The symptomatology of fever: A step towards qualitative definition of fever.

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The symptomatology of fever: A step towards qualitative definition of fever

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The old definitions of fever are based on cross-sectional surveys of the population without analyzing the associated symptomatology as fever is a sign, not symptom. Therefore, a longitudinal follow-up study is the need of hour to analyze associated symptoms with fever.

In a longitudinal study over one year, 196 participants recorded three temperature readings daily, one after waking up, one between 12 and 3 PM, one before sleeping, and filled the symptomatology questionnaire in a thermometry diary.

Per protocol analysis was done for febrile participants (n = 144). Fatigue (50.3%), warmth (47.3%), headache/head heaviness (47.0%), feeling malaise/general weakness (46.7%), loss of appetite (46.5%), muscle cramps/muscle aches (45.6%), chills/shivering (44.6%), increased sweating (43.0%), nausea (42.5%), irritability (38.9%), increased breathing rate (37.1%), and restlessness/anxiety/palpitations (36.5%) were the symptoms maximally seen during the febrile phase. A higher number of associated symptoms are associated with higher temperature readings. Dehydration suggested the numerically highest temperature values (100.86 ± 1.70°F) but seen in few febrile patients.

Incorporation of symptom analysis in febrile patients is the need of the hour. Fatigue and warmth are found to be the most prevalent symptoms during febrile phase. Associated symptoms can help in predicting the intensity of fever also.

temperature recording

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Fever has long been regarded as an important vital sign. Humans maintain their standard body temperature in a narrow range for the smooth functioning of the body.[

<mark>The ideal way to define fever is to follow-up healthy subjects prospectively.</mark> Moreover, when such individuals develop rise in baseline temperature with associated symptoms, fever is set to begin.

Thereby, in the study, we recruited healthy participants and longitudinally followed them up and analyzed their temperature in association with their symptoms that were present at that time. We analyzed which symptomatology suggested fever and whether there was any relationship between number of symptoms and the absolute temperature values.

A longitudinal study was conducted in a tertiary care hospital from July 2019 to September 2020. A sample size of 192 was calculated based on a prior study done by Mackowiak

The <mark>study was conducted in three phases: Non-febrile, febrile, and post-febrile phase.</mark> The participants recorded their temperature readings in all three phases. Minimum three oral temperature readings were recorded daily, one after waking up (AM), one between 12 and 3 PM (AN), and one before sleeping (PM). Participants filled a questionnaire related to the symptomatology of fever along with every temperature recording in provided clinical thermometry diary [

Supplemental Material 1

The febrile phase data were analyzed as per-protocol analysis (for those participants only who developed the febrile phase during the study) using Statistical Package for Social Sciences (SPSS) Version 23. The frequency distribution of the various symptoms associated with fever was analyzed. The <mark>association of absolute values of temperature with the various symptoms was also done.</mark> Taking confidence interval as 95%, a

The study screened 350 participants, and 144 were included in the analysis. The mean age of the participants was 24.24 ± 5.92 years (8-58 years). 26% (36) were <20 years, 72.1% (104) were in the age group 20-40 years, and 1.9% (4) were >40 years of age. 52.1% (75) were males. Various symptoms were present during the febrile phase, arranged in descending order [

Symptomatology of three temperature phases among participants (

(a and b): Box and Whisker plots: Association between febrile symptoms and temperature readings

We found that fatigue is the most common symptom associated with the febrile phase (50.3%), followed by warmth (47.3%). The febrile phase was associated with at least one symptom in 98.5% of the readings, whereas ≥ two were seen in 95.8%. The number of symptoms seen in various phases was: 0.01 ± 0.08 (non-febrile), 6.08 ± 2.42 (febrile), and 0.07 ± 0.36 (post-febrile) (P < 0.001). One symptom was confirmly present when mean temperature was 99.91 ± 1.55°F, while mean temperature for two associated symptoms was 100.22 ± 1.46°F. As per our knowledge, no other study has analyzed

the symptoms associated with fever.

As per classical teaching, fever is defined as an early morning temperature of >37.2°C (>98.9°F) or an evening temperature of >37.7°C (>99.9°F).[

It is essential to derive a symptom-based definition of fever, where patients can be taught about a specific set of symptoms to look out for, suspecting fever. In the present scenario of COVID-19, it gathers more importance as due to the shortage of amenities, even thermometers cannot be ensured in every nook and corner. Hence, the patients can lookout for a few symptoms which may most likely predict fever. The present study confirms fatigue is most common associated symptom (50.3%) during febrile phase followed by warmth (47.3%), headache/head heaviness (47.0%), feeling malaise/generalized weakness (46.7%), loss of appetite (46.5%), muscle cramps/muscle aches (45.6%), chills/shivering (44.6%), increased sweating (43.0%), nausea (42.5%), irritability (38.9%), increased breathing rate (37.1%), and restlessness/anxiety/palpitations (36.5%).

The presence of ≥ two symptoms was associated with higher temperature readings (100.22°F) compared to just one symptom (99.91°F). Similarly, dehydration correlated with higher temperature (100.86°F) followed by increase in breathing rate (100.61 ± 1.38°F). These findings can help in the early prediction of patients having a higher temperature and more likely to get sick. This may help in triaging the patients in the presently overburdened scenario of the COVID-19 pandemic also.

Our study has limitations too. Subjects were allowed to take antipyretics; hence, the symptoms could have resolved post drug use. The categorization among phases (febrile and non-febrile) was based on subjective parameters, varying from person to person. However, this itself forms the basis of our study as we propose that fever must be defined based on an individual's assessment of the symptoms. Future studies may establish objective measurements of these associated symptoms.

Fever must not be defined as a mere rise of temperature, as this may occur physiologically also. As fever is a sign, various symptomatology of fever should be defined. Fatigue is found to be the most prevalent symptom (50.3%) during febrile phase followed by warmth, headache, malaise, loss of appetite, muscle aches, chills, increased sweating, nausea, irritability, increased breathing rate, and palpitations. Simultaneously higher rise in temperature is associated with more number of symptoms, thus predicting the intensity of fever.

Fever is a sign, not a symptom.

Symptomatology of fever should be defined.

Fatigue is the most prevalent symptom during febrile phase.

Greater rise in temperature correlates with more symptoms, thereby predicting the intensity of fever.

Ethics and data sharing

The study was done after institute ethical approval and as per declaration of Helsinki. After obtaining approval from corresponding author, de-identified data can be shared.

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Physiology, Ovulation, Basal Body Temperature

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