COMMENTARY

Skin Mottling in Dark-skinned Indian Patients with Severe Septic Shock: A Window to the Circulation or a Closed Door?

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Abstract

Skin mottling has been found to be useful as a marker of peripheral hypoperfusion in shock in studies performed on fair-skinned patients. Whether skin mottling may be less apparent in dark-skinned patients, thus limiting its value in this patient population has not been studied. Jog et al. have performed an elegant study addressing this question, which is important and especially relevant to the Indian situation. They found that mottling is not easily visible in dark-skinned Indian patients, and when it becomes apparent, it is associated with a very high mortality. This study also throws up some areas for future research, including interobserver variability in the detection of mottling, and the hemodynamic and microcirculatory parameters associated with the appearance of mottling. Based on this study, the utility of skin mottling as a tool to guide hemodynamic management in severe septic shock in dark-skinned Indian patients is questionable.

Keywords: Dark-skin color, Mortality, Peripheral tissue perfusion, Septic shock, Skin mottling.

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Septic shock, characterized by the presence of sepsis, and the need for vasopressors despite fluid resuscitation and elevated lactate levels, is associated with high mortality. In the second Indian intensive care case-mix and practice patterns study (INDICAPS-II), 30-day mortality in patients with septic shock was 53%.[1] Circulatory shock is characterized by inadequate oxygen utilization by the cells, leading to impaired tissue perfusion and dysoxia. Impaired tissue perfusion is clinically recognized through three windows, namely, the skin (cutaneous perfusion), kidney (hourly urine output), and brain (mental status).[2] Peripheral cutaneous perfusion is receiving increasing attention as it is simple, easily amenable to frequent physical examination, and does not entail any costs. In particular, the capillary refill time (CRT) has been evaluated extensively in the ANDROMEDA-SHOCK study. In that study, there was no difference in mortality when a resuscitation strategy targeting normalization of CRT was used, compared with a strategy targeting serum lactate levels in patients with septic shock. Furthermore, CRT demonstrated greater specificity as a marker of tissue perfusion and was associated with superior real-time assessment of response to fluids and had faster dynamics of recovery with resuscitation than serum lactate.[3] The other indicator of peripheral cutaneous hypoperfusion is the presence of skin mottling around the knee joint. A high incidence of mottling has been reported in patients with septic shock, and severe skin mottling correlated with mortality.[4,5] However, in these studies, the vast majority of patients were Caucasian and fair-skinned, in whom early skin mottling is easily visible. The majority of Indians have darker skin, in whom the presence of mottling may not be readily apparent. It has been our clinical observation that visible mottling in dark-skinned patients occurs at an advanced stage of shock, and may not be useful as a monitor of adequacy of resuscitation. These clinical observations have been scientifically tested in a study by Jog et al. that was published in the December 2023 issue of the *Indian Journal of Critical Care Medicine*.[6] This is an outstanding example of a study that addresses a specific problem relevant to the practice of critical care medicine in India and is also important and interesting from a global perspective. The authors are to be congratulated for undertaking this study.

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This was a prospective observational study in 108 Indian patients with septic shock requiring a norepinephrine dose of ≥0.2 μg/kg/minute after fluid optimization. Patients were included if they were dark-skinned, defined as having skin color category 21–34 on the von Luschan scale or skin type IV–VI on the Fitzpatrick scale.[7,8] Fair-skinned patients with lower scores on both scales were excluded. Skin color was determined by two experts (a dermatologist and a cosmetic surgeon) who independently assessed the skin type based on the image of the normal skin area provided to them. Intensivists assessed the patients every 12 hours for the appearance of new mottling, and if mottling was suspected, photographs were sent to the two experts blinded to the clinical status of the patient. Mottling was recorded only if both experts were in agreement, and in case they differed on the grade of mottling, the higher grade was recorded. This unique study design inspires confidence that the skin color and presence of mottling were classified in a rigorous, non-biased manner.

Severity scores including the sequential organ failure assessment (SOFA) and acute physiology and chronic health

evaluation (APACHE) II scores, as well as hemodynamic parameters including CRT, mean arterial pressure, hourly urine output, arterial lactate, central venous oxygen saturation ($ScvO_2$) and venoarterial PCO_2 gap were obtained only at the time of enrolment of a patient in the study when the dose of norepinephrine had escalated to ≥0.2 μg/kg/minute. It is worth noting that these hemodynamic parameters were not recorded again when mottling was diagnosed. The end-point was 90-day mortality.

Mottling was infrequent (being apparent in only 20% of patients with severe septic shock). This is much lower than the 51–70% incidence reported in the Western literature. Mottling occurred on an average of about 4 days (range, 1–126 hours) after entering the study (septic shock with a dose of norepinephrine ≥0.2 μg/kg/minute), was high grade at first discovery [median mottling score was 5 [interquartile range (IQR) = 4] and 68% patients had severe mottling (a score of ≥4)], and was associated with a 91% mortality, compared to 67% mortality in patients without mottling. Most patients with higher grades of mottling died within 24 hours after the onset of mottling. The authors concluded that the appearance of mottling predicts mortality. However, it appears that mottling was virtually a prelude to death in very sick patients with severe septic shock. Patients who developed mottling had higher vasopressor dose requirements at baseline. Higher SOFA scores and lactate levels at study enrolment were associated with both the appearance of mottling as well as mortality, suggesting that sicker patients developed mottling prior to death.

Capillary refill time at baseline was prolonged above 3 seconds in 55 out of 108 patients (51%) and was similar in patients who developed mottling and those who did not. Capillary refill time at baseline had a lower predictive value for mortality. However, it is difficult to compare values of CRT and other hemodynamic parameters at baseline with mottling which occurred an average of 4 days after enrolment into the study.

There are some questions that remain unanswered. The skin color and presence of mottling were determined by experts. Would results be similar if intensivists were to diagnose mottling in the routine clinical course? The study protocol required both experts to agree on the presence of mottling once it had been reported by the intensivist. Would the incidence of mottling and the mortality be different if the diagnosis of mottling had been made more sensitive, for example, based on the observation of the intensivist or the confirmation by any one expert? Why was the grade of mottling high at first discovery? Did the strict criteria again lead to delayed diagnosis? It is unlikely that the intensivists missed early mottling, as by protocol they were looking for it every twelve hours. Is early mottling so difficult to see in dark-skinned patients? When mottling appears in dark-skinned patients, does it represent a stage of advanced and irreversible shock? Is it then merely an indicator of poor cutaneous perfusion or of something more sinister such as microcirculatory failure? Perhaps measurement of hemodynamic parameters such as serum lactate, $ScvO_2$, CRT, etc. or even visualization of the microcirculation at the time mottling is noticed may shed more light. Does the presence of mottling in septic shock represent a different phenotype with poor outcome, or does it reflect the failure of resuscitation? In the study by Jog et al., the progression of mottling was not recorded.[6] However, it would be interesting to note whether the grade of mottling worsened in patients who died, and more so, whether mottling improved in the two patients who survived. Perhaps a future study could include fair-skinned Indian patients as well. This would allow us to directly compare the incidence and significance of mottling in fair-skinned versus dark-skinned patients. Advanced technology such as laser Doppler scanning of the area superposed to the area of mottling score classification may give additional information such as quantification of perfusion in areas of mottling, and sequential measurements can help to follow up the results of resuscitation.[9]

Guidelines recommend integrating peripheral perfusion parameters in the management of septic shock, especially as cutaneous perfusion parameters are easy to use at the bedside, and can be used in resource-limited settings. However, based on this study, the utility of skin mottling as a tool to guide hemodynamic management in severe septic shock in dark-skinned Indian patients is questionable. This study provides valuable confirmation of the clinical observation that mottling is not easily visible in dark-skinned Indian patients, and when it becomes apparent, it is associated with a very high mortality.

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