into outbreaks and surveillance. In low-resource settings in Asia and Africa, the diagnosis of acute undifferentiated febrile illnesses (AUFIs), which are frequently brought on by a variety of pathogens including Plasmodium species, dengue virus, Salmonella enterica serovar Typhi, Salmonella enterica serovar Paratyphi A, Orientia tsutsugamushi, Rickettsia typhi, Leptospira species, chikung Although clinically "undifferentiated," these organisms are distinct in terms of their clinical course and require accurate diagnosis for the right kind of care [44]. The diagnosis and treatment of malaria have greatly improved with the availability of high-quality rapid diagnostic tests (RDTs) at the point of care (POC). However, even in regions where malaria is widespread, nonmalarial infections account for a sizable portion of AUFIs. Organization for World Health Currently advises using malaria RDTs to diagnose fever; if negative, evaluation for other reasons is advised, however without any additional details. Patients who present with a fever are frequently empirically treated with antimalarial medications in malaria-endemic areas and with antibiotics in non-endemic areas, or frequently with both. Rapid test platforms have developed during the past few decades, resulting in commercially available RDTs for some of the causes of nonmalarial febrile diseases; nevertheless, the accuracy of these tests is subpar. Multiplex POC assays, which can simultaneously evaluate numerous antigens/antibodies for many diseases from a single sample, are currently being investigated. Despite their poor accuracy, the currently available commercial RDTs can help provide better patient care when used correctly. There is a need for protocols to direct the right use of solitary and multiplex RDTs given their growing availability and continued development. One of the most typical initial symptoms of pediatric diseases is fever. Children under the age of five who have fever are often experiencing systemic inflammation as a result of a viral, bacterial, parasitic, or, less frequently, a noninfectious cause. If local epidemiology is well understood, the ages of the patients and their geographical locations can aid in directing the proper diagnostic strategy and therapy [45]. For children aged one to 59 months, the combined proportion of mortality caused by AIDS, diarrheal illnesses, pertussis, tetanus, measles, meningitis/encephalitis, malaria, pneumonia, and sepsis was 58.5 percent in 2015; for newborns, it was 23.4 percent[46]. Variable evidence exists regarding the frequency of fever with a mean of 5.88 fever episodes per kid under the age of five per year and a weekly active case detection range of two to nine febrile episodes per child under the age of five per year[47]. An estimated 655.6 million fever episodes in children under five occurred in 42 Sub-Saharan African nations in 2007, according to national survey data. Of these episodes, 32% took place in 11 outpatient facilities in the Democratic Republic of the Congo, Ethiopia, and Nigeria[48]. Fever is unquestionably the most frequent pediatric presenting symptom at the level of the medical center and the community. The most widespread presenting symptoms at the facility and community levels are highlighted by a number of studies that are described in table 8.1. Prior to the development of accessible and reliable malaria rapid diagnostic tests (RDTs), the majority of healthcare professionals in malaria-endemic nations assumed that fevers were caused by malaria; in the early 1990s, the emphasis was to reduce malaria mortality by all means possible. Children in malaria-endemic areas who were suspected of having a severe illness and exhibited warning signs were advised to take injectable antimalarials and antibiotics, according to the World Health Organization's (WHO) initial Integrated Management of Childhood Illness (IMCI) guidelines from 1997. Prior to 2010, the initial WHO recommendations for treating malaria advised empiric, oral, antimalarial medication for fever with children under the age of five living in malaria-endemic areas, without other source (WHO 2006). The effectiveness of the presumed treatment of febrile illnesses has been called into question due to the decline in malaria incidence, increase in antimicrobial resistance, and accessibility of accurate, affordable point-of-care diagnostics. This has reopened the debate over the most precise and economical methods for fever diagnosis and treatment. In places where there is a high risk of malaria transmission and few diagnostic tests are available, presumptive therapy is the most feasible and economical option[49]. (D'Acremont, Lengeler, and Genton 2007; D'Acremont and others 2009; English and others 2009) In 2009, specialists argued over whether there was enough data to abandon presumptive treatment standards and shift to a focus on diagnosis before treatment. There is growing evidence that showed the national and international efforts to combat malaria. More than US$2.5 billion was invested in 2012 by international partners, including the Bill & Melinda Gates Foundation's Malaria Control and Evaluation Partnership in Africa, the World Bank Malaria Booster Program, the U.S. President's Malaria Initiative, and the Roll Back Malaria Partnership[50]. Malaria incidence is declining in countries with previously identified high-transmission zones, making the management of nonmalarial fevers crucial[51]. The WHO updated its recommendations for treating fever in 2010 and now only advises antimalarial medication for patients who have a positive malaria test result either a point-of-care or a microscopy outcome (WHO 2010a). Through the majority of Sub-Saharan African nations, this new strategy is being implemented in the public sector[52]. To better understand treatment decision-making in this setting, as well as how to prevent the overuse of antibiotics and guarantee adequate care, more research is required. However, many patients initially seek care in the informal private sector. Understanding the etiology of nonmalarial fevers in each context is the logical next step to improve pediatric clinical outcomes of other treatable serious febrile illnesses, such as pneumonia, sepsis, bacterial meningitis, enteric fever, rickettsioses, and influenza. The epidemiology of pediatric febrile illness is undoubtedly changing. Because antimicrobial drug resistance is widespread and growing throughout the world, caution must be used when using antibiotics only where appropriate, and to create thorough recommendations when resources are scarce. Current recommendations are based on clinical characteristics, which are regrettably not very reliable indicators of the illnesses that cause fever. To guide the most efficient use of antibiotics, low-cost, accurate point-of-care diagnostics are required to identify which children may benefit from antibacterial therapy [53].

Diagnostic Challenges

Clinical Diagnosis

In many resource-constrained situations, the clinical history and examination are the cornerstones of diagnosis, and clinical algorithms have been created for the diagnosis of febrile disease. In accordance with the then-current WHO standards, a study involving over 1100 kids discovered that a mother's report of fever in her child was 93% sensitive and 21% specific for the identification of malaria parasitemia on a blood smear. Clinical algorithms, on the other hand, typically lack precision and are unable to effectively differentiate between different fevers etiologies [54].

Culture-Based Methods

Although bacterial cultures are still the gold standard for diagnosis, they are sluggish and resource-intensive. Additionally, the fluid and volume collected, host characteristics like age and comorbidities, prior antibacterial agent use, and the stage of sickness all affect how sensitive they are. Blood cultures, for instance, are 40% to 80% sensitive for invasive Salmonella spp. detection and are much more sensitive during the first week of illness when the bacterial concentration is higher than it is during subsequent weeks. Similar to stool cultures, which have only around 40% sensitivity to the detection of Salmonella spp., bone marrow cultures have about 90% sensitivity and are relatively unaffected by antibiotics. Some bacteria, like Rickettsia and Leptospira species, need cell-based systems to survive or enriched culture media for cultivation are not typically used in diagnostic laboratories since they could pose risks to lab personnel. A significant part of febrile illnesses is caused by respiratory tract disorders, yet only a small percentage of individuals with community-acquired pneumonia have positive blood cultures [55].

Differential diagnosis

Protozoal infections

In some parts of East Africa, visceral leishmaniasis, which can induce fever, significantly increases morbidity, especially in HIV-positive individuals. Despite being endemic in some areas of Central and West Africa, human African trypanosomiasis (HAT) incidence is declining as a result of control measures aimed at eliminating the disease as a public health concern. It is unknown how common these illnesses are in febrile sickness in unselected people; however, this is likely to vary greatly by region [56].

Fungal Infections

Both HIV-infected and HIV-uninfected hospitalized patients continue to experience febrile illnesses from under-recognized fungi infections. Despite the increased availability of ART, the primary cause of death for HIV-positive individuals in Africa is still cryptococcal infection, which can cause meningitis and disseminated illness. While it is still most frequently diagnosed at first presentation with HIV, the epidemiology of cryptococcal disease is evolving. Presentation with cryptococcal disease is now more frequently linked to treatment failure, default from therapy, and immune reconstitution early in the course of ART. Despite the paucity of information, it is likely that histoplasmosis is widespread throughout Africa and frequently misdiagnosed as tuberculosis [57].

Implications for diagnosis and treatment

Correct antibiotic medication and suitable supportive care are required for the management of individuals who come with fever. The results of malaria and HIV RDTs, the local epidemiology of fever and AMR, the patient's HIV status, and these data should all be considered when making empiric treatment decisions. Due to silent parasitaemia, even in the presence of positive malaria RDT, non-malaria etiology must be taken into account in countries with a high frequency of malaria parasitaemia. Management difficulties for ambulant patients in the outpatient setting are distinct from those faced by patients with severe febrile illness who are hospitalized because of pronounced disparities in disease severity and etiology.

Management of patients in first level health facilities

Guidelines for the Integrated Management of Childhood Illness (IMCI) and the Integrated Management of Adolescent and Adult Illness (IMAI) have been proposed by the World Health Organization (WHO) (IMAI). This advice helps management decide who needs anti-microbial medications, who needs supportive care, and who should be referred to a higher-level medical facility. In order to maintain the safety and efficacy of the guidelines, updates that reflect epidemiologic and management advancements are required. The use of malaria RDTs has resulted in more prudent antimalarial drug use in regions where the disease is endemic, but unexpectedly excessive antibacterial medicine prescribing. Finding individuals from whom antibacterial medications can be safely withheld presents a challenge in the management of ambulatory patients due to the high occurrence of self-limiting viral illnesses at first level healthcare institutions. research initiatives to Investigating the improvement of clinical severity criteria and utilizing biomarkers to identify severe bacterial disease are two ways to prevent over-prescription. A supplementary review in this issue describes studies that deal with biomarkers. Healthcare professionals are guided in managing feverish patients by an understanding of the local epidemiology of fever etiology and the use of diagnostic tools like malaria and HIV fast diagnostic tests. Clinicians currently face issues determining which of their hospitalized patients have infections that are resistant to empiric antibacterial regimens as well as determining which of their ambulatory patients need antibacterial medications[58].

Differential diagnosis of acute febrile illness

Numerous different infections have the potential to result in acute fever. The term "non-specific fever" or "fever of unknown origin" is used when one of them is accompanied by localized symptoms, such as respiratory tract, urinary tract, or gastrointestinal illnesses, while the other is not. Tropical regions are prone to these latter illnesses. Plasmodium spp. is a primary cause (etiology) of non-specific fever and was implicated in 219 million new cases and 435,000 deaths reported globally in 2017—the vast majority of which (90 percent) were reported in the Sub-Saharan African region[59]. Despite intense efforts and remarkable progress toward its eradication. Recent investigations examined the causes of fever and discovered a Numerous vague, non-malaria febrile illnesses are found. Therefore, due to the frequency of co-infections (such as salmonellosis and malaria), a lack of precise, specific, and sensitive equipment, and inadequately qualified workers, accurate diagnosis becomes difficult in this complex epidemiological landscape. Given that numerous bacteria can cause febrile sickness infections, varied patient therapy is necessary in this setting. Plasmodium, Salmonella, Rickettsia, and Leptospira are a few examples of pathogens (dengue, chikungunya or Zika virus). Inadequate treatment can therefore result in a significant risk of mortality, continuing disease transmission, and increased antimicrobial resistance. These factors all contribute to the misinterpretation of non-specific fever and the use of only empirical diagnoses. For the identification of illnesses associated with fever, a number of cutting-edge techniques, such as a microscope inspection of stained thick blood film. Lateral Flow Tests (LFTs), thick and thin blood smears, and tests for both malaria and non-malaria disorders. The former, however, might be prone to mistakes because it depends on the staff's level of expertise to visually identify the parasite when using the microscope. The latter, despite being less expensive and simpler to operate, also relies on the user's subjective judgment during the visual readout, particularly when the test line of the LFT is difficult to detect. Studies have also demonstrated that both approaches may not be sensitive enough. Both bacterial and viral cultures are employed, however they both require complex laboratory equipment, trained personnel, and are labor-intensive, time-consuming, and difficult to carry out [60,61,62]. Using nucleic acid amplification technology, precise species identification can be made easier. The majority of them provide varying degrees of multiplexity, time-to-result, and integration, as reviewed by Mitsakakis/D'Acremont et al., but do not typically cover the malaria/non-malaria distinction. These methods are generally more specific, suitable for a wide range of diseases, and have been integrated in some point-of-care (POC) or near-patient systems already on the market or in near-commercialization phase, such as the GeneX[63]. It is thought that a clinical case of malaria, which is brought on by parasites of the genus Plasmodium, is a serious medical ailment with the potential to be life-threatening. This is particularly pertinent to low-income nations in tropical and subtropical areas of the world where significant rates of morbidity and mortality associated with malaria are documented. Rapid and accurate diagnosis continues to be the first line of defense in the fight against this serious worldwide public health threat in order to launch a prompt and effective medical intervention. Rapid diagnostic tests, or RDTs, are the most user-friendly and economical of all the methods used to detect parasites. But some of this methodology's drawbacks might make it difficult to treat patients effectively. The fact that only one of the five species of human malaria, P. falciparum, is detected by the great majority of commercially available RDTs is a severe problem. Despite being the primary cause of infection in many regions, this rule outs infections with other parasites (such as P. vivax, P. ovale, P. malariae, and P. knowlesi) or infections involving multiple parasite species the identification of Malaria other than P. falciparum is overlooked. In consequence, an incorrect diagnosis of a bacterial illness based solely on signs and symptoms frequently leads to an erroneous prescription of antibiotics in resource-constrained situations where good microscopy is not accessible. Here, we describe how the development of novel multiplexing RDTs that detect two or more species of Plasmodium may address both the effective diagnosis of malaria and the indiscriminate use of antibiotics in sub-Saharan Africa, a hotspot for P. falciparum transmission [64]. An elevated body temperature is referred to as a fever. It is the most typical symptom people seeking medical attention present with in hospitals. There are numerous causes of fever, but infection (viral, bacterial, fungal, or protozoan) is the one that causes it the most frequently, with malaria being the most frequently blamed in tropical nations, such as Nigeria. This is because malaria is endemic in these areas, yet endemicity does not necessarily mean that a person would get malaria. In these areas, fever cases are routinely over diagnosed with malaria while other fever etiologies go unrecognized and uninvestigated, leading to poor patient outcomes as well as additional public health problems such antimalarial resistance and improper patient care. Other infectious conditions other than malaria that are frequently mistaken as malaria include bacterial sepsis, arbovirus infection, pediatric otitis media, and so on. According to studies, many febrile patients are misdiagnosed as having malaria and treated with antimalarial medications they don't require. Lack of knowledge or bias, a lack of fever management guidelines, and other factors all contributed to this misdiagnosis. Misdiagnosis has a number of negative effects, such as patient suffering for an extended period of time, increased chance of mortality, and the possibility of an epidemic breaking out. The solution entails recognizing that not all cases of fever are caused by malaria, putting fever management policies into place, conducting research to identify other causes of fever in Nigeria besides malaria, testing for these other causes of fever alongside malaria, and using better diagnostic tools for fever diagnosis[65].

2.2 Theoretical Review

A paradigm-shift in the treatment of febrile illnesses in areas where malaria is widespread has been ushered in by the development of rapid diagnostic tests (RDTs) based on the malaria antigen. Historically, presumptive antimalarial therapy was common policy and practice, with malaria being assumed to be the primary cause of fever. In 2010, the World Health Organization (WHO) changed the advice for treating acute fever case management for all populations and endemic regions from presumptive antimalarial medication to parasite-based diagnosis. Although there are still issues with the adoption of malaria RDTs, it is now simpler to exclude malaria from the differential diagnosis thanks to the accessibility of relatively straightforward, trustworthy, and affordable point-of-care tests. The "test before treat" strategy has shown that overestimating the frequency of malaria was caused by the incorrect classification of many febrile illnesses in the past. Since the clinical manifestations of febrile episodes are frequently vague, a complete diagnosis necessitates a variety of laboratory tests, many of which are not readily available at the point of care. Where tests are used, a sizable portion of feverish patients go undetected. Wide geographic swaths in many African nations lack information on the etiologies of febrile diseases because diagnostic resources are scarce, surveillance networks are frequently concentrated around research institutes, and there are few diagnostic facilities available. Health care professionals frequently turn to prescribing empiric antimicrobial therapy in the lack of trustworthy evidence, thereby fostering the formation and spread of antibiotic resistance (AMR). Due to the recent influx of studies documenting the etiologies of non-malarial febrile disorders, improving fever case management has become a top global health goal (NMFI) in nations with low and medium incomes. When there are no good diagnoses available, understanding the distribution of pathogens might help doctors prescribe antibiotics empirically and wisely. Information on the distribution of pathogens in various African regions is still scarce. Furthermore, it is challenging to examine dispersion across time and location because there is currently no agreement on how to report NMFI etiology data. An online, open-access, interactive map was created using the findings of a systematic evaluation of published research from 1980 to 2015 in order to start filling in this knowledge gap. One of the most frequent causes of pediatric hospital admissions is febrile illness, and treating it can sometimes be difficult. Most feverish kids will have self-limiting infections that can be safely handled at home, frequently without the use of antibiotics. However, a small percentage of children will have potentially serious illnesses, and differentiating these kids from the others can be challenging because children's clinical symptoms and indications are sometimes ambiguous. As a result, patients can be given unnecessary antibiotic prescriptions, put through invasive procedures, and admitted for observation while awaiting microbiological findings. In addition to the distress, expense, and difficulty that this may cause children and parents directly, there may be indirect effects on the development of antibiotic resistance [64]. Rapid point-of-care testing (POCTs) are encouraged by the WHO as a way to decrease the need for antibiotics.

POCTs have the potential to increase the use of clinical decision-making, reduce the usage of other invasive tests, and general medical resources However, attaining these outcomes depends on a number of variables, including the uptake of POCTs by healthcare professionals and how they affect clinical judgments. This cannot be expected, for instance, as many doctors continued to administer antimalarial medications even after the introduction of malaria POCTs and patients tested negative. Urine dipsticks, rapid tests for Group A Streptococcal throat infections (rapid strep test), rapid respiratory virus tests for respiratory syncytial virus (RSV) or influenza, and blood-based tests like C reactive protein (CRP) and blood gas analyzers are examples of POCTs that are currently available for the management of childhood infections. General practitioners (GPs) treating patients with infections have received the majority of attention in studies investigating physicians' perspectives on the use of POCTs for managing patients with infections. To the best of our knowledge, there is only one study that addresses hospital-based healthcare professionals' opinions on the use of POCTs in children [65].

Management of Febrile Illness

99 percent of the 5.2 million worldwide deaths of children under the age of five occurred in low- and middle-income (LMIC) nations in 2019. Despite significant declines, infectious diseases like malaria, diarrhoea, and pneumonia still have a big impact on child mortality. By halting the progression of mild illness into severe illness and death, early and effective treatment can significantly lower infectious cause-related mortality. Thus, meeting the Sustainable Development Goal 3.2 aim of lowering under-five mortality to 25 per 1,000 live births depends critically on prompt and adequate treatment seeking. The severity of an illness effects how people seek medical care reciprocally. The scientific literature now in circulation

has a number of reviews of pediatric sickness therapy that use the severity of the illness as a criterion for care such as pneumonia, diarrhea, and/or malaria. On the other hand, etiology research has recommended a syndromic approach for study on severe febrile illness because to the clinical overlap of malaria with pneumonia and other infectious diseases as well as the high case fatality ratio among admitted patients with febrile illness (SFI). Due to the fact that caregivers identify and categorize their child's condition based on observed signs and symptoms, this technique is especially pertinent to studies on treatment seeking. From a syndromic viewpoint, a synthesis of the information on treatment seeking for SFI in children can offer important insights into the mechanisms linking illness presentation, care seeking, and health outcomes. Understanding the validity and comparability of the available evidence will be facilitated by an analysis of the underlying methodological approaches used in such investigations. Numerous researches have made reference to the idea of SFI. SFI is defined differently in the scientific literature, despite the fact that Roddy et al. call it "a commonly documented and globally known cause of morbidity and mortality." Integrated Management of Childhood Illness (IMCI) standards describe SFI as fever with danger signals, but some writers have emphasized on clinical diagnosis or causal agents. The significance of perceived severity for health-related behavior, such as seeking treatment, has also been highlighted by health behavior theories. Due to the vagueness of SFI definitions in the scientific literature currently available and the significance of severity for treatment seeking and health outcomes in children under the age of five, fever in neonates and babies 3 months of age is defined as a temperature measured directly was 38°C. These patients frequently enter the emergency room and outpatient clinics for fever-related reasons, many of whom have no diagnostically significant signs and symptoms and are given the diagnosis of fever without a source (FWS) following initial clinical evaluation. For many years, these newborns have been split into two categories. Patients in the second group, which makes up 5 percent to 15 percent of cases, have fevers brought on by serious bacterial infections (SBI), such as pneumonia, urinary tract infections (UTI), soft tissue and bone infections, or severe, exceptionally invasive bacterial infections. The first group of patients includes those with mild, clinically inconsequential viral infections. Despite being challenging, identifying newborns and early babies at risk of SBI from persons who do not have substantial clinical difficulties is thought to be essential. SBI patients must be identified and treated quickly in order to ensure positive illness outcomes. Additionally, choosing individuals with low risks of SBI might make it possible to avoid pointless antibiotic treatments, hospital stays, and intrusive laboratory procedures. Several algorithms based on analytical and clinical indicators have been devised to help differentiate between newborns at low and high risk. While these algorithms were relatively similar in certain steps, they varied in the way they used certain diagnostic techniques, which led to a spirited discussion among the authors. In many children's hospitals in the USA, they were not consistently implemented in clinical practice and were frequently replaced by handmade standards. The discussion of the Evidence of steadily changing epidemiology, aetiology, and characteristics of SBIs over the past 15 years has further encouraged the development of the optimum treatment strategy for infants with FWS. Additionally, when additional biomarkers have become accessible over time, their incorporation into the algorithms was believed to have the potential to dramatically increase their diagnostic efficacy. This study's major goals are to outline the traditional treatment for young infants with FWS and to talk about how new information on the subject is affecting clinical practice [66]. Over four decades have passed since attempts were made to create an evidence-based strategy for the assessment and treatment of early febrile infants. Concerns concerning the onset and quick spread of group B strep (GBS) infection in newborns, whose clinical manifestation and Evidence of steadily changing epidemiology, aetiology, and characteristics of SBIs over the past 15 years has further encouraged the development of the optimum treatment strategy for infants with FWS. Additionally, when additional biomarkers have become accessible over time, their incorporation into the algorithms was believed to have the potential to dramatically increase their diagnostic efficacy. This study's major goals are to outline the traditional treatment for young infants with FWS and to talk about how new information on the subject is affecting clinical practice. Over four decades have passed since attempts were made to create an evidence-based strategy for the assessment and treatment of early febrile infants. Concerns concerning the onset and quick spread of group B strep (GBS) infection in newborns, whose clinical manifestation and cellulitis. Others included bacterial gastroenteritis in children who had diarrhea, as well as pneumonia, which can be viral or bacterial. All of these included bacterial meningitis, bacteremia, and urinary tract infections (UTI), but because UTI is so much more prevalent than the other diseases, it throws off models that try to pinpoint all possible causes. These prediction models used clinical and laboratory test factors that weren't derived from the original data but instead were based on a priori criteria. Each variable was created arbitrarily, without any genuine physiologic or biological foundation, using terms like age groupings in weeks or months and integers that end in zero. As an illustration, the variable that indicated whether a white blood cell (WBC) count was abnormal was 5000 per mm3 or >15 000 per mm3 was established beforehand as an indication and evaluated in combination with other predictor variables; it was not statistically derived. Clinical appearance, age, urinalysis, WBC count (and/or absolute neutrophil count [ANC], band count, and/or immature to total neutrophil ratio), and cerebrospinal fluid (CSF) analysis were the main factors used to make recommendations (except for the Rochester criteria, which did not require CSF). The sensitivity, specificity, and predictive values of all were somewhat similar. The models were released because to their strong negative predictive values (NPVs) (97 percent to 99 percent) and fairly high sensitivity (90 to 95 percent). The rare occurrence of the most severe infections, together with modest specificities (20 percent to 40 percent), also explained the relatively low positive predictive values and contributed to the high NPVs.Midway through the 1980s, Powell et al. in Rochester made a significant change when they realized that it was impossible to anticipate who would be at high risk and instead tried to determine who would be at low risk, even in the first month of life. It became clear that infants under 29 days of age should all receive thorough assessments, hospitalization, and empirical antimicrobial treatment, while infants between 29 and 90 days of age could be managed with presumptive intramuscular ceftriaxone as outpatients while waiting for the results of blood, urine, and CSF cultures [67]. Over time, other teams employed strategies to create clinical prediction rules that depend on obtained information to determine and define the best, most accurate and sparse set of factors that predict a predetermined result that can be converted into advice. The progressive application of predetermined clinical and laboratory criteria was yet another strategy. Despite these significant efforts, there is persistent evidence that emergency and community physicians do not always adhere to these recommendations in practical contexts. It has not been demonstrated that worse clinical results result from disregarding current standards of care. Different methods for treating very young febrile children have shown the need for a current, evidence-based guideline that was created by a national professional association or organization with wide representation. Due of this, the American Academy of Pediatrics (AAP) decided to create this recommendation with the aid of an evidence review that the Agency for Healthcare Research and Quality had commissioned (AHRQ).

Bacteriology is evolving

Numerous variables, such as prenatal GBS screening and the addition of vaccination against Streptococcus pneumoniae, have contributed to changes in the incidence of bacterial illnesses in newborns and infants during the 1980s. Additionally, advancements in food safety might have reduced the frequency of Listeria monocytogenes-related illness in this age range. Escherichia coli is currently the most frequent bacteria to cause bacteremia, according to recent research, whereas GBS continues to be the most frequent cause of meningitis in most studies. L monocytogenes infections are now uncommon in the US. The choice of tests, how values are interpreted for decision-making, and the choice of antimicrobial medications are all affected by the transition from Gram-positive to Gram-negative dominance. Making use of the decision models between 23.3 and 32.1 percent of instances of bacterial meningitis nowadays can result in incorrect diagnosis[68].

Advances in Testing

Inflammatory Markers

Earlier clinical prediction models were built on the WBC, ANC, and band count in addition to the clinical exam and urine. These markers are no longer as helpful because E coli has supplanted GBS as the most prevalent bacterial infection in this age range. Point-of-care testing for C-reactive protein (CRP), an inflammatory marker (IM) produced by the liver in response to infections and many other diseases, is now accessible. Procalcitonin is produced quickly in response to infection and other tissue damage, and it is mostly expressed by thyroid C cells. Compared to other IMs, it is more specific for bacterial infections and increases to abnormal values more quickly. Although it's not currently accessible at many locations in the United States, procalcitonin has emerged as the most reliable IM for risk classification available[69].

Pathogen Identification

Improvements have made it possible to identify bacterial, viral, and fungal pathogens more quickly and precisely as well as to screen for invasive infections more accurately. Most bacterial infections can now be identified within 24 hours using automated blood culture methods. Most recently, bacterial infections and antibiotic resistance genes can be found in about an hour using nested multiplex polymerase chain reaction (PCR) testing of positive blood cultures. Similar to this, data on CSF for 14 possible CSF pathogens can be obtained in 1 hour with multiplex meningoencephalitis panels.

Viral Testing

Emerging agents, including the par echovirus, have been identified thanks to the development of rapid viral PCR and multiplex respiratory viral testing. These discoveries spurred investigations of their impact on risk categorization of young febrile infants. Although the incidence of IBIs in febrile babies is reduced by the presence of known respiratory viral infections (see Inclusion Criteria 5, Positive viral test), it is still not apparent how subsequent laboratory evaluation and care should be affected, particularly in the first month of life. A viral test result that is positive also raises the question of whether or not hospitalization will be avoided or cut short. Researchers found no difference in duration of stay between febrile children with and without multiplex viral testing in research that examined data from 2000 to 2012 before its widespread availability. Future Research lists this as an important subject that needs more investigation[70].

Emerging Technologies

The field of genomic diagnostics for IBIs, which encompasses both the genomic detection of viral and bacterial genetic material as well as the discovery of host genomic responses to viral or bacterial infections, is still in its relative infancy. Both require more research to determine how these technologies stack up against customary diagnostic methods in terms of timing and accuracy. However, RNA transcriptional profiling and next-generation sequencing of microbial cell-free DNA are making progress[71].

Changing Research Methods

Although the majority of the early studies came from single-site inner-city emergency departments (EDs), more recent studies carried out by sizable, geographically extensive research networks and integrated regional health care systems have produced more generalizable findings. Comparative gains are provided by improvements in data analysis and storage, as well as the use of statistical techniques for creating clinical prediction criteria. Larger and more precise data sets are being produced through collaborative efforts between primary care offices, EDs, hospitals, and integrated health systems. The committee believes that customized treatment, made possible by these enormous data sets and developing modeling approaches capable of studying children on dozens of characteristics, will lead to the concept of "one child, one recommendation" in the future. For today's doctors, this recommendation, which is based on constantly developing data and takes advantage of emerging technologies, should serve as the cornerstone for developing an effective plan for assessing and treating each febrile newborn. The committee recommends using the three age-based algorithms as a starting point for choosing the optimum strategy. Approaches may vary slightly depending on a number of perinatal or neonatal factors among other things, the expertise of the clinician, the skills and values of the parents, the relationship the clinician has with the infant's family, the features of the clinical facility, and the capacity to get lab results quickly. Withholding antibiotics and patient follow-up in the setting of difficult-to-reach populations is frequently unrealistic because the majority of febrile illnesses in the community are probably brought on by self-limiting viral infections. Given the overlapping non-specific symptoms for treatable and non-treatable febrile infections, clinical algorithms for the identification of individuals needing antimicrobials have little promise. Given the high incidences of leptospirosis and scrub typhus in fever studies conducted in Laos and Cambodia, as well as the fact that almost none of the patients from whom the samples were taken had been prescribed doxycycline, it is clear that antimicrobials are not being prescribed to the right patients. According to estimates, 13 percent, 12 percent, 8 percent, and 2 percent of patients in rural Laos would have experienced significant benefits from azithromycin, doxycycline, ceftriaxone, and ofloxacin, respectively. It was recommended that individuals with "undifferentiated" fever and negative results from fast diagnostic testing for malaria and dengue should get empirical doxycycline treatment[72]. The management of fever may be improved with the introduction of new pathogen-specific point-of-care tests (POCTs) for common infections like dengue or scrub typhus, but their value and cost-effectiveness will differ greatly regionally, seasonally, and in response to longer-term epidemiological trends like climate change. Most patients will go undetected, even in places where POCT target infections are reasonably common. In fact, even studies with ample funding can only, at best, discover an etiological factor in 50% of patients. The detection of infections in the majority of patients in the context of normal care is still an unattainable goal, despite the fact that they offer helpful insights into prevalent causes of fever at the population level, potentially improving empirical treatment guidelines. Utilizing host indicators of bacterial infection is one method for improving fever control. The use of C-reactive protein (CRP) in febrile patients in South-East Asia is becoming more and more clear as a reliable biomarker for the management of respiratory illnesses. A major advantage of bacterial infection biomarkers over pathogen-specific testing is their applicability throughout the gamut of bacterial pathogens, giving medical professionals consistently helpful information in the face of geographical and seasonal variation in disease etiology. Their drawback is that while they can assist in identifying which individuals need antibiotics, they are unable to independently establish which antibiotic is required. Geographical variation in the deteriorating AMR situation and a lack of AMR data from numerous judgments on empirical therapy are greatly complicated, especially for ESBL bacteria. In order to supplement their utilization, current empirical guidelines built on aetiological and AMR data are still needed. It is necessary to continue the pioneering work on integrated algorithms started in Africa. However, there hasn't been much research done on how algorithms should change depending on the region. White et al. indicated that with even only slight spatial variation, spatially explicit treatment algorithms may result in a significant improvement in the outcome of fevers by modeling spatial heterogeneity in therapy across the vast north-south range of Laos. It is highly challenging to establish fever treatment standards throughout Asia due to data gaps; where local knowledge is present, it is crucial. HIV-positive, diabetic, pregnant, and pediatric patients are high-risk febrile categories with a higher likelihood of morbidity and fatality. The evidence base is weak due to issues with conducting clinical research in the latter two groups, yet understanding is critically needed. The causes of pregnant fevers and their effects on Asia's high rates of maternal and neonatal death are topics of growing study. The fact that dengue infection is linked to higher rates of fetal mortality in Brazil has important ramifications for dengue endemic regions throughout South and South-East Asia. Similar to this, the rising incidence of diabetes mellitus in Asia has significant implications for a variety of fevers, including tuberculosis, infection with Burkholderiapseudomallei, and likely bacterial meningitis. Interventions in public health to lower the prevalence of diabetes and enhance diabetes management are likely to have significant advantages for the management of infectious illnesses. Key pathogen vaccinations continue to be essential and cost-effective interventions. A large impact on lowering the incidence of individuals presenting with JEV fever without central nervous system disease, for instance, is predicted to result from vaccination against JEV, which is motivated by its significance as a cause of disease of the central nervous system[73].

2.3 Review of Empirical Studies

Febrile Illness among Nigerian Nomads

The formal health system appears to be poorly suited to providing services to nomadic populations that are continuously on the move, and local authorities frequently ignore the presence of nomads when it comes to the provision of health care. For instance, guinea worm case detection scouts in Southwestern Nigeria "failed" to include trips to nomad camps and ivermectin distribution in the fight against onchocerciasis frequently neglected nomadic Fulani villages. Nomadic camps, which are situated on the outskirts of populated places, are frequently disregarded to the point where, in some regions, fewer than 3% of children under the age of two may benefit from full immunization services. Nomads are excluded from ongoing malaria management initiatives while being disproportionately more susceptible to infectious diseases like malaria. Malaria is to blame for up to 20% of maternal mortality in sub-Saharan health facilities, making up more than 10% of the continent's overall illness burden. Malaria continues to be the leading cause of pediatric morbidity and mortality in Nigeria. Malaria accounted for 63.4 percent of all diseases recorded in 2000, with 50% of the population experiencing at least one episode, which resulted in between 30 and 50% of inpatient admissions and 50% of outpatient visits to medical institutions. The headman, his wives, children, and dependents make up the traditional Fulani family. A wuro (camp) is formed when about 15 households congregate in one place, and there are many wuro comprise a gure. In their quest for health, Nomadic Fulani are widely known for their reliance on herbal remedies and private medical facilities. Even though the government is currently working to reduce the disease burden by distributing and promoting the use of insecticide-treated nets (ITNs), straightforward diagnostic tools, behavior change communication, appropriate chemotherapy, intermittent preventive treatment, and community management of febrile illnesses, the nomads still have difficulty accessing these services. Given that the idea of illness is influenced by cultural identity, one of the key health challenges in Africa is how beliefs about health and illness are used in the administration of healthcare. The way the Fulani accept illness, for instance, illustrates how they vary from other communities in this regard. Being Fulani requires tenacity and resilience, character, self-control, and showing others how to behave. Integration with the malaria control program is hampered by the lack of understanding of their cultural experiences with malaria. But even when the disease eventually declines to a level below public health importance among settled people, if the issue is not addressed, nomads will continue to represent an epidemiologically significant group. Prior to the creation of a suitable intervention program, a study on the malaria disease experiences of nomadic Fulani populations that camp in the valleys of rivers Benue and Gongola of Northeastern Nigeria during the dry season was conducted [74,75].

The epidemiology of febrile illness in Africa

In developed nations where vaccination campaigns against Streptococcus pneumoniae and Haemophilus influenzae type b have seen widespread adoption and significant drops in invasive illness rare cases of systemic bacterial infection[76]. In these areas, localized bacterial illnesses including pneumonia and urinary tract infections are the most common bacterial causes of fevers in children; nevertheless, viruses account for up to 76 percent of fevers without obvious cause [77,78,79,80]. There is little information on the burden of invasive bacterial disease in LMICs, where introduction of the H influenzae type b and pneumococcal vaccines is ongoing but not yet ubiquitous in most regions and where typhoidal and non-typhoidal Salmonella remain significant sources of disease. caused by children's febrile illnesses. Instead of widely evaluating the causes of febrile disease in their population, researchers frequently focus on certain syndromes, like pneumonia [74], or specific infections, like malaria. We searched the literature going back to the 1970s for studies that involved or had a pediatric group as their primary subject and investigated the etiologies of acute febrile illness in both inpatient and outpatient settings, as well as any related clinical disorders. Using the search phrases "acute febrile sickness," "undifferentiated fever," "low- and middle-income nations," and "developing countries," as well as the names of continents and regions, we were able to locate relevant publications in PubMed/Medline (e.g., South Asia). By looking through bibliographies and the Worldwide Antimalarial Resistance Network, further studies were found [75]. We only considered prospective studies where acute febrile illness was a primary enrolment criterion or, in the case of sero-epidemiology research, a primary justification for blood culturing in order to determine the percentage of patients with febrile illness who had an identified pathogen. We searched for patients of different ages, but we concentrated on research involving children under the age of 18. Studies that focused on certain risk populations, those that utilized arbitrary or ill-defined inclusion criteria, and those with discrepancies in the methodology or the data were all disregarded. With the use of predefined data fields, data were extracted from the articles [81].

	Study population	Study size	Testing	Main diagnoses	Comment and limitations
D'Acremont, Tanzania, 2006 [38]	Paediatric Outpatient District Hospital HIV prevalence: not stated	1005	Blood culture, respiratory virus and arboviral nucleic acid amplification testing (NAAT); arboviral serology; *Leptospira, Coxiella*, and *Toxoplasma* serology	Viral aetiology in 78% of systemic infections, 100% of nasopharyngeal infections, and 51% of lower respiratory infections Overall: 9% malaria, 4.2% bacteraemia	Challenging to determine causation due to high prevalence (76.9%) of co-infection and lack of healthy controls.
Crump, Tanzania, 2007–08 [39]	Paediatric/ adult Referral hospitals Inpatient HIV prevalence <13 years 12.2% ≥13 years : 39.0%	870	Antigen detection for *Cryptococcus, Histoplasma capsulatum, Legionella pneumophila, Streptococcus pneumoniae;* blood culture (aerobic and mycobacterial); NAAT for arboviruses; serology for *Brucella, Leptospira, Coxiella*, and *Rickettsia;* thick and thin blood film for parasites	<13 years: chikungunya 10.2%, leptospirosis 7.7%, 7.4% spotted fever group rickettsiosis (SFGR), 3.4% bacteraemia, 2.6% Q fever, 2.0% brucellosis, 1.3% malaria, 0.9% fungaemia, ≥13 years: 17.1% bacteraemia, 10.1% leptospirosis, 8.7% SFGR, 7.9% Q fever, 5.3% brucellosis, 5.7% chikungunya, 5.2% fungaemia, 3.5% mycobacteraemia, 2% malaria	Large proportion of patients (64.0% aged <13 years, and 33.2% ≥ 13 years without a aetiologic diagnosis. Respiratory viruses not sought.
Baba, Nigeria,	Adult Referral	310	Serology for chikungunya, dengue,	67% dengue, 50.2%	The high prevalence

	Study population	Study size	Testing	Main diagnoses	Comment and limitations
2006 [40]	hospital Hospitalisation and HIV status not reported		typhoid, West Nile virus (WNV), yellow fever; thick and thin film for malaria	chikungunya, 32.6% typhoid, 29.4% malaria, 24.9% WNV,	of co-infection of mlalaria, serologically diagnosed typhoid, and arboviral infections highlights challenges of making diagnoses through non-reference standard tests
Jacob, Uganda, 2008-09 [41]	Adult Referral hospital Inpatients with severe sepsis HIV prevalence 100%	368	Antigen detection of *Cryptococcus*, blood culture (aerobic and mycobacterial); serology for HIV; thick and thin blood film for malaria,	23.4% *Mycobacterium tuberculosis*, 11% bacteraemia, 4% non-tuberculous mycobacteria, 2% *Cryptococcus neoformans*	Highly selected population, with limmited breadth of pathogens investigate
Chipwaza, Tanzania 2013 [42]	District hospital Outpatient/ Inpatient HIV prevalence not stated	370	NAAT for influenza and dengue; serology for brucellosis, chikungunya, dengue, leptospirosis, typhoid; thick and thin blood films for malaria; urine microscopy for	<5 years: 31.3% dengue, 22.9% malaria, leptospirosis 19.5%, brucellosis 13.2%, typhoid 6.8%, 5.4% chikungunya, 1% influenza	High prevalence of co-infection of serologically diagnosed typhoid

	Study population	Stud y size	Testing	Main diagnoses	Comment and limitation s
			bacteria	≥5 years: 81.1% dengue, 49.7% brucellosis, 31% leptospirosis, 22.6% malaria, typhoid 14.4%, 4.1 influenza	and zoonotic infections highlights the challenges o determinin g causation when non-reference standard tests are used
O'Meara, Maine Kenya, 2011-12 [43]	Paediatric District hospital Outpatient HIV prevalence 0.4%	370	Antigen detection for group A *Streptococcus*, NAAT for adenovirus, influenza A and B, human metapneumovirus, parainfluenza virus 1-3, malaria, respiratory syncitial virus (RSV); serology for *Rickettsia, Coxiella*; thick and think films for parasites	22.4% SFGR, ' 20.3% influenza A/B, 10.5% adenovirus, 10.1% parainfluenza virus 1-3, 8.9% Q fever, 5.3% RSV 5.2% malaria 5.2%, 3.6% scrub typhus, hMNV 3.2%, group A *Streptococcus* 2. 3%, 1.0% typhus group *Rickettsia*	Study notable for inclusion of healthy controls, in whom ≥1 pathgen was detected in 49.1%. Limitation s include a limited selection of pathogens sought.

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Few studies have examined the various possible causes of fever, and for many participants, the causative organism or co-infecting microbes have not been discovered. This makes it difficult to determine the exact source of the fever. Self-limiting arboviral infections and viral upper respiratory infections are widespread among ambulatory patients, affecting up to 60% of children who visit health facilities. There is a high occurrence of potentially lethal illnesses among hospitalized patients that call for specialized care. Major causes of fever include bacterial zoonoses and bloodstream infections [82]. Antibiotic resistance has become more common among bacterial isolates in recent years, particularly with the emergence of Salmonella enterica and extended spectrum -lactamase-producing Enterobacteriaceae. Up to 34. 8 percent of individuals with sepsis who had human immunodeficiency virus (HIV) infection have Mycobacterium tuberculosis bacteremia confirmed, and fungi-related illnesses like histoplasmosis and cryptococcosis continue to be significant. 2.4 Mapping febrile illness the COVID-19 pandemic has brought to light the infectious illnesses' profound influence on the world's 7.8 billion inhabitants. As we do today, our ancient ancestors understood the devastation that epidemic fevers caused and the immense impact they had on their lives. However, endemic infectious diseases would have probably had a bigger influence on people's daily life before urbanization. Except for those that have attracted public, research, and policy attention, such as TB, HIV, malaria, and dengue, endemic infectious illnesses have generally been neglected. Chikungunya, Ebola, and Zika epidemics have made headlines in the past ten years, but they were frequently seen as local tropical problems. Diseases that are endemic can develop into pandemic diseases [83]. In order to prioritize interventions and funding, as well as to inform preventative and public engagement programs, treatment guidelines for both specific pathogens and syndromic empirical treatment, we need to know where infectious illnesses are prevalent [84]. Without such knowledge of public health, we will be waiting for the next catastrophe in the dark. Malaria has been overestimated as a cause of fever, despite still being a focally important cause in many areas [85]. This has been proven by the widespread implementation of affordable and accurate malaria rapid diagnostic tests (RDTs), usable by health workers in rural malarious areas with little training. In most endemic areas, the incidence of malaria has decreased. Consequently, there is a critical requirement to comprehend fever epidemiology [86]. Many policy and operational decisions are based on the epidemiology of fevers other than malaria. The three papers in this series, which were derived from the work of Ancestor, describe systemic reviews of what is known about the locations of various non-malarial fevers in south and Southeast Asia, Africa, and Latin America. A fourth paper in this series, describing the data from China, is awaited[87]. A total of 69,104 records from 101 countries, published between 1980 and 2015, were reviewed, including 29,558 from Asia, 16,523 from Africa, and 23,023 from Latin America (19 in Asia, 48 in Africa, 34 in Latin America). 4099 of them (2409 in Asia, 1065 in Africa, and 624 in Latin America) satisfied the selection requirements[88.89,90].

Causes of Febrile Illness

In a febrile illness, the hypothalamus raises body temperature in reaction to stress. Although fevers can have infectious or non-infectious etiologies, they are frequently brought on by an infectious disease. The severity of the sickness does not always correlate with the body's temperature. Fever-related infectious causes:

Infections caused by bacteria include typhoid, which can be contracted through contaminated food or water, meningococcus, staphylococcus, and streptococcus (which causes strep throat) (meningitis of brain), virus infection - Common viruses include the measles, mumps, rubella, dengue fever, coronavirus, and influenza. Giardiasis (contaminated water), Lyme disease (tick bite), Malaria (mosquito bite), and Candida (yeast), Cryptococcus (meningitis), and Pneumocystis (fungal infection) are all examples of parasitic infections (pneumonia) Etiologies of acute febrile fever that are not infectious: Malignant cancer, autoimmune illness, heat exhaustion or heat stroke, malignant malignancy, Prescription drugs and vaccinations Finding the underlying cause of the fever is the first step in treating a febrile disease when it presents to a medical professional [91.92]. One of the most frequent reasons for consultations, particularly in poorer nations, is febrile sickness [93]. There may be a wide variety of infectious pathogens implicated; yet clinical manifestations are frequently non-specific, undermining the accuracy of a diagnosis based solely on clinical symptoms [94]. There has been a decrease in the percentage of confirmed malaria cases as a result of the recent widespread adoption of rapid diagnosis tests (RDTs) for the diagnosis of malaria infection. Since clinical laboratory resources are sorely limited in low-income settings, clinical care guidelines for febrile illnesses have been produced, although they are frequently based on syndromes and clinical diagnoses are rarely verified [95]. Clinicians commonly deal with febrile non-malarial illnesses with few paraclinical options for patient diagnosis and care. Studies in Eastern Africa and Asia have emphasized the significance of many non-malarial illnesses that, if biologically proved, may be avoided or properly treated, including bacterial zoonoses or arboviral infections [96]. Madagascar, a sizable island in the South-Western Indian

Ocean, with a variety of bioclimates and a wide range of malaria transmission. Since 2007, when the Ministry of Public Health (MoH) and the Institut Pasteur de Madagascar (IPM) implemented the Fever Sentinel Surveillance Network (FSSN), which is made up of 34 basic healthcare facilities across the nation, fever cases have been monitored [97]. The following epidemic-prone diseases will be closely monitored by this network: malaria, influenza-like illnesses (ILI), dengue-like syndromes (DLS), and diarrheal syndromes. From From 2008 to 2011, this surveillance revealed that fever accounted for 11.1 percent of all outpatients. Malaria made up 12.0 percent of febrile cases, ILI was responsible for 20.7 percent, DLS was responsible for 8.7 percent, and diarrheal illnesses were responsible for 4.7 percent. Only malaria, however, is lab-verified using RDTs in accordance with national policies. On the incidence of other non-malarial illnesses in people, such as leptospirosis, relapsing fever, rickettsia infection, and other less common infections, there is little information available in Madagascar. Our study's main goal was to determine the common causes of fever among outpatients visiting medical facilities in Madagascar [98]. The lack of resources and the wide variety of acute febrile illness (AFI) etiologies in tropical areas make it difficult to diagnose, treat, and implement public health measures for endemic and epidemic diseases. This is further complicated by the fact that the majority of patients come with vague symptoms (such as low-grade fever, generalized. Malaria made up 12.0 percent of febrile cases, ILI was responsible for 20.7 percent, DLS was responsible for 8.7 percent, and diarrheal illnesses were responsible for 4.7 percent. Only malaria, however, is lab-verified using RDTs in accordance with national policies. 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A useful tool to routinely identify and record the causes of acute fever is syndromic-based illness surveillance. Trop Net Europa and a project created by the U.S. Centers for Disease Control and Prevention (CDC, Atlanta, GA) for the same goal along the U.S.-Mexico border have both used this method to identify fevers of unknown origin in Turkey, China, and India. In Southeast (SE) Asia, the etiologies of more than 40% of cases of acute undifferentiated febrile illness were identified in a prospective study of Thai patients, with the most common cause being illnesses caused by rickettsia, dengue, and influenza. In Latin America, surveillance discovered a variety of pathogens that had not previously been isolated in the region as the cause of acute undifferentiated febrile illness in Ecuador in 40% of enrolled individuals. SE Asia is experiencing a dynamic period of population growth, urbanization, and international movement, which raises concerns about new and re-emerging illnesses. Populations in SE Asia have been demonstrated to be affected by infections with the dengue virus, malaria parasites, influenza viruses, hepatitis viruses, rickettsia, and Leptospira in the past. Limited information is available, though, on the causes of AFI in the Kingdom of Cambodia among the SE Asian countries. The populations of Cambodian refugees who either relocated to the United States or lived in refugee camps in Thailand were documented to have ailments in earlier research. These Studies have shown how diseases caused by parasites such malaria, hepatitis, cryptosporidium, and tuberculosis manifested in a patient group that was frequently undernourished and stressed out. Recent research in Cambodia have combined prospective and/or syndromic methods. 35 of 88 (40 percent) patients with encephalitic syndromes who were admitted to a provincial hospital outside of Phnom Penh had infectious etiologies, including 11 bacterial, 1 fungal, and 23 viral infections (Japanese encephalitis virus [JEV] the principal causative agent of disease). In order to detect hemorrhagic fever, encephalitis, or hepatitis in children, a hospital-based study in Phnom Penh was carried out. The results revealed that hepatitis A and JEV significantly contributed to the disease burden in this population. We started clinic-based observation in 2006 to determine the causes: the prevalence of AFI among Cambodian patients seeking care at peri-urban, rural, and hospital outpatient departments. In this article, we outline the characteristics, signs, and known etiologies of the patients who sought medical attention for AFI from December 2006 to December 2009 [99]. One of the most prevalent signs of illness or disease in children is fever, which can have a variety of reasons. Feverish illnesses can be caused by bacterial, viral, protozoal, or fungal infection [90]. Clinical diagnosis can be challenging because many febrile infections have some similar overlapping characteristics [91]. There is a possibility of diagnosis delay due to the wide range of differential diagnoses for fever in youngsters [100]. The majority of fevers in the tropics and areas where malaria is prevalent are assumed to be caused by malaria and are treated accordingly. But there is growing evidence that some of these febrile infections are caused by things other than malaria [101]. The term "infectious disorders in patients who present with undifferentiated fever and require malaria quick diagnostic testing/microscopy, but in whom these tests were negative has been used to describe these non-malarial febrile illnesses. Since non-malarial febrile illnesses have been found to have a greater global fatality rate than malaria, even in malaria-endemic areas, they are significant contributors to morbidity and mortality[102]. Numerous cases of malaria with a clinical diagnosis have, according to studies, been caused by other infections, particularly bacteria. This means that when fevers are presumed to be caused by malaria, other sources of fever are disregarded, which may have unintended consequences. Malaria is typically over-diagnosed when more serious infections are left untreated, and it is thought that overtreating malaria can hasten the emergence of antimalarial drug resistance. The World Health Organization advises artemisinin-based combination therapy (ACT) exclusively for parasitologically proven patients and test-based management of malaria. Fever is still treated empirically in places with limited resources, nevertheless. Rapid diagnostic tests (RDTs) have been successfully used to distinguish between malaria and non-malarial febrile illnesses. They are based on the detection of the malaria antigen [103]. The percentage of fever that can be attributed to malaria varies depending on the locale. In Nigeria generally, and the Niger Delta region in particular, the etiology of non-malarial febrile sickness is not well understood[104].

Etiologies of Acute Undifferentiated Febrile Illness

Data were only available for a few significant disorders; therefore, it has not been possible to estimate the true burden of acute undifferentiated febrile illness (AUFI). One of these is dengue, which has gained worldwide attention recently despite being ignored for decades. A prior study indicated that patients with dengue had a greater hospitalization rate than those with other febrile illnesses, despite the fact that dengue infection does not require a special antiviral therapy. Leptospirosis is a reemerging zoonosis that can have a severe form that can result in up to 40% mortality. In the past, rickettsioses, such as scrub typhus and murine typhus, were among the under-recognized causes of acute fever. Unfortunately, in the majority of AUFI cases, neither clinical symptoms nor routine laboratory tests are precise enough and conventional examinations are time-consuming and not available everywhere. Its problematic diagnoses and method of treatment are still based on scant information from regional epidemiology research. Empirical antibiotic treatment is still necessary due to the lack of trustworthy techniques for quick diagnosis, which results in excessive costs and, more significantly, antibiotic resistance. Leptospirosis and scrub typhus were the two most frequent etiological factors in AUFI, according to earlier etiology investigations conducted in Thailand. However, the majority of these investigations were carried out in rural and agricultural environments. Additionally, there are few statistics on AUFI in urban and suburban locations. To ascertain the prevalence of prevalent infectious diseases endemic in Bangkok, Thailand, this prospective epidemiological study was conducted predominantly in AUFI patients attending the fever clinic of the Hospital for Tropical Diseases (HTD) in Bangkok. Additionally, to help with the triage of dengue patients, to reduce the need for unnecessary antibiotic treatment, and to enable early treatment for diseases that require antibiotic treatment, clinical traits that can be used to distinguish dengue infection, which do not require antibiotic therapy, from bacterial and tropical diseases were determined [105].

Diagnosis

In low-resource tropical countries, fever is one of the most often reported symptoms by people seeking medical attention. It may occur alone or in conjunction with other widespread symptoms like cough or diarrhea; Prasad, Sharples, and others 2015. Health care professionals and healthcare systems face particular difficulties when treating fever without localizing symptoms because it can be brought on by a variety of bacterial, fungal, parasitic, viral, and bacterial infections as well as noninfectious conditions. Clinical evaluation is not always accurate in determining the probable etiology of a condition or in identifying patients who will eventually develop a serious or fatal illness. Adding to the shortcomings of clinical evaluation is the lack of epidemiologic information on prevalent causes of fever that is readily available as well as the paucity of clinical laboratory services in many places [106]. Malaria has long been the frequent default diagnosis for fever without localizing symptoms in the tropics due to its ubiquity and severity. In regions where malaria has historically been endemic, vertical strategies are used to manage and control fever. However, an increasing number of research on the causes of fever and a greater use of malaria diagnostic tests have helped to reveal the issue of overdiagnosis of malaria in patients who are febrile in many regions [107]. Since 2004 there have been documented decreases in malaria and Health care professionals are dealing with an increasing number of patients who have fever but a negative malaria diagnostic test as a result of the rise of nonmalarial illnesses like dengue and the widespread use of diagnostic testing for malaria. This increase is alarming since people who visit hospitals with fever that is not related to malaria are just as likely to pass away as those who do. Additionally, febrile infections other than malaria are rarely treated with vertical programs. One of the most difficult diagnoses in clinical medicine is that of individuals who present with an acute febrile illness[108]. Fever has long been mistakenly treated as malaria in Africa and other tropical areas. The improvement in the creation and usage of fast diagnostics for malaria but it resulted in unacceptable levels of assuming that patients with negative results from a quick test for malaria should take antibiotics. This unanticipated effect has major implications for antibiotic conservation for future generations since it increases antimicrobial resistance. Yukari C. Manabe and colleagues demonstrated in their article published in The Lancet Infectious Diseases that highly accurate multiplex molecular tests for identifying some of the causes of fever are now available outside of laboratory settings, requiring only 2-3 minutes of hands-on time and yielding results in under an hour. These multiplex molecular assays that can be run on-demand are yet another significant step towards resolving the conundrum of acute febrile illness differential diagnosis, and they have increased utility as a public health tool for investigations into outbreaks and surveillance. In low-resource settings in Asia and Africa, the diagnosis of acute undifferentiated febrile illnesses (AUFIs), which are frequently brought on by a variety of pathogens including Plasmodium species, dengue virus, Salmonella enterica serovar Typhi, Salmonella enterica serovar Paratyphi A, Orientia tsutsugamushi, Rickettsia typhi, Leptospira species, chikung Although clinically "undifferentiated," these organisms are distinct in terms of their clinical course and require accurate diagnosis for the right kind of care [109]. The diagnosis and treatment of malaria have greatly improved with the availability of high-quality rapid diagnostic tests (RDTs) at the point of care (POC). However, even in regions where malaria is widespread, nonmalarial infections account for a sizable portion of AUFIs. Organization for World Health Currently advises using malaria RDTs to diagnose fever; if negative, evaluation for other reasons is advised, however without any additional details. Patients who present with a fever are frequently empirically treated with antimalarial medications in malaria-endemic areas and with antibiotics in non-endemic areas, or frequently with both. Rapid test platforms have developed during the past few decades, resulting in commercially available RDTs for some of the causes of nonmalarial febrile diseases; nevertheless, the accuracy of these tests is subpar. Multiplex POC assays, which can simultaneously evaluate numerous antigens/antibodies for many diseases from a single sample, are currently being investigated. Despite their poor accuracy, the currently available commercial RDTs can help provide better patient care when used correctly. There is a need for protocols to direct the right use of solitary and multiplex RDTs given their growing availability and continued development. One of the most typical initial symptoms of pediatric diseases is fever. Children under the age of five who have fever are often experiencing systemic inflammation as a result of a viral, bacterial, parasitic, or, less frequently, a noninfectious cause. If local epidemiology is well understood, the ages of the patients and their geographical locations can aid in directing the proper diagnostic strategy and therapy [110]. For children aged one to 59 months, the combined proportion of mortality caused by AIDS, diarrheal illnesses, pertussis, tetanus, measles, meningitis/encephalitis, malaria, pneumonia, and sepsis was 58.5 percent in 2015; for newborns, it was 23.4 percent (Liu and others 2016, chapter 4 of this volume). Variable evidence exists regarding the frequency of fever with a mean of 5.88 fever episodes per kid under the age of five per year and a weekly active case detection range of two to nine febrile episodes per child under the age of five per year (Gething and others 2010). An estimated 655.6 million fever episodes in children under five occurred in 42 Sub-Saharan African nations in 2007, according to national survey data. Of these episodes, 32% took place in 11 outpatient facilities in the Democratic Republic of the Congo, Ethiopia, and Nigeria (Gething and others 2010). Fever is unquestionably the most frequent pediatric presenting symptom at the level of the medical center and the community. The most widespread presenting symptoms at the facility and community levels are highlighted by a number of studies that are described in table 8.1. Prior to the development of accessible and reliable malaria rapid diagnostic tests (RDTs), the majority of healthcare professionals in malaria-endemic nations assumed that fevers were caused by malaria; in the early 1990s, the emphasis was to reduce malaria mortality by all means possible. Children in malaria-endemic areas who were suspected of having a severe illness and exhibited warning signs were advised to take injectable antimalarials and antibiotics, according to the World Health Organization's (WHO) initial Integrated Management of Childhood Illness (IMCI) guidelines from 1997. Prior to 2010, the initial WHO recommendations for treating malaria advised empiric, oral, antimalarial medication for fever with children under the age of five living in malaria-endemic areas, without other source (WHO 2006). The effectiveness of the presumed treatment of febrile illnesses has been called into question due to the decline in malaria incidence, increase in antimicrobial resistance, and accessibility of accurate, affordable point-of-care diagnostics. This has reopened the debate over the most precise and economical methods for fever diagnosis and treatment. In places where there is a high risk of malaria transmission and few diagnostic tests are available, presumptive therapy is the most feasible and economical option (DCP3 volume 6, Babigumira, forthcoming). (D'Acremont, Lengeler, and Genton 2007; D'Acremont and others 2009; English and others 2009) In 2009, specialists argued over whether there was enough data to abandon presumptive treatment standards and shift to a focus on diagnosis before treatment. There is growing evidence that showed the national and international efforts to combat malaria. More than US$2.5 billion was invested in 2012 by international partners, including the Bill & Melinda Gates Foundation's Malaria Control and Evaluation Partnership in Africa, the World Bank Malaria Booster Program, the U.S. President's Malaria Initiative, and the Roll Back Malaria Partnership (D'Acremont, Lengeler, and Genton 2010; Feachem and others 2010; Leslie and others 2012; WHO 2013a). Malaria incidence is declining in countries with previously identified high-transmission zones, making the management of nonmalarial fevers crucial (Feachem and others 2010; WHO 2013a; Hertz and others 2013; Ishengoma and others 2011) [111]. The WHO updated its recommendations for treating fever in 2010 and now only advises antimalarial medication for patients who have a positive malaria test result either a point-of-care or a microscopy outcome (WHO 2010a). Through the majority of Sub-Saharan African nations, this new strategy is being implemented in the public sector (Bastiaens and others 2011). To better understand treatment decision-making in this setting, as well as how to prevent the overuse of antibiotics and guarantee adequate care, more research is required. However, many patients initially seek care in the informal private sector. Understanding the etiology of nonmalarial fevers in each context is the logical next step to improve pediatric clinical outcomes of other treatable serious febrile illnesses, such as pneumonia, sepsis, bacterial meningitis, enteric fever, rickettsioses, and influenza. The epidemiology of pediatric febrile illness is undoubtedly changing. Because antimicrobial drug resistance is widespread and growing throughout the world, caution must be used when using antibiotics only where appropriate, and to create thorough recommendations when resources are scarce. Current recommendations are based on clinical characteristics, which are regrettably not very reliable indicators of the illnesses that cause fever. To guide the most efficient use of antibiotics, low-cost, accurate point-of-care diagnostics are required to identify which children may benefit from antibacterial therapy [112].

Bacterial bloodstream infection

In Africa, bloodstream infection is a primary factor in hospitalized fever. In patients with severe febrile illness, bacteremia has been found in 10.4% of East African patients and 12.4% of West African patients. Significant risk factors for bacteremia continue to be severe malnutrition and HIV-related immunosuppression. Nontyphoidal serovars of S. enterica and S. enterica serovar Typhi, which combined accounted for 46.2% of bacterial bloodstream isolates in Blantyre, Malawi between 1998 and 2016, are the most common bloodstream infections. In several locations in Africa, the incidence of invasive nontyphoidal Salmonella (iNTS) sickness has been predicted to reach 100 cases per 100,000 people per year by the Typhoid Surveillance in Africa Program (TSAP) study. HIV infection, malnutrition, sickle cell illness, recent malaria infection, and severe poverty are risk factors for iNTS. The decreasing prevalence of iNTS in some places may be attributed to reduced malaria incidence and broad accessibility to ART. The re-emergence of S. enterica serovar Typhi is suggested by longitudinal data. In Malawi, it was found in 1.0 percent of patients with bloodstream infections from 1998 to 2009 and in 43.0 percent of blood cultures that came back positive from 2014 to 2016. More than 100 cases of S. enterica serovar Typhi bacteremia were reported annually in TSAP in various rural and urban locations in West Africa and East Africa. The incidence was frequently higher in preschoolers. Another typical cause of bacteremia, particularly in kids, is streptococcus pneumoniae. Recent findings demonstrate a decrease in invasive pneumococcal disease linked to use of the vaccine, despite some replacement by non-vaccine strains among individuals with the disease. Other frequently found infections include Enterobacteriaceae and Staphylococcus aureus, the latter of which was the most prevalent bloodstream pathogen among children from Guinea-Bissau with 54 percent of isolates [113]. A major worry is the prevalence of antimicrobial resistance (AMR). Resistance to ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole has grown widespread among Salmonella isolates. Between 2010 and 2014, 56% of S. enterica serovar Typhi isolates and 63% of iNTS isolates in Ghana were multi-drug resistant, and similar percentages have also been observed in Burkina Faso, Kenya, and Tanzania. S. enterica is also developing fluoroquinolone resistance, which reduces the range of available oral outpatient treatments. According to reports, extended-spectrum cephalosporin resistance is becoming more common throughout Africa [114]. In western Kenya, nontyphoidal Salmonella bloodstream isolates made up to 56.5% of this resistance. resistance to cephalosporins with a wider spectrum among Salmonella enterica serovar Typhi is still uncommon, however it was just discovered in the Democratic Republic of the Congo. Along with other invading microorganisms, AMR is rising. It is concerning that fluoroquinolone and extended-spectrum beta-lactam resistance

Enterobacteriaceae have rapidly increased in Malawi, and it is likely that comparable trends exist throughout Africa [115].

Mycobacterial blood stream infections

Although less common in children, Mycobacterium tuberculosis is a significant contributor to bloodstream infections in adults with HIV. According to a recent comprehensive analysis, M. tuberculosis caused bacteremia in 0.4% of children and 13.5% of adults with HIV. Despite the availability of ART, M. tuberculosis continues to be a significant source of bloodstream infection in Zambia and Uganda [116].

Bacterial zoonoses

Bacterial zoonoses are under-recognized causes of febrile illness in Africa. Major bacterial zoonoses include brucellosis, leptospirosis, Q fever, and rickettsiosis. The close association between people, livestock, and wildlife in both rural and urban areas of many African countries is a key driver of the high prevalence of zoonotic infection [117].

Brucellosis

According to recent studies, between 2.6 percent and 22.4 percent of febrile patients in East Africa had brucellosis [118,119]. The most typical bloodstream isolate was Brucella melitensis in a pastoral region of rural Tanzania [120]. The information that is currently available on brucellosis risk factors in Africa suggests that consuming raw milk and giving birth to animals are important in sub-Saharan Africa, just as they are everywhere else [121].

Leptospirosis

Leptospirosis testing is reported infrequently in feverish patients, but when it is, it has been found in up to 8.4% of patients admitted to hospitals with fever [122]. Tropical African nations may have some of the highest leptospirosis rates in the world, despite significant seasonal variation [123]. Both rural and urban settings seem to be prevalent places for leptospirosis to occur[124]. In Africa, livestock may be a significant cause of human disease in addition to rats [125].

Q fever

According to a recent comprehensive study, 3 to 8% of African patients with undifferentiated febrile illness and 6 to 9% of those with community-acquired pneumonia had C. burnetii, the cause of Q fever [126]. Additionally, findings from Togo and the Gambia indicate a significant prevalence of human seropositivity. Cattle, goats, sheep, and camels have all been found to have strong seroreactivity to C. burnetii and are therefore likely to be significant infection reservoirs[127].

Rickettsial infections

When people leave Africa and return, rickettsioses frequently induce fever. African tick-bite fever, which is brought on by Rickettsia africae, is the main SFGR on that continent. R. conorii, the germ that causes Mediterranean spotted fever, has been found in at least nine sub-Saharan African nations, though. It is acknowledged that rickettsioses are widespread in Southern Africa and could be found elsewhere on the continent. Studies from Ethiopia and Tanzania also reported a significant prevalence of SFGR, as did a recent study from Kenya that found it in 22.4 percent of children with fever. The prevalence of SFGR is less well known in West Africa, where ticks are the main vectors and human seropositivity is widespread, but it is anticipated to be substantial. Additionally, Rickettsia felis believed to be widespread in Western likewise Central Africa. R. felis has been found in healthy people, however studies indicate that it may also be a prevalent cause of fever [128].

Relapsing fever

The relapsing fever-causing bacteria Borrelia spp. has been found throughout Africa, although it is rarely investigated in studies of the causes of fever and may go unnoticed by doctors. B. crocidurae, the tick-borne relapsing fever-causing bacteria, was found in 7.3% of fever-stricken adult and pediatric patients in Senegal. Using blood films, B. recurrentis was found to be the source of louse-borne relapsing fever in 6.1 percent of healthy yekolotemaries (religious scholars) and 4.9 percent of healthy street children in Ethiopia. The difficulty in establishing the frequency of relapsing fever among patients with acute febrile illness is highlighted by the high prevalence among community members [129].

2.4 Conceptual Framework

One of the most prevalent signs of illness or disease in children is fever, which can have a variety of reasons. Feverish illnesses can be caused by bacterial, viral, protozoal, or fungal infection [130]. Clinical diagnosis can be challenging because many febrile infections have some similar overlapping characteristics [131]. There is a possibility of diagnosis delay due to the wide range of differential diagnoses for fever in youngsters [132]. The majority of fevers in the tropics and areas where malaria is prevalent are assumed to be caused by malaria and are treated accordingly. But there is growing evidence that some of these febrile infections are caused by things other than malaria [125]. The term "infectious disorders in patients who present with undifferentiated fever and require malaria quick diagnostic testing/microscopy, but in whom these tests were negative has been used to describe these non-malarial febrile illnesses. Since non-malarial febrile illnesses have been found to have a greater global fatality rate than malaria, even in malaria-endemic areas, they are significant contributors to morbidity and mortality[126]. Numerous cases of malaria with a clinical diagnosis have, according to studies, been caused by other infections, particularly bacteria. This means that when fevers are presumed to be caused by malaria, other sources of fever are disregarded, which may have unintended consequences. Malaria is typically over-diagnosed when more serious infections are left untreated, and it is thought that overtreating malaria can hasten the emergence of antimalarial drug resistance. The World Health Organization advises artemisinin-based combination therapy (ACT) exclusively for parasitologically proven patients and test-based management of malaria. Fever is still treated empirically in places with limited resources, nevertheless. Rapid diagnostic tests (RDTs) have been successfully used to distinguish between malaria and non-malarial febrile illnesses. They are based on the detection of the malaria antigen [133]. The percentage of fever that can be attributed to malaria varies depending on the locale. In Nigeria generally, and the Niger Delta region in particular, the etiology of non-malarial febrile sickness is not well understood[134].

Etiologies of Acute Undifferentiated Febrile Illness

Data were only available for a few significant disorders; therefore, it has not been possible to estimate the true burden of acute undifferentiated febrile illness (AUFI). One of these is dengue, which has gained worldwide attention recently despite being ignored for decades. A prior study indicated that patients with dengue had a greater hospitalization rate than those with other febrile illnesses, despite the fact that dengue infection does not require a special antiviral therapy. Leptospirosis is a reemerging zoonosis that can have a severe form that can result in up to 40% mortality. In the past, rickettsioses, such as scrub typhus and murine typhus, were among the under-recognized causes of acute fever. Unfortunately, in the majority of AUFI cases, neither clinical symptoms nor routine laboratory tests are precise enough and conventional examinations are time-consuming and not available everywhere. Its problematic diagnoses and method of treatment are still based on scant information from regional epidemiology research. Empirical antibiotic treatment is still necessary due to the lack of trustworthy techniques for quick diagnosis, which results in excessive costs and, more significantly, antibiotic resistance. Leptospirosis and scrub typhus were the two most frequent etiological factors in AUFI, according to earlier etiology investigations conducted in Thailand. However, the majority of these investigations were carried out in rural and agricultural environments. Additionally, there are few statistics on AUFI in urban and suburban locations. To ascertain the prevalence of prevalent infectious diseases endemic in Bangkok, Thailand, this prospective epidemiological study was conducted predominantly in AUFI patients attending the fever clinic of the Hospital for Tropical Diseases (HTD) in Bangkok. Additionally, to help with the triage of dengue patients, to reduce the need for unnecessary antibiotic treatment, and to enable early treatment for diseases that require antibiotic treatment, clinical traits that can be used to distinguish dengue infection, which do not require antibiotic therapy, from bacterial and tropical diseases were determined [135].

2.5 Summary of Gaps

According to (Manuel Raab et al, 2022) on "Clinical presentations, diagnostics, treatments and treatment costs of children and adults with febrile illness in a tertiary referral hospital in south-eastern Guinea: A retrospective longitudinal cohort study" that the wide reliance on rapid diagnostic tests to diagnose febrile patients not only risks to over- or under-diagnose certain diseases but also leaves the possibility of highly infectious diseases in febrile patients unexplored. , the study only focused on the collection of patient data at one particular hospital which reduced generalizability of our findings, the period of three months is relatively short and the study was not designed to verify the aetiology of febrile illness in patients[136].

According to (Jeanne Elven et al, 2020) on “non-malarial febrile illness: a systematic review of published aetiological studies” stated that more emphasis is needed in rural areas that remain beyond the reach of many research and surveillance efforts. A mechanism such as the recently inaugurated African Centers for Disease Control and Prevention may be able to reform this area. As the threat of antimicrobial resistance looms large, knowledge of the distribution of pathogens causing febrile illness should facilitate priority setting in the development of new diagnostic tools and improved antimicrobial stewardship[122]. According to (Michael WandanjeMahero et al, 2022) on “There are many fevers”: Communities’ perception and management of Febrile illness and its relationship with human animal interactions in South-Western Uganda” elucidated that further research is needed in understanding strategies for improving; i) community members utilization of the health system, ii) NMFI treatment algorithms and iii) the link between conservation and public health in such settings[132].

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Chapter Three

Methodology

3.1 Research Design

A cross-sectional study design was adopted. A 45-item self-administered questionnaire was designed to assess the management of febrile illness cases in selected primary healthcare Centres in Ibadan, Oyo state**.** The questionnaire was used to obtain information on the socio demographic characteristics of the respondents, their priorities in diagnostic process, diagnostic procedure and tools as well as the factors that facilitate or mitigate the adoption of treatment guidelines in Primary Healthcare Centres in Ibadan, Oyo State.

***Study Location/Area*:** Oyo South is a senatorial zone/district in Oyo State, comprising of the entire geographical areas of:

1. Ibadan North Local Government Area
2. Ibadan North East Local Government Area
3. Ibadan North West Local Government Area
4. Ibadan South-east Local Government Area
5. Ibadan South West Local Government Area
6. Ibarapa Central Local Government Area
7. Ibarapa East Local Government Area
8. Ibarapa North Local Government Area
9. Ido Local Government Area

Senatorial zones in Nigeria are typically made up of a group of local government areas in a particular state and are represented by a Senator at the National House of

Assembly at National level; however, all the LGA are statutorily govern by State Government and Federal Government.

The study was carried out in selected PHC facilities and randomly selected 5LGAs in Ibadan Oyo

3.2 Population of the Study

The study was conducted among healthcare workers who were Doctors, Nurses, Community Health Officers, Community Health Extension Workers and Junior Community Health Extension Workers - the frontline healthcare workers- at the Primary Healthcare Centres in the selected Local Government Areas (LGAs) in Ibadan, that manage the patients.

3.3 Sample and Sampling Techniques

Multi-stage sampling technique was employed to select respondents from the list of all the PHCs in the 5 selected Local government areas in Ibadan, Oyo State.

Stage 1: The identification of all the LGAs, in the 3 Senatorial Zones/Districts in Oyo State.

Stage 2: 2 out of the 3 Senatorial Districts which have 11 LGAs in Ibadan were selected.

Stage 3: The Oyo Central and Oyo South Senatorial districts which contain 11 LGAs, 5 LGAs (Ibadan North East, Ibadan North West, Ibadan South East, Ibadan South West and Ibadan North) were randomly selected from the 2 Districts and this formed the population.

3.3.1 Sample Size

The sample size was based on the number of the recruited frontline health workers in all the selected Primary Healthcare Centres in the 5 LGAs in Ibadan, Oyo State.

3.3.2 Method

Using Slovin's Formula for sample size determination, $n = N/(1+Ne^2)$, where n is the sample size, N is the population size and e is the margin of error at 5%.

Calculation of Sample Size Using Slovin's Formula

Slovin's Formula $n = N/1+Ne^2$

Where, N= Population size

e= Margin of error

Therefore, N= 669

e= 5% or 0.05

$n = 669/1+669 \times (0.05)^2$

$n = 669/1+ (669 \times 0.0025)$

$n = 669/1+ 1.6725$

$n = 669/2.6725 = 250.3$

Sample size, n = 250

The Sample Size was 250 respondents/Frontline Health workers was shared among 5 LGAs.

3.4 Description of the Research Instrument

A self-administer and pre-designed questionnaire was used. Study variables questions were included in four sections. All questions are open and close ended, easy, short, and understandable in nature. Questions were answered after consent has been taken from respondents.

3.5 Validity of Research Instrument

A Content validity was adopted which showed whether all the aspects of the test/measurement are covered. A language test was designed to measure the writing and reading skills, listening, and speaking skills. It indicates that a test has high content validity.

3.6 Reliability of the Research Instrument

A Test-Re-tests was adopted which measures the consistency of the results at different points of time. It identified whether the results are the same after repeated measures. For instance, a questionnaire was shared among a group of health workers to check the quality of the instrument at first and after which was repeated with many groups. Same response was gotten from a various group of participants, it means the validity of the questionnaire is high as it has high test-retest reliability.

Inclusion Criteria

Enrollees were potential study participants who work in Primary Health Centres that possess professional qualifications like the Medical Doctors, Community Health Officer/Community Health Extension, who attend to patients and gave consent for the study or survey.

Exclusion Criteria

Potential study participants with professional qualifications who did not give consent, non-professional and who do not work in Primary Health Centre. These can interfere with the success of the study or increase their risk for an unfavorable outcome.

3.7 Data Collection

The data collected was made possible through the use of self-structured questionnaire which was opened and closed ended, self-administered version designed to identify methods of diagnosis for case management, to determine what factors influence on how they evaluate, diagnose, and treat a child who presents to the hospital acutely ill with a fever, professional qualifications, factors that facilitate or mitigate the adoption of treatment guidelines, and to identify areas to improve quality of care in PHCs. Hardcopies for those who found it convenient and softcopies for those who had internet access were administered to the respondents after their consent have been obtained and assured that all information provided would be treated confidentially and use for research purposes only.

3.8 Data Analysis

Data was analyzed with SPSS version 25 statistical packages, Google form and Excel. Descriptive statistics such as mean, frequency, and proportion was used to describe the management of febrile illness cases among Under 5 years in selected PHCs in Ibadan, Oyo States. The results were presented using Tables, Pie-charts and Bar-chart.

3.9 Ethical Approval

The approval for the research was obtained from the Lead City University research ethical committee and the Oyo State Primary Healthcare Board research ethical committee respectively.

Chapter Four

Results and Discussion of Findings

4.1 Demographic Data Analysis

The result of table 4.1 shows that out of 250 respondents, 29.6% are between the age of 20-31years while 38% are between the ages of 50-55 years. The study shows that 7.6% of the respondent is attending community health centers while 92.4% are attending primary healthcare centers, the result shows that 45.6% of the respondents are from rural area while 54.4% are living in the urban area. 31.6% of the respondent said the PHC functions for 24 hours while 68.4% of the respondent said the PHC function 24 hours. The result from the study shows that 11.6% are community health officers while 62.8% are community health extension workers. 84% of the respondents are married while 16% are single. The findings show that 97.6% of the respondent has tertiary education while 2.4% have no formal education. The result shows that 64.8% of the respondents are practicing Christianity while 35.2% are practicing Islam. The result also shows that 34% of the respondent said they had no training specific to malaria while 66% said they had training specific to malaria. 62% of the respondent said they had no training specific to typhoid and enteric fever while 38% said they had training specific to typhoid and enteric fever. However, 62.4% of the respondent said they had no training specific to other febrile illnesses while 37.6% said they had training specific to other febrile illnesses.

Table 4.1: Percentage Distribution of the Background Characteristics

Variable	**Frequency**	**Percent**
Age of the respondent		
20-31 years	74	29.6
40-41 years	81	32.4
50-55 years	95	38.0
Category of health centre		
Community health centre	19	7.6
Primary health centre	231	92.4
Location of PHC		
Rural	114	45.6
Urban	136	54.4
Population covered by the PHC		
<2500	128	51.2
5000-10000	122	48.8
Whether the PHC functions for 24 hours		
No	79	31.6
Yes	171	68.4
Designation of the respondent medical officer		
Community health officer	29	11.6
Community health extension workers	157	62.8
Lab technologist	64	25.6
Marital status		
Married	210	84.0
Single	40	16.0
Level of Education		
Post secondary	244	97.6
No formal education	6	2.4
Religion		
Christianity	162	64.8
Islam	88	35.2
Have you had any training specific to Malaria?		
No	85	34.0
Yes	165	66.0
Have you had any training specific to Typhoid/Enteric fever?		
No	155	62.0

Yes	95	38.0
Have you had any training specific to other febrile illness?		
No	156	62.4
Yes	94	37.6

4.2 Presentation of data

4.2.1 What is the knowledge of febrile illness management guideline in selected Primary Healthaare Centres in Ibadan, Oyo State?

Table 4.2 shows that 18.4% of the respondent answered incorrectly the first line of drug for treating malaria while 81.6% answered the same question correctly. 10.45% of the respondent answered incorrectly the common route of administration of anti-malaria drugs while 89.6% of the respondent answered the same question correctly. The result shows that 56.4% of the respondent answered incorrectly the cases of resistance of malaria to the following anti-malaria drug while 43.6% answered the same question correctly. 6.8% of the respondent answered correctly what is responsible for malaria parasites resistant to anti-malaria drug while 93.2% answered the same question incorrectly. The study shows that 72.8% of the respondent answered incorrectly how many cases do you seek laboratory diagnosis of malaria before treatment while 27.2% of the respondent answered the same question correctly. 62% of the respondent answered correctly what proportion of attendance at your PHC is due to malaria disease while 38% of the respondent answered the same question incorrectly. The study also shows that 14% of the respondent answered incorrectly the common symptoms of malaria diseases showed by children that visit the PHC while 86% of the respondent answered the same question correctly. 8% of the respondent answered incorrectly the common symptoms of malaria disease showed by adults that visit the PHC while 92% answered the same question correctly. The findings revealed that 39.2% of the respondent answered incorrectly the most important things to look for when deciding how to diagnose a child who presents with a fever while 60.8% answered the same question correctly. 36.8% of the respondent answered incorrectly what symptoms make you the most concerned about a patient while 63.2% of the respondent answered the same question correctly. 57.2% of the respondent answered incorrectly the potential diagnoses that you look for when you determine that a child with fever does not have malaria while 42.8% answered the same question correctly. 90% of the respondent answered incorrectly the first line of drug for treating typhoid while 10% answered the same question correctly. 24% of the respondent answered incorrectly the most common route administration of antibiotics used for typhoid while 66% of the respondent answered the same question correctly. 4% of the respondent answered incorrectly has you come across cases of resistance of typhoid to any of the following antibiotics while 96% answered the same question correctly. 48.8% of the respondent answered incorrectly what is responsible for typhoid resistant to antibiotics while 51.2% answered the same question correctly. 68.4% answered incorrectly how many cases they seek laboratory diagnosis of typhoid before treatment while 31.6% answered the same question correctly. 56% of the respondent answered incorrectly the common symptoms of typhoid showed by children that visit the PHC while 44% answered the same question correctly. 46.8% of the respondent answered incorrectly the common symptoms of typhoid showed by adults that visit the PHC while 53.2% answered the same question correctly. 80% of the respondent answered incorrectly what symptoms make you the most concerned about a patient while 20% answered the same question incorrectly. The result also shows that 18.8% of the respondent answered incorrectly the other potential diagnoses that you look for when you determine that a child with fever does not have typhoid while 81.2% answered the same question correctly.

Table 4.2: Percentage Distribution of Knowledge

Variables	**Incorrect %**	**Correct %**
First line of drug for treating malaria	18.4	81.6
Common route of administration of anti-malaria drugs	10.4	89.6
Cases of resistance of malaria to the following anti-malaria drug	56.4	43.6
What is responsible for malaria parasites resistant to anti-malaria drug?	6.8	93.2
How many cases do you seek laboratory diagnosis of malaria before treatment	72.8	27.2
What proportion of attendance at your PHC is due to malaria disease?	62.0	38.0
Common symptoms of malaria diseases showed by children that visit the PHC?	14.0	86.0
Common symptoms of malaria disease showed by adults that visit the PHC?	8.0	92.0
Most important things to look for when deciding how to diagnose a child who presents with a fever	39.2	60.8
What symptoms make you the most concerned about a patient?	36.8	63.2
Potential diagnoses that you look for when you determine that a child with fever does not have malaria?	57.2	42.8
Which of the following is the first line of drug for treating typhoid?	90.0	10.0
Most common route administration of antibiotics used for typhoid	24.0	76.0
Have you come across cases of resistance of typhoid to any of the following antibiotics?	4.0	96.0
What do you think is responsible for typhoid resistant to antibiotics?	48.8	51.2
In how many cases do you seek laboratory diagnosis of typhoid before treatment?	68.4	31.6
Common symptoms of typhoid showed by children that visit the PHC?	56.0	44.0
Common symptoms of typhoid showed by adults that visit the PHC?	46.8	53.2

What symptoms make you the most concerned about a patient?	80.0	20.0
What are other potential diagnoses that you look for when you determine that a child with fever does not have typhoid	18.8	81.2

Figure 4.1: Percentage Distribution of Knowledge of Febrile Illness Management Guidelines

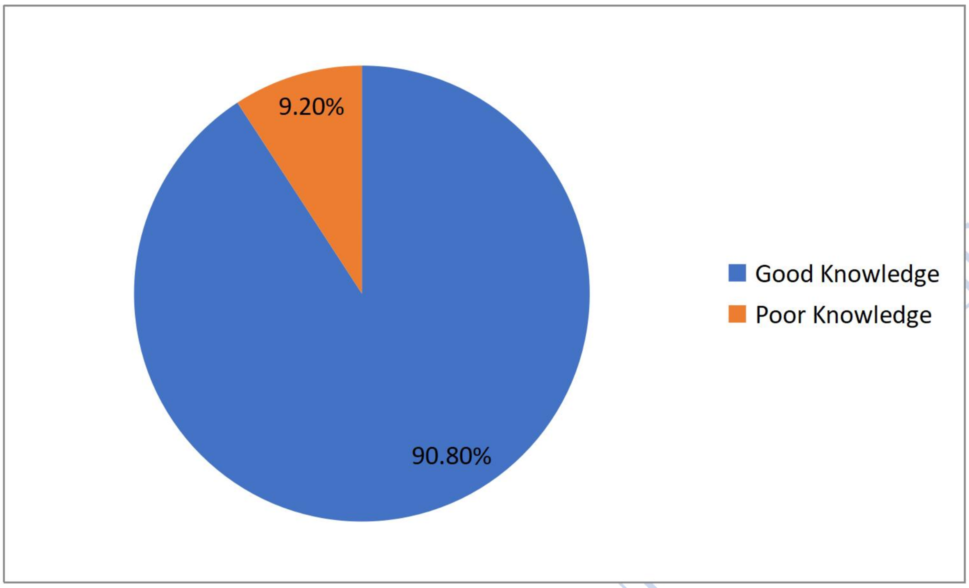

Figure 4.1 shows that only 9.20% of the respondent have poor knowledge of febrile illness management guideline

4.2.2 What is the adoption of national guideline for febrile illness managent in selected Primary Healthcare Centres in Ibadan, Oyo State?

Figure 4.2: Percentage Distribution of the Adoption of national guideline for Febrile Illness Management

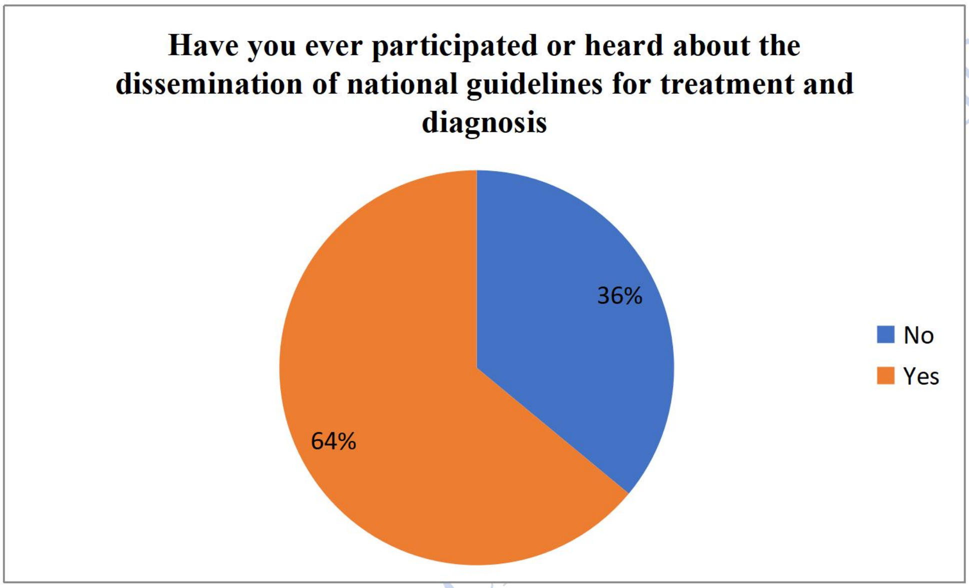

Figure 4.2 shows that only 36% of the respondent said they have never participated or heard about the dissemination of national guidelines for treatment and diagnosis

Table 4.3 shows that 74.8% of the healthcare worker used Mrdt diagnostic tool to see a patient with fever, 17.2% used Microscopy diagnostic tool, 1.6% used cultural media while 6.4% used serology diagnostic tool. The findings shows that 71.6% of the healthcare worker said they find Mrdt tool useful, 26.4% said they find microscopy tool useful while 2% said they find cultural media useful. 58.8% of the workers said they find it useful because of its simple technique while 1.2% said they find it useful because it is cost effective. The study also shows that 42.8% of the respondent said availability of Mrdt can make healthcare improved while 2% of the respondent said community mobilization can make healthcare improved.

Table 4.3: Percentage Distribution of Diagnostic Procedure and Tools

Variables	**Frequency**	**Percent %**
What diagnostic tools do you have at the clinic to use when you see a patient with fever?		
Mrdt	187	74.8
Microscopy	43	17.2
Culture media	4	1.6
Serology	16	6.4
Which ones do you find most useful?		
Mirdt	179	71.6
Microscopy	66	26.4
Culture media	5	2.0
Why?		
Highly sensitive	52	20.8
Simple technique	147	58.8
Affordable.	16	6.4
Reliable	29	11.6
Cost effective	3	1.2
Reduce turnaround time	3	1.2
In what ways can healthcare be improved upon in the facility?		
Training of health workers	66	26.4
Provision of well equipped laboratory	19	7.6
Efficiency of service	26	10.4
Community mobilization	5	2.0
Availability of mRDT	107	42.8
Availability of skilled personnel	27	10.8

4.2.3 What are the factors influencing the adoption of national guideline for febrile illness management?

Table 4.4 shows the factor influencing the adoption of national guideline for febrile illness management. From the result respondent between ages 20-31years are 2.43 less likely not to have ever heard or participated about the dissemination of national guidelines for treatment and diagnosis of malaria compared to their counterpart who are 50-55years at (0.185, 0.910 CI). It also shows that respondents between ages 31-40 years are 2.24 less likely not to have ever heard or participated about the dissemination of national guidelines for treatment and diagnosis of malaria compared to their counterpart who are 50-55 years at (0.220, 0.902 CI). The result shows that <2500 population covered by PHC are 1.31 times less likely not to have ever heard or participated about the dissemination of national guidelines for treatment and diagnosis of malaria compared to their counterpart that covered 5000-10000 at (0.431, 1.349 CI). The result shows that community health officer are 1.50 times less likely not to have ever heard or participated about the dissemination of national guidelines for treatment and diagnosis of malaria compared to their counterpart who are lab technologist at (0.248, 1.776 CI). It also shows that community health extension workers are 1.25 more likely not to have ever heard or participated about the dissemination of national guidelines for treatment and diagnosis of malaria compared to their counterpart who are lab technologist at (0.644, 2.450 CI). The findings show that respondent that are married are 1.09 less likely not to have ever heard or participated about the dissemination of national guidelines for treatment and diagnosis of malaria compared to their counterpart who are single at (0.378, 2.195 CI). The findings also shows that respondent who had tertiary education are 1.81 more likely to have ever heard or participated about the dissemination of national guidelines for treatment and diagnosis of malaria compared to their counterpart who have no formal education at (0.320, 10.251 CI). The result shows that participant who had no training specific to malaria are 4.23 less likely to have ever heard or participated about the dissemination of national guidelines for treatment and diagnosis of malaria compared to their counterpart who had training specific to malaria at (0.107, 0.521 CI). It also revealed that respondent who had no training on typhoid and enteric fever are 1.92 more likely to have ever heard or participated about the dissemination of national guidelines for treatment and diagnosis of malaria compared to their counterpart who had specific training on typhoid and enteric fever. The result also shows that participant who have good knowledge are 1.91 less likely not have ever heard or participated about the dissemination of national guidelines for treatment and diagnosis of malaria compared to their counterpart who have poor knowledge at (0.177, 1.550 CI).

Table 4.4: Factors influencing the adoption of national guideline for febrile illness management

Variable	UOR	95% CI	P-value	AOR	95% CI	P-value
Age of the respondent						
20-31 years	0.318	0.164, 0.615	0.001	0.410	0.185, 0.910	0.028
40-41 years	0.461	0.240, 0.886	0.020	0.446	0.220, 0.902	0.025
50-55 years	1					
Category of health centers						
Community Health centers	1.111	0.451, 2.734	0.819			
Primary Health Centers	1					
Location of PHC						
Rural	1.375	0.948, 1.994	0.093			
Urban	1					
Population covered by the PHC						
<2500	1	1.165, 2.384	0.005	0.763	0.431, 1.349	0.352
5000-10000	1.667					
Whether the PHC functions for 24 hours?						
No	1.324	0.848, 2.066	0.217			
Yes	1					
Designation of the respondent medical officer						
Community health officer	1.231	0.592, 2.559	0.578	0.663	0.248, 1.776	0.414
Community health extension workers	2.340	1.663, 3.293	0.000	1.257	0.644, 2.450	0.503
Lab technologist	1					
Marital status						
Married	1	1.501, 2.665	0.000	0.911	0.378, 2.195	0.835
Single	2.000					
Level of education						
Tertiary	1	1.389, 2.345	0.000	1.812	0.320, 10.251	0.501
No formal education	1.805					
Religion						
Christianity	1	0.645, 1.894	0.716			
Islam	1.105					

Have you had any training specific to?						
Malaria						
No	0.333	0.193, 0.576	0.000	0.236	0.107, 0.521	0.000
Yes	1					
Typhoid/Enteric						
No	1					
Yes	1.672	1.208, 2.315	0.002	1.920	0.886, 4.162	0.098
Febrile illnesses						
No	1					
Yes	1.294	0.943, 1.776	0.110			
Knowledge						
Good Knowledge	1					
Poor Knowledge	1.671	1.277, 2.186	0.000	0.523	0.177, 1.550	0.242

4.3 Discussion of Findings

4.3.1 Background Characteristics of the Respondent

The aim of this study is to evaluate the management of febrile illness cases among Under 5 years in selected Primary Healthcare Centers in Ibadan, Oyo State. The age of the respondent documented in this study is consistent with the one documented in Southwestern where 8.8% are from ages below 30 years, 43.7% are from age 40-49 years and 34.1% are 50 years and above.

Also, the result of the study shows that the majority of respondent has post secondary education 97.6%, this consistent with the study carried out in Nigerian Southwestern Metropolis where 92.7% of the respondent has post secondary education. However, the result from the study shows that 11.6% of the respondents are community health officers, 62.8% are community health extension workers and 25.6% are lab technologist, this is not in agreement with the study carried out in Southwestern where the respondents are 21.8% CHO, 39.5% CHEW and 8.8% Lab technologist.

Finally, the study also shows that 92.4% of the respondents are working in Primary Healthcare Centers and minorities are working in Community Health Centers, this is consistent with the study carried out in Nigerian Southwestern Metropolis where 90% of the respondents are from primary healthcare center and only 4.6% are from community health centers.

4.3.2 Knowledge of Febrile Management Guideline

This study revealed that majority of the respondent has good knowledge of Febrile Illness Management Guideline while only few have poor knowledge on it. This is consistent with that study carried out in Southern Metropolis where, 81.6% of the respondents have good knowledge of febrile illness management guideline and 18.4% of the respondents have poor knowledge of febrile illness and management guideline.

4.3.3 Factors influencing the Adoption of Guideline for Febrile Illness Management

It is observed from this study that respondent who have post secondary education are 1.81 more likely to have heard or participate in dissemination of national guideline for treatment and diagnosis of malaria, this is not in agreement with a study carried out in Southwestern where respondent who have secondary education and below are 1.36 more likely to have participated in good malaria practices.

The result of the study also shows that respondent who are community health extension nurse are 1.25 times more likely to have heard or participate in dissemination of national guideline for treatment and diagnosis of malaria at (0.644, 2.450 CI). This is not in line with the study carried out in Southwestern Metropolis where they are 1.88 times more likely to have participated in good malaria practices.

The study also shows that respondent who are between ages 21-31 years are 2.43 less likely not to have ever heard or participated about the dissemination of national guidelines for treatment and diagnosis of malaria at (0.185, 0.910 CI). Also, it also shows that respondents between ages 31-40 years are 2.24 less likely not to have ever heard or participated about the dissemination of national guidelines for treatment and diagnosis of malaria at (0.220, 0.902 CI). This is not consistent with the study carried out in Southwestern Metropolis where, respondent that are below 30 years are 11.23 more likely to have participated in good malaria practices and respondent between 40-49 years are 1.92 more likely to have participated in good malaria practices.

Chapter Five

Conclusion

5.1 Summary of Findings

Management of febrile illness is guided by the national policy and guideline on diagnosis and treatment of malaria and other febrile illness in health facility in Nigeria, the policy and guideline have provided how illness cases due to under 5 years can be successfully managed with a very good outcome, the guidelines have been updated with most recent updates from WHO guidance hence providing a robust knowledge base for frontier health care workers across board.

5.2 Conclusion

In line with World Health Organization recommendation, Nigeria has adopted the Test, Treat and Track (3Ts) Strategy with all suspected cases of malaria and other diagnosed illnesses using either Rapid Diagnostic Test or Microscopy, with confirmed cases treated promptly with effective ACT and all cases track through the surveillance system.

The approved national guidelines widely disseminated to health care facilities workers in both private and public across Nigeria as an important step in standardizing diagnosis and treatment practices. Accordingly, it is imperative for health care providers to strictly comply with it, to harmonize management of febrile illness practices within Nigeria.

From the results and findings of this study it was reveal that health care workers at primary health facility in Nigeria are guided by approved FMOH, Abuja policy on management of febrile illness, with appropriate testing procedures before treatment, however the adoption and use of the treatment guidelines in the management of febrile illnesses among children under the age of five in Ibadan, Oyo State Nigeria has been impacted by the lack of some basic amenities, such as lack of access to the internet due to the high cost in Nigeria, coupled with some health workers' inability to use smartphones, lack of a computer system at the facility, then workload which does not create room to access the national guideline, and lack of technology support.

5.3 Recommendation(s)

The following are recommendation from the study:

i. External Quality Assurance should be maintained to input standard of operation to healthcare Centres.

ii. Initiate steady Training/Workshops/seminar to update knowledge of health care workers at primary health care level, knowing full well the dynamics of science and disease transition.

iii. Making available standard laboratory service, Diagnostic materials and drugs for management of illness cases at the PHC will create robust and quality services for the patients at the grassroot who access health care deliver services at PHC which is closer to the people.

5.4 Contribution to Knowledge

The study was able to identify knowledge gap of health workers on the use of current treatment guidelines in the management of febrile illnesses and had also identified factors that have mitigated access to National Guidelines for routine management of patients at the health facilities.

5.5 Suggested Areas for Future Researchs

(1) To determine the level of knowledge of health workers in case management of fever in Primary Health Centres in Ibadan, Oyo State

(2) Assessment of the role of Medical Laboratory in healthcare delivery.

(3) Assessment of clinical and Laboratory investigation of Febrile illnesses in health facilities in Ibadan, Oyo State.

(4) Assessment of variety of data reporting tools at Primary Healthcare Centres in Ibadan, Oyo State.

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Appendix I

Consent Form

Consent for Participation in Study

Description: I am Oyetunde Timon OYEBAMI, a final year post graduate student on MPH programme of Lead City University. I want to carry out a study on the management of febrile illness cases in PHCs in 4 selected LGAs within Ibadan.You will be asked to participate in a structured interview. This information may be shown at scientific meetings, published in a written format, or used to develop new education modules, diagnostic tools, or treatment protocols.

Time Involvement: Your participation will take approximately one hour.

Risks and Benefits: There is a minimal risk that can be associated with your participation in this study in case any information you provide can be directly linked to you. Study ID codes will be used to protect your identity from study directors, your employers, and the general public. There will be no dissemination of any identifying information alluding to who provided which responses and results will be presented without any identifying factors.

The benefits which may reasonably be expected to result from this study are a better understanding of what factors influence how you evaluate, diagnose, and treat children with fever. We will not provide individual instruction or feedback in order to protect your identity. We will, however, use this information for potential development of new education modules, diagnostic tools, and treatment protocols. We cannot and do not guarantee or promise that you will receive any benefits from this study**.** Your decision whether or not to participate in this study will not affect your employment or role in data collection for the current study.

Payments: You will not receive any payment for your participation.

Participant's Rights: If you have read this form and have decided to participate in this project, please understand your participation is voluntary and you have the right to withdraw your consent or discontinue participation at any time without penalty or loss of benefits to which you are otherwise entitled. The alternative is not to participate. You have the right to refuse to answer particular questions. The results of this research study may be presented at scientific or professional meetings or published in scientific journals. Your identity or any identifiable data will not be included in these results.

Contact Information:

Whom to Contact

Questions: In case you have any question about the study you can ask it. You can also raise your questions, concerns or complaints about this research, its procedures, risks and benefits, on that ground, you are free to contact the principal investigator with any information needed.

Oyetunde Timon OYEBAMI

Department of Public Health

Lead City University Ibadan, Oyo State

Livingvessel2002@gmail.com

OR

The Chairman Lead City Health Research and Ethic Committee

Lead City University Ibadan Oyo State

Email: lcu.hrec@lcu.edu.ng

Phone Number: 07033171050

I give consent to participate in this study.

Name of Participants: ________________________________

Signature or Thumb Print: ___________________

Date: ____

Name of Interviewer: _______________________________

Signature/Date: ____________________________________

Name of Witness (If Applicable): ____________________________

Signature/Thumb print and Date

Appendix II

Questionnaire (Study Tool)

Management of Febrile Illness Cases in Selected Primary Healthcare Centres in Ibadan, Oyo State

Email ………………………………………………………

1) Category of Health Centre (1) Community Health Centre (2) Primary Healthcare Centre (3) Health Post (4) Basic Health Post

2) Location of PHC: 1. Rural 2. Urban 3. Sub-Urban

3) Number of subcenters catered by the PHC (1) 0 (2) 0 – 4 (3) 4 – 8 (4) 9 - 12

4) Population covered by the PHC (latest) year (immunization) (1) $\leq$_2500 (2) 5000 - 10000

5) Whether the PHC functions for 24 hours: i. Yes ii. No

A. Sociodemographic

6) Designation of the respondent medical officer

i. Doctor

ii. Med. Lab. Scientist

iii. Nurse

iv. Pharmacist

v. Community Health Officers (CHO)

vi. Community Health Extension Workers (CHEW)

vii. Junior Community Health Extension Workers (JCHEW)

viii Mid-wife

vix Lab. Technologist

viii. Ward maid

ix. Other (specify)____

7) How old are you? (1) 20 – 25 (2) 26 – 30 (3) 31 – 40 (4) 41 – 50 (5) 51 – 55 (6) >60

8) Marital Status: i. Married ii. Single iii. Separated/Divorced iv. Widowed

9) Level of Education: i. Tertiary ii. Secondary school iii. Primary school iv. No formal education

10) Religious affiliation: i. Catholic ii. Anglican iii. Pentecostal iv. Islam v. African traditional religion

11) Have you had any training specific to?

Malaria? i. Yes ii. No

Typhoid/ Enteric fever i. Yes ii. No

Other febrile illnesses? i. Yes ii. No

12) If yes to any of the above, who ran it? ____

13) When/how often? ____

B. Priorities In Diagnostic Process

14) Which of the following is/are the first line of drug for treating malaria?

i. Chloroquine derivatives ii. S.-Pyrimethamine derivatives iii. Artesunate derivatives

iv. Herbal medicines v. Quinine derivatives vi. None

16) Which of the following is/are the most common route(s) of administration of anti-malarial drugs used for childhood malaria? i. Oral ii. Intra-muscular iii. Intra-venous iv. Rectal

17) Have you come across cases of resistance of malaria to any of the following anti-malarial drug(s)?

i. Chloroquine derivatives ii. S.-Pyrimethamine derivatives iii. Artesunate derivatives

iv. Quinine derivatives v. None

18) What do you think is/are responsible for malaria parasites resistant to antimalaria drug?

i. Drug abuse ii. Incomplete dosage iii. Fake drug iv. Mutation v. Other reasons

19) In how many cases do you seek laboratory diagnosis of malaria before treatment?

i. 1-3 persons in 10 cases ii. 4-6 persons in 10 cases iii. 7-10 persons in 10 cases

iv. >10 persons in 20 cases

20) What proportion of attendance at your PHC is due to malaria disease?

i. 0-20% ii. 21-50% iii. 51-70% iv. >70%

21) What is/are the common symptom(s) of malaria disease showed by children that visit the PHC?

i. Fever ii. Vomiting iii. Headache iv. Convulsion v. Cough/catarrh vi. Body pain vii. Loss of appetite viii. Nausea vix. Chill/Cold x. Abdominal pain xi. Anemia

22) What is/are the common symptom(s) of malaria disease showed by adults that visit the PHC?

i. Fever ii. Vomiting iii. Headache iv. Convulsion v. Cough/catarrh vi. Body pain vii. Loss of appetite viii. Nausea vix. Chill/Cold x. Abdominal pain xi. Anaemia

23) What are the most important things to look for when deciding how to diagnose a child who presents to the clinic with a fever?

i. Fever ii. Vomiting iii. Headache iv. Convulsion v. Cough/catarrh vi. Body pain vii. Loss of appetite viii. Nausea vix. Chill/Cold x. Abdominal pain xi. Anaemia

24) What symptoms make you the most concerned about a patient?

i. Fever ii. Vomiting iii. Headache iv. Convulsion v. Cough/catarrh vi. Body pain vii. Loss of appetite viii. Nausea vix. Chill/Cold x. Abdominal pain xi. Anaemia

25) What are other potential diagnoses that you look for when you determine that a child with fever does not have malaria? (1) Clinical diagnosis (2) Mrdt (3) Microscopy

26) Which of the following is/are the first line of drug for treating typhoid?

27) i. ciprofloxacin ii. Chloramphenicol iii. Ampicillin iv. Azithromycin (v) Ceftriaxone

28) Which of the following is/are the most common route(s) of administration of antibiotics used for typhoid? i. Oral ii. Intra-muscular iii. Intra-venous iv. Rectal

29) Have you come across cases of resistance of typhoid to any of the following antibiotics?

i. ciprofloxacin ii. Chloramphenicol iii. Ampicillin iv. Azithromycin

30) What do you think is/are responsible for typhoid resistant to antibiotics?

i. Drug abuse ii. Incomplete dosage iii. Fake drug iv. Mutation v. Other reasons____________

31) In how many cases do you seek laboratory diagnosis of typhoid before treatment?

i. 1-3 persons in 10 cases ii. 4-6 persons in 10 cases iii. 7-10 persons in 10 cases

iv. >10 persons in 20 cases

32) What proportion of attendance at your PHC is due to typhoid?

i. 0-20% ii. 21-50% iii. 51-70% iv. >70%

33) What is/are the common symptom(s) of typhoid showed by children that visit the PHC?

i. Fever ii. Vomiting iii. Headache iv. Convulsion v. Cough/catarrh vi. Body pain vii. Loss of appetite viii. Nausea i×. Chill/Cold ×i. Abdominal pain ×ii. Anaemia

34) What is/are the common symptom(s) of typhoid showed by adults that visit the PHC?

i. Fever ii. Vomiting iii. Headache iv. Convulsion v. Cough/catarrh vi. Body pain vii. Loss of appetite viii. Nausea i×. Chill/ Cold ×i. Abdominal pain ×ii. Anaemia

35) What symptoms make you the most concerned about a patient? i. Fever ii. Vomiting iii. Headache iv. Convulsion v. Cough/catarrh vi. Body pain vii. Loss of appetite viii. Nausea i×. Chill/ Cold ×i. Abdominal pain ×ii. Anaemia

36) What are other potential diagnoses that you look for when you determine that a child with fever does not have typhoid? (1) Clinical diagnosis (2) Mrdt (3) Microscopy

C. Diagnostic Procedure and Tools

37) What diagnostic tools do you have at the clinic to use when you see a patient with fever?

(1) Mrdt (2) Microscopy (3)Culture media (4) Serology(widalrxn)

38) Which ones do you find most useful? (1) Mrdt (2) Microscopy (3)Culture media

(4) Serology(widalrxn)

39) Why? (1) Highly sensitive (2) Simple technique (3) Affordable (4) Reliable

(5) Cost effective (6) Reduce Turn-Around-Time

40) In what ways can healthcare be improved upon in this facility? ____

D) Factors That Facilitate the Adoption of Treatment Guidelines in Phc

41) Have you ever seen or in possession of the National Guideline for treatment and diagnosis of malaria as signed by Hon Minister for Health? Yes ( ), No( )

42) If yes which edition of the guidelines, do you have? 2007 edition, 2015 edition, 2020 edition. None

43) If No, kindly state the reason for not having access to this document ------

44) Have you ever participated or heard about the dissemination of national guidelines for treatment and diagnosis of malaria? Yes() , No( ).

45.) Which of these factors prevent you from accessing the online /e-copy of national guidelines on treatment and diagnosis of malaria:

1. Access to the internet ( )

2. Inability to use smartphone ( )

3. Lack of computer system ( )

4. Lack of training in IT ( )

5. Workload ( )

6. User's computer skill ( )

7. Lack of technology support ( ).

8. None

Appendix III

Bio –Data

Full Name:	Oyetunde Timon OYEBAMI
Address:	No. 3, Popoola Street, Bolumola Area, Ibadan. Oyo State
E-mail Address:	livingvessel2002@gmail.com
Phone No:	8034002918
Date of Birth:	5th February, 1979
Place Birth:	Ibadan
Nationality:	Nigerian
Next of Kin:	Oyebami Olusola Omoyemi
Address:	No. 3, Popoola Street, Bolumola Area, Ibadan. Oyo State

Education Background:

Medical Laboratory Science	2000
MPH in Epidemiology (Lead City University Ibadan	2020-2020

Work Experience:

NYSC **-** Federal Medical Centre, Calabar	2001
Oyo State Primary Healthcare Board	2006 – till date
EQA- Quality Assurance Officer (QA) Oyo State on State malaria Elimination program (SMEP)	2014 - till date
Presidential Malaria Initiatives- USAID	2012-2022
Consultancy- Walter Reed Army Institute of Research (WRAIR)	2016 - till date
Facilitator - PMIS/MSH	2021 - till date

University Compliance Certificate

This is to certify that the thesis by Oyetunde Timon OYEBAMI, with the Matric Number **LCU/PG/001965** in the Department of Public Health, Faculty of Basic Medical and Applied Sciences, Lead City University Ibadan, is in full compliance with the approved University format and style.

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Signature Date