

Amos Grünebaum*, Frank A. Chervenak, Laurence B. McCullough, Joachim W. Dudenhausen, Eran Bornstein and Philip A. Mackowiak

How fever is defined in COVID-19 publications: a disturbing lack of precision

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Abstract

Objectives: Fever is the single most frequently reported manifestation of COVID-19 and is a critical element of screening persons for COVID-19. The meaning of “fever” varies depending on the cutoff temperature used, the type of thermometer, the time of the day, the site of measurements, and the person’s gender and race. The absence of a universally accepted definition for fever has been especially problematic during the current COVID-19 pandemic.

Methods: This investigation determined the extent to which fever is defined in COVID-19 publications, with special attention to those associated with pregnancy.

Results: Of 53 publications identified in which “fever” is reported as a manifestation of COVID-19 illness, none described the method used to measure patient’s temperatures. Only 10 (19%) publications specified the minimum temperature used to define a fever with values that varied from a 37.3 °C (99.1 °F) to 38.1 °C (100.6 °F).

Conclusions: There is a disturbing lack of precision in defining fever in COVID-19 publications. Given the many factors influencing temperature measurements in humans, there can never be a single, universally accepted temperature cut-off defining a fever. This clinical reality should not prevent precision in reporting fever. To achieve the precision and improve scientific and clinical communication,

when fever is reported in clinical investigations, at a minimum the cut-off temperature used in determining the presence of fever, the anatomical site at which temperatures are taken, and the instrument used to measure temperatures should each be described. In the absence of such information, what is meant by the term “fever” is uncertain.

Keywords: covid-19; fever; pregnancy; temperature; thermometer.

Introduction

Physicians since antiquity have regarded fever as an entity worthy of unremitting attention, and for nearly two centuries have had instruments with which to verify its existence. Given the medical profession’s intense interest in fever since time immemorial, one would expect there to be a universally accepted definition of the entity. In physiological terms, there is such a definition: “a state of elevated core temperature, which is often, but not necessarily, part of the defensive response of multicellular organisms to invasion by live microorganisms or inanimate matter recognized as pathogenic or alien by the host” [1, 2]. Unfortunately, this particular definition is clinically useless, because lack of agreement as to the meaning of “a state of elevated core temperature.” Despite millennia of clinical attention devoted to elevated body temperatures, no universally accepted thermal definition of fever exists to this day.

The absence of such a universally accepted definition has been especially problematic during the current COVID-19 pandemic. “Fever” is the single most frequently reported manifestation of the illness and, as such, its detection is a critical element of programs screening persons for the infection. In one of the earliest published series of COVID-19 cases, Huang [3], detected fever in 40 of 41 (98%) of cases, cough in 31 (76%), and myalgia or fatigue in 18 of 41 (44%). In another report by Guan [4], 43.8% of COVID-19 cases were febrile on admission to hospital, whereas 88.7% were febrile at some time during the hospitalization. In pregnant women infected with COVID-19 fever has been equally common. In a review of 13 publications concerned with the infection in pregnant women,

*Corresponding author: Prof. Amos Grünebaum, Department of Obstetrics & Gynecology, Lenox Hill Hospital, New York, NY, USA; and Zucker School of Medicine at Hofstra/Northwell, New York, NY, USA, E-mail: amosgrune@gmail.com

Frank A. Chervenak, Laurence B. McCullough and Eran Bornstein, Department of Obstetrics & Gynecology, Lenox Hill Hospital, New York, NY, USA; and Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY, USA

Joachim W. Dudenhausen, Faculty of Health Sciences, Joint Faculty of University Potsdam, B-TU and MHB, Germany

Philip A. Mackowiak, Department of Medicine, University of Maryland School of Medicine, Emeritus Professor of Medicine and the Carolyn Frenkil and Selvin Passen History of Medicine Scholar-in-Residence at the University of Maryland School of Medicine, Baltimore, ML, USA

fever, along with cough and chest pain were the most common manifestations of the illness [5, 6].

While universally accepted normal ranges have been established for other vital signs, temperature continues to be a notable exception. There is no agreement as to the upper limit of the normal temperature range in humans (i.e., the temperature that defines the lower limit of the febrile range). Moreover, publications involving “febrile” patients rarely include a definition of fever or the method and anatomic location employed in measuring patients’ temperatures. These oversights are critical, given the fact that patients’ temperatures vary according to the location at which measurements are taken (e.g., oral, tympanic, axillary, rectal, skin), the type of thermometer used (e.g., contact, non-contact, handheld thermal scanner), time of day, and patients’ gender and race [7, 8].

A reliable means of detecting the presence of fever is especially important during pregnancy, because of its relevance not just to the health of the mother, but also that of the fetus and in turn, that of the newborn baby. Pregnant women’s temperatures are routinely taken on admission to the labor and delivery suite [9]. However, given the complexities surrounding patients’ temperatures described above and the absence of a universal definition of what constitutes a “fever,” interpretation of such measurements with regard to the febrile state is far from straight forward.

In undertaking this investigation, we sought to determine the extent to which fever is defined and the methods used to measure patients’ temperatures are described in published reports of COVID-19-infected patients in general and pregnant women in particular. Given that detection of fever is the principal method used to screen persons for COVID-19 (and for that matter infections in general), and that fever is the most common symptom reported in COVID-19 patients, we believe that such information should be included in every publication concerned with the clinical characteristics of the infection.

Methods

We conducted a literature search using PubMed and Google Scholar, covering the period January 2020 to June 2020. We focused on pregnancy during the COVID-19 pandemic because of its growing clinical significance world-wide and also to limit our search to a manageable size. Publications considered for analysis were identified by the presence of the following search terms in the title or abstract: COVID **OR** coronavirus **OR** SARS-CoV-2 **AND** pregnancy. We also reviewed other online coronavirus/COVID-19 publications cited frequently in the COVID-19 pregnancy literature. Publications mentioning an elevated temperature or fever as a manifestation of COVID-19 were examined for their definition of fever (i.e., a specific temperature defining the lower limit of the febrile

Table 1: Fever cut-off for COVID-19 pregnant patients.

Temperature cut-off defining a fever	Measurement site ^a	Source
≥37.3 °C (≥99.2 °F)	NG	Yang H et al. [10]; Chen Y, et al. [11]
>37.5 °C (>99.5 °F)	NG	Mao et al. [12]; Chen S, et al. [48]; González R, et al. [14]
>37.5 °C (>99.5 °F)	NG	Chen et al. J [11]
≥37.6 °C (≥99.7 °F)	NG	Liu, Y et al. [13]; Liu D, et al. [15]
≥37.8 °C (≥100 °F)	NG	Breslin N et al. [16]
≥38.0 °C (≥100.4 °F)	NG	Acog.org accessed 7/6/2020; Ellington S, et al. MMWR Morb Mortal Wkly Rep 2020 [18]
>38.0 °C (>100.4 °F)	NG	Richardson et al. JAMA 2020 [17];

^aNG, not given.

range) and a description of the method used in measuring patients’ temperatures (i.e., instrument used and anatomic site examined).

Results

Three hundred thirty-four publications with COVID **OR** coronavirus **OR** SARS-CoV-2 **AND** pregnancy in the abstract or title were identified. Of these, 53 included the term “fever” [10–35] [36–62] as a manifestation of COVID-19. None of these 53 publications (0/53) described the method used in measuring patients’ temperatures. Only 10/53

Table 2: Fever cut-off for COVID-19, non-pregnant patients.

Temperature cutoff defining a fever	Measurement site ^a	Reference
≥37.0 °C (≥98.6 °F)	Axilla	Zhuang SF, et al. [63]
≥37.2 °C (≥99 °F)	NG	Liu Y, et al. [64]
≥37.3 °C (≥99.2 °F)	NG	Na Du, et al. [65]
>37.3 °C (>99.2 °F)	NG	Lauxmann MA [66]
≥37.5 °C (≥99.5 °F)	Axilla	Guan W, et al. [4]; González R, et al. [14]; Ciceri F, et al. Clin Immunol 2020 [67]
>37.5 °C (>99.5 °F)	NG	Mao B, et al. [12]
>37.8 °C (>100 °F)	NG	Brill SE, et al. BMC Med 2020 [68]; Chen/Guo [55]
≥38.0 °C (≥100.4 °F)	NG	Mitra B, et al. Emerg Med Australas 2020 [69]
≥38.0 °C (≥100.4 °F)	Oral	Alsofayan YM, et al. J Infect Public Health 2020 [70]
>38.0 °C (>100.4 °F)	NG	Hashmi HAS, Asif HM [71]
		Pongpirul WA, et al. [72]; Okoh AK, et al. [73]
>38.5 °C (>101.3 °F)	NG	Li TZ, et al. [74]

^aNG, not given.

Table 3: Fever cut-off for non-COVID-19, pregnant patients.

Fever definition	Measurement site	Measurement site reference
Morning: >37.2 °C (98.9 °F) or >37.7 °C (>99.9 °F)	Oral	https://www.uptodate.com/contents/pathophysiology-and-treatment-of-fever-in-adults [75]
>37.8 °C (>100.0 °F)	NG	Romero et al. [76]; Yoon [77]
≥38 °C	NG	Towers et al. [79]
>38 °C (>100.4 °F)	NG	Hospital-based Triage of obstetric patients ACOG Committee Opinion number 667; July 2016 [80]

Table 4: Fever cut-off for non COVID-19, non-pregnant patients.

Fever definition	Measurement site	Measurement site reference
37.7 °C (99.9 °F) upper limit normal	Oral	Mackowiak [81]
38.0 °C (100.4 °F) upper limit normal	Axilla	Wunderlich [82, 83] ^a
≥38.3 °C (101 °F), A-M >37.2 °C (>98.9 °F) or P-M >37.7 °C (>99.9 °F)	NG	Laupland [84]
There is not a single agreed-upon upper limit for normal temperature with sources using values between 37.2 and 38.3 °C (99.0 and 100.9 °F) in humans	Oral	Dinarelli [85]
≥38.0 °C (≥100.4 °F)	NG	Wikipedia [86]
		CDC [78]

^aWunderlich's thermometers were calibrated 1.6–1.8 °C (2.9–3.2 °F) higher than current thermometers (7).

(19%) specified a minimum temperature used to define fever. Of those COVID-19/Pregnancy publications giving a minimum temperature used to define fever, values varied from a low of 37.3 °C (99.1 °F) to a high of 38.1 °C (100.6 °F) (Table 1). Similarly varied minimum temperatures used to define fever appeared in publications dealing with COVID-19-related fevers in non-pregnant patients (Table 2), in publications dealing with non-COVID-19-induced fevers in pregnant patients (Table 3), and in non-COVID-19/no pregnancy publications (Table 4).

Discussion

Our investigation revealed that, whereas most COVID-19 publications identify fever as a cardinal manifestation of

the illnesses, a distinct minority of such publications gives the minimum temperature used to define fever. Almost none, including those containing a definition of fever, describes the method used to measure patients' temperatures. In effect, the authors of these publications, including a recent review of the pathophysiology of COVID-19 [86] almost universally ignore the clinical reality that patients' temperatures vary according to the site at which measurements are made, by the type of thermometer used, by time of day, by the patient's age, and whether the patient is pregnant.

The failure to describe the anatomic site at which measurements are taken is especially problematic, given the variation in temperature existing at various sites throughout the human body. Singh, for example, found temperatures measured with an electronic thermometer to differ between the right and left axilla [87]. The extent of such variation is illustrated further in a recent review by Geneva [88] that identified the following average temperatures for sites most often used in measuring patients' temperatures: rectal, 37.04 °C (98.7 °F), tympanic, 36.64 °C (98.0 °F), urine, 36.61 °C (97.9 °F), oral 36.57 °C (97.80 °F) and axillary, 35.97 °C (96.7 °F).

Temperature readings can also vary according to the type of instrument used. Traditionally, contact thermometers that are placed on the forehead or in the mouth, ear, axilla, or rectum have been used to monitor patients' temperatures. Non-contact thermometers, which have become the preferred instruments from an infection control standpoint when screening patients for COVID-19, allow temperatures to be taken with minimal (tympanic) or no (non-contact infrared thermal scanners) physical contact with the person being examined. There is no consensus as to the optimal cut-off temperature for determining the existence of a fever for each device.

Even among the few publications reviewed that do state clearly a minimum cut-off temperature for fever, considerable variation exists both as to what cut-off temperatures were chosen and the anatomic site at which temperature measurements were obtained. In a publication cited over 5,000 times in other works, Guan [4] identified fever (defined by them as an axillary temperature ≥37.5 °C [≥99.5 °F]) as the most common manifestation of COVID-19-induced illness, without specifying the type of thermometer used or the method by which axillary temperatures were obtained. In a study of COVID-19-infected, pregnant women, Breslin [16] defined fever as a temperature of "at least 37.8 °C (100.0 °F) without specifying either the type of thermometer used or the site at which measurements were taken. In a review of 108 pregnant women with COVID-19, Zaigham and Anderson [43] identified fever in 68% of cases

without defining the term. Moreover, only 5 of the 14 references they reviewed defined a cutoff for fever and none indicated how temperatures were measured. Reviews of COVID-19 during pregnancy by Dashraath [52], Rasmussen and Jamieson [38], Galang [89] and Della Gatta [90] also identified fever as a prominent manifestation of the illness without defining temperature cutoffs for fever or describing the methodology involved in measuring patients' temperatures.

Carl Reinhold Wunderlich (1815–1910) is credited with offering one of the earliest evidence-based definitions of fever derived from the results of an analysis of a vast number of axillary temperatures taken from patients in his clinic in the latter part of the 19th century [81, 82]. Based on these observations, he defined a *slight fever* as 38–38.4 °C (100.4–101.1 °F), a *moderate fever* as 38.5–39 °C (101.3–102.2 °F) and *considerable fever* as 39.5–40.5 °C (103.1–104.9 °F), with cutoffs lower in the morning than in the evening. Currently, according to *Harrison's Principles of Internal Medicine* [91], fever is defined as a core temperature (rectal) of 37.5–38.3 °C (99.5–100.9 °F), a skin temperature (axillary) >37.2 °C (>99 °F), a morning oral temperature >37.2 °C (>99 °F), or late afternoon oral temperature >37.7 °C (>99.9 °F), with lower thresholds applicable to frail elderly persons. The Merck Manual defines fever as an elevated body temperature (>37.8 °C (100.0 °F) orally or >38.2 °C (100.8 °F) rectally) or an elevation above a person's known normal daily value [92].

How fever is defined in pregnant women also varies. Based, in part, on a study of temperatures of normal parturients, which ranged from 34.6–37.6 °C (94.3–99.7 °F) upon admission to the labor unit, Acker [93] defined intrapartum fever as a maternal temperature ≥38 °C (100.4 °F) orally. Herbst [94] defined fever in pregnancy as "... at least one recorded temperature of ≥38.3 °C (≥101 °F)," whereas an expert panel [95] recommended defining fever during pregnancy as a single oral temperature of ≥39 °C (≥102.2 °F) or two readings of ≥38 °C (100.4 °F) taken 30 min apart.

Given the many factors influencing the results of temperature measurements in humans, there can never be a single, universally accepted temperature cut-off defining a fever. This clinical reality, however, should not prevent precision in reporting fever. To achieve the needed precision and thereby improve scientific and clinical communication, when fever is reported in clinical investigations, the cut-off temperature used in determining the presence of fever, the anatomical site at which temperatures are taken, and the instrument used to measure temperatures should each be described. In the absence of such information, what is meant by the term "fever" will remain uncertain.

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