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Glasgow Coma Scale in Anticipation of Sepsis and Septic Shock: Review Article

Mohammed Saeed M Alalawi[1], Hussain Abdullah M Aljabran[2], Abdullah Mohammed Alkhamri[3], Abdulrahman Mohammed Alwahbi[4], Zahra Ibrahim AlQarrash[2], Hussain Abdulillah M Iraqi[5], Mohammed Saleh M Alonazi[6], Abdulaziz Raja Najim Alotaibi[7], Majed Ali Mohammed Alahmari[6], Ahmed Abdalmuhssen A Alnuwaiser[8], Feras Khalid A. Mimarji[5], Abdullah Atallah Al-Enezi[9], Naif Ahmed A Alabbad[10], Alaa Hassan Alhayki[2], Mashail Hashim H Farran[11]

Department of Emergency Medicine

[1]Anak General Hospital, Anak, Saudi Arabia, [2]Imam Abdulrahman bin Faisal University, Dammam, Saudi Arabia, [3] King Saud University, Riyadh, Saudi Arabia, [4]Qassim University, Qassim, Saudi Arabia, [5] Jeddah University, Jeddah, Saudi Arabia, [6]Imam Muhammad ibn Saud Islamic University, Riyadh, Saudi Arabia, [7]Taif University, Taif, Saudi Arabia, [8] King Faisal University, Hofuf, Saudi Arabia, [9]Majmaah University, Al Majmaah, Saudi Arabia, [10]University of Warmia and Mazury in Olsztyn, Olsztyn, Poland, [11]Ibn Sina National College, Jeddah, Saudi Arabia

Corresponding Author: Mohammed Saeed M Alalawi, Email: mohd.s.alawi@gmail.com Mobile: +966598157904

ABSTRACT

Evaluation of level of consciousness has become essential for anticipation of sepsis and septic shock. Both the Sequential Organ Failure Assessment (SOFA) score and the quick SOFA score utilize the Glasgow Coma Score (GCS) for screening of sepsis. **Objectives**: the aim of this review is to determine and study the role of Glasgow coma score in anticipation of sepsis and septic shock. **Methods**: To achieve this aim, we have searched online database, namely PubMed and Cochrane Library for studies and review articles assessing the significance of assessment of Glasgow Coma Scale (GCS) for anticipating sepsis or septic shock. Thirteen appropriately-related studies were selected for review. **Results:** Disturbed sensorium was found to be a sensitive early indicator for sepsis, thus GCS is used for assessment of both the Sequential Organ Failure Assessment (SOFA) and quick SOFA scores qSOFA scores. Lower GCS scores were associated with high mortality rates. **Discussion:** Encephalopathy is an early sign of sepsis and septic shock. Glasgow Coma score (GCS) was a good indicator of neurological dysfunction evaluated by the SOFA and qSOFA scores. The use of GCS was also a predictor of mortality in patients with sepsis. Some researchers, however, reported that GCS was not the best tool for measuring brain dysfunction in sepsis. **Conclusions**: Glasgow coma score can anticipate sepsis and septic shock, and predict the outcome of sepsis.

Keywords: Glasgow Coma score, Sepsis, Septic shock.

INTRODUCTION

Sepsis in a major health problem and an important cause of mortality in intensive care units (ICUs) worldwide. It is estimated that about 300 every 100 population in the United states develop severe sepsis[(1)]. Septic shock is a significant cause of mortality with a mortality rate reaching up to 50%[(1)]. In spite of the continuous efforts to put solid criteria for early diagnosis of sepsis, physicians still find a challenge to accurately identify patients with sepsis in wards and/or emergency departments. In the past, the systemic inflammatory response syndrome(SIRS) diagnostic criteria was used to detect sepsis in different clinical situations[(2)]. The previous consensus definitions of sepsis(Sepsis-2) required the presence of infection, along with at least two criteria for SIRS, as well as organ failure for diagnosis of sepsis[(2,3)]. However, recent researchers claimed that these criteria were neither sensitive nor specific, and had hindered the accurate detection and identification of sepsis. Because there is no gold standard test for diagnosis of sepsis, researchers focused on developing, as well as evaluating the efficacy of, tools that can anticipate sepsis among hospitalized patients with likelihood of infection**(4)**. The currently used tool for screening of sepsis is the Sequential Organ Failure Assessment (SOFA) score**(5)**. The development of this score was based on the new definition of sepsis as "life-threatening organ dysfunction caused by a deregulated host response to infection"**(6)**. Eventually, sepsis can be diagnosed when a patient scores two or more points on the SOFA score. SOFA score is based on evaluation of the function of six systems, namely the respiratory, neurological, cardiovascular, hepatic, renal, and coagulation systems. Because it is time-consuming, the task force developed a shorter easily-applicable score for detection of sepsis, the quick SOFA score or qSOFA**(7)**.The qSOFA score indicates that sepsis is very likely if the patient has any 2 of the

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following; Glasgow Coma Scale <15, systolic blood pressure <100 mm Hg, and respiratory rate >22/min.

Septic shock, on the other hand, is currently defined as "a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone."[6] Certain criteria were proposed for defining septic shock, namely a mean arterial pressure of <65 mm Hg, hypotension requiring vasopressors, or elevated serum lactate of >2 mmol/L[6].

Altered mental state, measured by Glasgow Coma Scale (GCS), is an important category for prediction of sepsis measured in both SOFA as well as qSOFA score. The aim of this review article was to evaluate the benefit and impact of using Glasgow Coma Scale in anticipation of septic shock.

METHODS

For conducting this review, we have searched online database, namely PubMed and Cochrane Library for studies and review articles assessing the significance of assessment of Glasgow Coma Scale (GCS) for anticipating sepsis or septic shock. Abstracts with related titles were investigated and evaluated for selecting appropriately-related articles. Of about 75 results, 13 appropriately-related studies were selected for reviews. We included the studies which evaluated the pathophysiology of central nervous system involvement in sepsis, the impact of utilizing Glasgow Coma Score in sepsis anticipation, and GCS predictive values as regards the overall outcome.

The study was approved by the Ethics Board of *Imam Abdulrahman bin Faisal* University.

RESULTS

Glasgow coma scale (GCS) was reported as a significant indicator for sepsis many decades ago. ***Kieft*** *et al.*[10] studying sepsis syndrome included the alternation of level of consciousness as one of the criteria of sepsis that had significantly increased the risk for development of septic shock among the studied sample[8].Similarly, many researchers later on stated that low GCS in patients with sepsis was significantly associated with high mortality rates[9–11].

After changing the definition of sepsis and septic shock, Glasgow coma scale remained an important indicator for sepsis. ***Freund*** *et al.*[19] in their multicenter prospective cohort study conducted a study between May and June 2016 on 879 patients with suspected infection, reported that qSOFA was superior to SIRS in early prediction of sepsis and sepsis-related mortality, with an area under the receiver operating curve (AUROC) of 0.80 and 0.65 for qSOFA and SIRS, respectively. The mortality rate was 3%among patients with qSOFA score <2 and 24% among patients with SOFA score 2 or more[12]. Similarly, further studies approved the superiority of SOFA and qSOFA criteria for early detection of sepsis and sepsis-related mortality than SIRS criteria[4,13].

Sheetrit *et al.*[14] in their research studied 2,560 cases derived from the MIMIC-III database by multivariate analysis to evaluate factors aiding the early discovery of accurate sepsis in intensive care units' patients. They reported that Glasgow Coma Score was a significant factor for early diagnosis of sepsis[14].

However, some researchers did not agree with the usage of Glasgow Coma Scale as a predictor for sepsis. ***Frank*** *et al.*[15] in their report stated that some sepsis cases may present with acute brain dysfunction with normal GCS. They reported an illustrative case with unrecognized urinary tract infection presented significant cognitive impairment and behavioral dysfunction with normal Glasgow Coma score, thus not fulfilling the current proposed criteria for sepsis[15].

Similarly, ***ÅsaAskim*** *et al.*[16] in their prospective cohort study conducted in Norway in 2012 on all patients suspected with infection who were followed from January 1 to December 31, 2012, reported that the use of qSOFA score – with GCS<15 as one subcategory, was not sensitive in detecting sepsis early, and that it missed up to two thirds of sepsis patients[16].

Glasgow coma scale (GCS) was reported to be an indicator for mortality as well. ***Knaus*** *et al*[9] evaluating the definition of sepsis and sepsis syndrome stated that patients with low GCS had a higher mortality rate[9]. Similarly, a prospective case series study conducted on 1996 reported that septic encephalopathy was associated with high risk of mortality proportionally correlated with the GCS[10]. Researchers reported patients with a GCS of 15 had 16% mortality, those with a score of 13 to 14 had 20% mortality, those with GSC of 9 to 12 had 50% mortality, and those with GCS of 3 to 8 had 63% mortality ($P < .05$)[10].

On the contrary, ***Russell*** *et al.*[17] in their retrospective study on 437 patients reported that the GCS was not significantly associated with high in-hospital mortality (p0.36).

DISCUSSION

Encephalopathy as an early presentation of sepsis:

Altered mental state seems to be a significant component of sepsis syndrome and septic shock. Sepsis often presents early by encephalopathy and/or disturbed consciousness[10,18]. The previous consensus definition of sepsis (Sepsis-2) did not high-lighten the importance of encephalopathy in early detection of sepsis, and altered consciousness was not a defined criteria for diagnosis[2,3]. The third international consensus definition of sepsis, however, added the level of consciousness, measured by Glasgow Coma Scale, as an important predictor indicating the development of sepsis in both SOFA and qSOFA[6].

Of note, even before the development of third consensus definition of sepsis, ***Kieft et al.***[10] reported that the alternation of level of had increased the risk for development of septic shock [8]. Then, many researchers stated similar findings and approved that low GCS in patients with sepsis was significantly associated with high mortality rates[9–11].

Pathophysiology of Septic-Associated Encephalopathy (SAE):

Sepsis associated encephalopathy represents neurological dysfunction resulting from the dysregulated host response to infection. It is a diffuse dysfunction without a cerebral structural pathology or direct infection. The pathophysiology of sepsis-associated encephalopathy is sophisticated. Different types of brain cells are involved by both inflammatory and non-inflammatory processes. Vagus nerve and circumventricular organs (CVOs) are the main neurological structures involved in sepsis pathophysiological process[19]. Vagus nerve is involved in the inflammatory reflex responsible for modulation of different chemical and hormonal pathways encountered in sepsis, whereas, the circumventricular organs (CVOs) are considered components of express components of adaptive and innate immune systems[19]. Early diagnosis of sepsis associated encephalopathy is essential for proper management and improving prognosis. Neurological examination is the mainstay for diagnosis, however, brain imaging, electroencephalogram, and laboratory investigations are often essential for confirmation of diagnosis and identification of the cause. Management depends mainly on treatment of sepsis, correction of the cause, and control of aggravating factors such as metabolic disturbances, medications withdrawal or over dosage[20–24].

Glasgow Coma Score as a measure for encephalopathy:

Diagnosis of sepsis-associated encephalopathy (SAE) is essential for early detection of sepsis and accurate prediction of its outcome. Glasgow Coma Score (GCS) was the most commonly utilized tool for evaluation of cerebral dysfunction in patients suspected to have sepsis. The third international definition of sepsis and septic shock changed the concept of sepsis being a systemic inflammatory response syndrome to a dysregulated host response to infection leading to organ dysfunction. Organ dysfunction is determined when SOFA score is 2 or more points. Glasgow Coma Score is used for evaluation of neurological dysfunction in both SOFA as well as qSOFA score. In SOFA score, a value of 0-4 is given for GCS of 15, 13-14, 10-12, 6-9, and <6, respectively. In qSOFA score, on the other hand, any change in mentation (GCS <15) is considered pathological[5,6].

Criticism of using GCS in sepsis:

In contrary to the previous studies, some researchers still claim that the use of GCS is not sensitive in early prediction of sepsis. For instance, ***Frank*** *et al*. [15] believed that some cases with unrecognized source of sepsis might present with cognitive impairment and behavioral dysfunction with normal Glasgow Coma score[15]. Similarly, ***ÅsaAskim*** *et al*. [16] reported that the use of qSOFA score – with GCS<15 as one subcategory, was not sensitive in detecting sepsis early, and that it missed up to two thirds of sepsis patients[16]. Thus, the introduction of a more sensitive indicator for cognitive function is still recommended for early detection of sepsis.

Glasgow Coma Score and sepsis associated mortality:

Glasgow Coma score did not only predict the development of sepsis, but also had a prognostic value. Patients with low Glascow Coma Score had a high mortality rate[9–11]. Differences in Glasgow Coma Scales (GCS) had been associated with different mortality rates; it seemed very low GCS had mortality rates of more than two-thirds of the affected patients[10]. However, this was not reported in other studies [17].

CONCLUSIONS

In conclusion, brain dysfunction is an important and early sign of sepsis. Glasgow Coma Score, in spite of being a good predictor for sepsis, still is not accurate and reliable estimate of sepsis and could overlook some patients with sepsis-associated acute brain dysfunction. Further researches are recommended to be done to re-define neurological

dysfunction that can early anticipate sepsis and septic shock.

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