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FEVER IN FAMILY PRACTICE

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Abstracts:

Introduction: *Fever is considered a physiologic response characterized by an increase in the body temperature beyond the normal variant, It is considered as one of the most common causes for pediatric consultation, It is estimated that about twenty percent of the consultations in family medicine, primary care as well as emergency departments' visits. Fever could be concerning to parents and physicians, however the prevalence of serious infections in children is typically small. It is suggested that around less than one percent in family practice settings in developed countries. But this number could increase up to twenty five percent in the emergency departments.*

Methodology: *We did a systematic search for fever in children and fevers of unknown origins using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.*

Aim of the study: *In this study we will review the fever in pediatric population in family medicine practice*

Conclusion: *Assessment and treatment of fever in children may be improved by appropriate clinical practices. The worth and cost effectiveness of existing clinical prediction rules and guidelines in determining the risk of serious illness in febrile children should be better assessed. Studies integrating both in-hospital and post-discharge phases of children assessment are needed, particularly evaluating the reliability of parents in assessing the progression of illness and the efficacy of safety-netting strategies. Fevers of unknown origin continue to be one of the most difficult diagnostic challenges in medicine. Because fever of unknown origin may be caused by over two hundred malignant/neoplastic, infectious, rheumatic/inflammatory, and miscellaneous disorders, clinicians often order non-clue-based imaging and specific testing early in the fever of unknown origin work-up, which may be inefficient/misleading.*

Key words: *Fever, fever in family practice, fever of unknown origin*

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INTRODUCTION:

Fever is considered a physiologic response characterized by an increase in the body temperature beyond the normal variant [1], It is considered as one of the the most common causes for pediatric consultation, It is estimated that about twenty percent of the consultations in family medicine, primary care as well as emergency departments' visits [2].

Fever could be concerning to parents and physicians, however the prevalence of serious infections in children is typically small. It is suggested that around less than one percent in family practice settings in developed countries [3]. But this number could increase up to twenty five percent in the emergency departments [4]. In this study we will review the fever in pediatric population in family medicine practice

METHODOLOGY:

We did a systematic search for fever in children and fevers of unknown origins using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: fever, pediatric population, fever of unknown origins, family practice.

2. Measurement of Fever in Children

The physiological normal temperature is subjected to many variations. There are many factors affect the body temperature, including but not limited to time of the day [5]; activity; food intake; age [6]; and menstrual cycle. In infants, the core temperature could be as low as thirty-six during nocturnal sleep, however it could increase up to 37.8 ◦C in active times of the day. This inconsistency prevents the identification of a single universal limits of normal; so, fever could be defined as a thermoregulated increase in the body temperature beyond normal daily variation. But, for clinical and research purposes, fever is usually recognized as a core temperature of 38 ◦C or more.

The body temperature could be measured in different anatomical areas of the body such as the axilla, rectum, mouth, skin, and ear. There are significant changes in each measurement sites [7]. Rectal temperature is recognized to be the most reliable for estimating core body temperature. However, its usage is discouraged by many guidelines because of its [8]. Moreover, it is contraindicated in neutropenic or immunocompromised children [9]. There are other measurement sites which are less reliable than rectal temperature however they could be used in clinical practice. The oral temperature is recognized to be one of the most reliable anatomical sites, though it is on average 0.5 ◦C less than rectal temperature. But it is not suitable for children under five years of age, and some kids could find it uncomfortable. The axillary temperature measurement could be recognized a viable substitute. In newborns, the axillary temperature has been concluded to be as accurate as rectal temperature. Clinically, an axillary temperature is recognized to be abnormal when it is beyond 37.5 ◦C. The recommendations differ on the best site for temperature measurement in pediatric population. The National Institute for Health and Care Excellence (NICE) guidelines suggest measuring body temperature in the axilla, using an electronic thermometer for kids younger than four weeks of age and chemical dot or electronic thermometers in older children, However the American Academy of Pediatrics recommends rectal thermometry for kids less than 4 years of age and oral thermometry in older kids. Eventually, even though it is subjected to the observer differences, parental report of tactile fever should never be dismissed. A study that comparison of more than three hundred children with fever concluded that mothers could reliably detect fever by tactile assessment (sensitivity more than eighty percent, specificity around seventy five percent) [10].

3. Increased Body Temperature as a Diagnostic Sign

In any abnormal elevation of body temperature, the kid should be evaluated as a potential symptom of an underlying disease. Fever reflects an increase in body temperature occurs by an alteration of the hypothalamic temperature set-point because of exposure to the endogenous pyrogens. While hyperthermia happens when there is an increase in body temperature because of a failure of thermoregulation system, either because of increased heat absorption, heat production and/or reduced ability to dissipate it. Cases of hyperthermia are usually due to environmental one, due to heat exposure, which overwhelms the body's thermoregulation capabilities, this is common in "forgotten baby syndrome" when the kids are left in cars during hot season [11].

"Heat stroke" is known as a core temperature ≥ forty ◦C accompanied by central nervous system dysfunction due to environmental heat exposure [12]. The young kids have less effective heat dissipation system, in comparison to the older kids as well as the adults. Other factors that predispose the kids to heat

stroke include but not limited to conditions characterized by excessive fluids loss or that adversely affect water-electrolyte balance such as gastrointestinal illness, diabetes insipidus, and diabetes mellitus [13]. Other causes than environmental factors, could be directly caused by conditions resulting in abnormal thermoregulation or increased heat production. The central nervous system circumstances including insults to the hypothalamus could lead to temperature dysregulation and hyperthermia. Other important causes involve status epilepticus, thyrotoxicosis, and genetic syndromes linked to abnormal thermoregulation. Neuroleptic malignant syndrome is considered as a severe idiosyncratic reaction to antipsychotic medications, however also antiemetic medications such as metoclopramide, known for altered mental status, muscular rigidity, movement disorders, hyperthermia and autonomic dysfunction [14]. The malignant hyperthermia is a rare genetic disorder linked to many forms of congenital myopathy and triggered by succinylcholine or inhalational anesthetics agents; clinical features involve rapid onset of extremely high temperature, often heralded by masseters spasm, muscle rigidity, metabolic acidosis, and hemodynamic collapse. Specific management plan, with stopping of involved anesthetics, muscular relaxation with sodium dantrolene, and correction of metabolic acidosis, has effectively decreased the mortality rates.

Although the elevation of fever does not necessarily reflect the severity of the illness, there is an association with a greater likelihood of SBI for temperatures > thirty-nine ◦C. In a new study on more than twelve thousand children with febrile illness, fever >thirty-nine ◦C was linked to an increased risk of SBI, particularly in infants under six months of age [15]. But this cut-off still missed around eighty percent of SBI incidents; So, lower temperatures could not be considered reassuring.

The Value of Associated Clinical Findings

Collecting information as much as possible in the first, hands-off, phase of the visit is pivotal. Physical signs like pallor, mottled appearance, ashen or blue skin color, reduced activity (poor feeding, no smile, decreased response to stimuli, lethargy, weak high-pitched cry), tachypnea, capillary refill time >3 s, and a reduced urine output are all concerning for SBI ("red flags") , and should prompt a thorough evaluation. The meaning of some of them, however, may be put in context.

Tachypnea: though the WHO criteria for the diagnosis of pneumonia involve tachypnea alone, isolated tachypnea is a very poor indicator of pneumonia in the presence of wheezing. Moreover, fever could be itself alter respiratory rate and heart rate [16].

Non-blanching rash: though a non-blanching rash should often raise concern, well-appearing children with fever and petechiae (small, non-blanching, macular hemorrhagic skin spots<2 mm in diameter) are still at low risk of SBI.

In a study series of about four hundred patients between three and thirty-six months of age, none of the 357 well-appearing children had SBI, but six out of fifty-three ill-appearing children had SBI. Night sweats are a comparatively nonspecific symptom [17]. But, their presence in the context of prolonged and unexplained febrile illness should raise concern for occult infectious such as tuberculosis, and endocarditis. Eventually, clinician's intuition that has been also established to be of diagnostic importance. It likely imitates a gestalt evaluation of several clinical aspects that can be appreciated in the first, no touch approach to the ill child. These aspects have been further characterized and systematized. Nevertheless, gut feeling does not eliminate full clinical evaluation and prudent management; so, its importance could be to raise clinical suspicion in unclear situations rather than to forego proper standard evaluation [18].

Fever of Unknown Origin classes:

Prolonged fevers have been diagnostically problematic. There are a few infections are associated with prolonged fevers. Petersdorf and Beeson [19] developed criteria for prolonged fevers, that is, fever of unknown origin, defined as fever 38.3C for more than three weeks. Fever of unknown origin work-ups may be done as an outpatient. Petersdorf also classified fevers of unknown origin by category, that is, infectious, malignant/neoplastic, rheumatic/inflammatory, and miscellaneous disorders. Fevers of unknown origin could also be well-thought-out in the context of host subsets, for example, organ transplants, human immunodeficiency virus, returning travelers. It needs a focused fever of unknown origin-relevant history, physical examination, and selective nonspecific laboratory tests rather than excessive over testing [20].

Diagnostic Approach to Classic Fever of Unknown Origin

First of all, it is recommended to confirm the prolonged fever meets the fever-of unknown-origin definition [21]. The fever-of-unknown origin work-

up should be symptom (history) and sign (physical examination) driven. Secondly history and physical can provide clues. Thirdly within the fever-of-unknown-origin category, try to determine the pattern of organ involvement. Each disorder has a typical pattern of organ involvement that suggests the differential diagnosis. As an example, pattern of organ involvement of systemic lupus erythematosus includes multiple organs but highly, spares the liver. The most difficult fevers of unknown origin have no localizing signs [22].

HISTORY:

Malignant/Neoplastic Disorders.

Significant weight loss (more than lbs/week), especially if go with early anorexia, is a hallmark of malignant/neoplastic fevers of unknown origin. Post-hot bath pruritus proposes a malignant/neoplastic disorder. A malignant/neoplastic fever of unknown origin should be considered in those with a history of adenopathy or malignancy. Infectious Diseases. The history should include prior/ invasive procedures or surgeries (abscesses), dentition (apical abscesses, subacute bacterial endocarditis), antecedent/concomitant infections, and tuberculosis. Animal or pet contact suggests Q fever, brucellosis, toxoplasmosis, cat scratch disease, or trichinosis. Mosquito or tick exposure suggests ehrlichiosis/anaplasmosis, babesiosis, or malaria, while rodent exposure suggests rat bite fever, relapsing fever, or leptospirosis. Blood transfusions could be a vital sign to ehrlichiosis/anaplasmosis or human immunodeficiency virus [23].

Rheumatic/Inflammatory Disorders.

History is extremely important in inflammatory conditions. With arthralgias/myalgias, a rheumatic/ inflammatory fever of unknown origin is probable, but chills go against a rheumatic/inflammatory cause. Dry cough also may be a sign of giant cell arteritis/temporal arteritis. With a fever of unknown origin, oral ulcers propose Behçet's syndrome or systemic lupus erythematosus. A history of acalculous cholecystitis in a fever of unknown origin is an easily overlooked clue of systemic lupus erythematosus or periarteritis nodosa [24].

Miscellaneous Disorders.

If the history does not propose a specific group, miscellaneous causes of fever of unknown origin should be considered. Periodic fever may be the only clue to cyclic neutropenia. Neck/jaw pain, mistaken for dental pain may be a sign to subacute thyroiditis. Factitious fever is common in medical personnel [22].

Physical Examination

Malignant/Neoplastic Disorders.

Hectic fevers of lymphoma could reflect infection [25]. Bradycardia may accompany lymphoma or central nervous system cancers. Eye examination could be helpful; Roth spots (lymphoma, atrial myxoma), cytoid bodies (atrial myxoma), or retinal hemorrhages (preleukemia). A murmur is an important clue in subacute bacterial endocarditis, noninfectious culture-negative endocarditis, for example, marantic endocarditis or atrial myxoma. if there's sternal tenderness it could reflect a bone marrow disorder [26].

Infectious Diseases.

The method to diagnose infectious fevers of unknown origin starts with fever pattern analysis. Morning temperature spikes propose miliary tuberculosis, typhoid/enteric fever, or Whipple's disease. Relative bradycardia is a basic outcome in typhoid/enteric fever, malaria, babesiosis. double quotidian fevers occurs twice daily fever spikes propose malaria, miliary tuberculosis, or visceral leishmaniasis.

Two fever peaks per week (camel back fever curve) could be one of the few clues to ehrlichiosis/ anaplasmosis, leptospirosis, brucellosis, or rat bite fever. Fundoscopic findings may be a clue to toxoplasmosis, tuberculosis, histoplasmosis, or cat scratch disease [27].

Rheumatic/Inflammatory Disorders.

Morning temperature points are a significant sign to periarteritis nodosa whereas a double quotidian fever is an important finding in adult Still disease. In a fever of unknown origin, rash could suggest sarcoidosis, systemic lupus erythematosus, or adult Still's disease. Unequal pulse suggests Takayasu's arteritis. Lacrimal gland enlargement is a sign to late-onset rheumatoid arthritis, sarcoidosis, or systemic lupus erythematosus. External eye/fundi may provide many diagnostic signs in rheumatic/inflammatory fevers of unknown origin, for example, cytoid bodies, Roth spots in (systemic lupus erythematosus, periarteritis nodosa). In a fever of unknown origin, oral ulcers propose Behçet's disease or systemic lupus erythematosus. Lymphadenopathy proposes systemic lupus erythematosus, late-onset rheumatoid arthritis, or sarcoidosis. In a fever of unknown origin with systemic lupus erythematosus, a murmur with negative blood cultures suggests possible Libman-Sacks endocarditis. Hepatomegaly without

splenomegaly argues against a rheumatic/inflammatory fever of unknown origin etiology. Epididymitis/epididymal nodules are subtle clues to periarteritis nodosa, systemic lupus erythematosus, or sarcoidosis. Miscellaneous Disorders. Miscellaneous fevers of unknown origin are more likely to be diagnosed by historical clues rather than physical findings. Relative bradycardia is a clue to drug fever or factitious fever. Lipemia retinalis might be the only sign of hypertriglyceridemia. Lymphadenopathy might be due to pseudolymphoma or hyper-IgD syndrome. Cirrhosis is an often-overlooked cause of fever of unknown origin. Splenomegaly is an important clue to regional enteritis, cirrhosis, or hyper-IgD syndrome [28].

Therapy of Fever of Unknown Origin

Fevers of unknown origin represents a diagnostic challenge and not a therapeutic problem. Until a definite fever-of-unknown origin diagnosis, antipyretic or antimicrobial therapy may mask, delay, or obscure clinical manifestations and should be avoided. Empiric therapy is prudent in a few difficult-to-diagnose life-threatening fevers of unknown origin [22].

CONCLUSIONS:

Assessment and treatment of fever in children may be improved by appropriate clinical practices. The worth and cost effectiveness of existing clinical prediction rules and guidelines in determining the risk of serious illness in febrile children should be better assessed. Studies integrating both in-hospital and post-discharge phases of children assessment are needed, particularly evaluating the reliability of parents in assessing the progression of illness and the efficacy of safety-netting strategies.

Fevers of unknown origin continue to be one of the most difficult diagnostic challenges in medicine. Because fever of unknown origin may be caused by over two hundred malignant/neoplastic, infectious, rheumatic/inflammatory, and miscellaneous disorders, clinicians often order non-clue-based imaging and specific testing early in the fever of unknown origin work-up, which may be inefficient/misleading.

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