

Editorial

Sepsis, an Ancient Threat and Today's Challenge for Global Health

Laura Alberto, PhD, MEd, Esp.Ed., Com.Sc.(Dip), BN¹



Citation: Alberto L. Sepsis, an ancient threat and today's challenge for global health
International Journal of Critical Care
2023;18(3):1-6. doi:
10.29173/ijcc1034



Academic Editors:

Ged Williams, RN, Crit. Care Cert.,
LLM, MHA, FACN, FACHSM,
FAAN

Natalie L. McEvoy, PhD, MSc, BSc,
RGN, Pg Diploma, StAR Lecturer in
Critical Care, Royal College of
Surgeons, Ireland

Wendy Pollock, RN, RM PhD
FHEA, Associate Professor, Deputy
Director of Research, Monash
University, Australia

Managing Editor: Patricia Zrelak,
PhD, RN, NEA-bc, SCRn, CNRN,
ASC-BC, CCRN-K, PHN, FAHA

Published: October 2024

Acknowledgments: None



Copyright: © 2024 by the authors.
Open access publication under the
terms and conditions of the
Creative Commons Attribution (CC
BY NC) license
(<https://creativecommons.org/licenses/by-nc/4.0/>).

¹National Scientific and Technical Research Council (CONICET), Institute for Research in Medicine and Health Sciences, Universidad del Salvador, Argentina
Email: laura.alberto@usal.edu.ar

Sepsis is a challenging condition since ancient times.

In Egypt, 5000 years ago, a surgical practitioner treating a man with a broken arm and an external wound referred that the patient had reached a “decisive point” referring to the line between life and death and said with conviction “... an ailment with which I will contend” (Breasted, 1930). This story is told in Edwin Smith’s Surgical Papyrus, the oldest surgery treatise (Elsberg, 1931, Breasted, 1930). Interpreters of this story surmised this patient was suffering from blood poisoning (Breasted, 1930), a condition today known as sepsis.

Sepsis is a recognised global health concern, but the true epidemiology of sepsis is unknown. It is estimated 49 million people worldwide are affected annually, including 5,6 million women with maternal disorders, 4,9 million children and adolescents, and 5,1 million neonates (Rudd et al., 2020). Of those affected by sepsis, 11 million will die, including 2,9 million children younger than 5 years (Rudd et al., 2020). These estimations are the most robust epidemiological evidence available, however, it also has limitations. Modelling estimations were restricted to the information available on individual vital registries or admissions identified by the International Classification of Diseases (ICD) coding related to sepsis and definitions of sepsis (Rudd et al., 2020). The quality and availability of information vary across settings, with low- and low middle-income countries (L-LMIC) historically having suboptimal registration of health information, possible due to the lack of

resources to manage health registries (Fleischmann et al., 2016, Rudd et al., 2020). Therefore, the true global epidemiology of sepsis is unknown.

The knowledge of sepsis, diagnosis and treatment has evolved but disparities remain in the application of this knowledge. The first consensus on sepsis was followed by multiple iterations that lead to the latest definition, the Sepsis-3 (Singer et al., 2016, Bone et al., 1992). Today, sepsis continues to be an ailment clinicians contend, and despite the advances in medical science and clinical consensus on what sepsis is, there is no reliable test to diagnose sepsis nor a specific medicine to treat it. Clinicians suspect sepsis in the presence of life-threatening organ dysfunction caused by a dysregulated host response to an infection (Singer et al., 2016). Essential treatment includes: the administration of 1) antimicrobials prior the obtention of cultures, 2) fluids, 3) vasopressors if there is hypotension despite a proper fluid challenge, and 4) monitoring lactate levels and hemodynamic response (Evans et al., 2021). Over the last three decades, the emergence of the Surviving Sepsis Campaign movement has improved sepsis diagnosis and care but adherence to treatment guidelines varies widely (Levy et al., 2014). For example, in a study on 386 adult intensive care units (ICUs) from 22 Asian countries, the compliance to the sepsis 1hour bundle was 26% in L-LMIC, 22% in upper middle-income countries and 16% in high income countries, this adherence resulted in an overall hospital mortality of 36% with no difference across income settings (Li et al., 2022). On the contrary, in 45 ICUs from Turkey, researchers reported no adherence (0%) to the bundle elements within 3 to 6 hours of the suspicion of sepsis, and mortality for sepsis and septic shock were 22% and 78% respectively (Bahar et al., 2021). The reasons for this variation may be related to the insufficient training, the characteristics of the culture related to quality improvement and the disparities in the access to the diagnosis and treatment of sepsis. Nonetheless, in settings where improvement was well documented, more lives were saved (Levy et al., 2014), and at the same time a new clinical entity featuring a constellation of functional, cognitive and psychological impairments was described (Mostel et al., 2019). These impairments represent additional burden to sepsis survivors, their families and the health systems.

There is emerging evidence highlighting the health burden experienced by sepsis survivors in the long term. Researchers found a large proportion (60%) of sepsis survivors reporting cognitive complains up to 1year and experiencing different levels of physical impairment for more than 3-years after hospital discharge, and they remain prone to new infections and readmission (Ehlenbach et al.,

2018, Cuthbertson et al., 2013, Prescott et al., 2016). In addition to the individual suffering, the impact of sepsis in the survivor’s families, the health systems and the society is unclear. In L-LMIC it is likely the same disparities observed in the access to treatment may affect the access to care in the long-term, preventing the adequate management of post sepsis comorbidities. It is in these low resource settings were most of the burden of sepsis resides (Rudd et al., 2020, Fleischmann et al., 2016, Cassini et al., 2020), where sepsis research is limited and where the true burden of sepsis in the long term is unknown. In the fight against sepsis, no one should be left behind.

Sepsis requires a sustained, integrated global public health response. The Global Sepsis Alliance (GSA), a global advocate for sepsis, is leading the international sepsis agenda. In parallel to the past World Health Assembly of May 2024, during the “Multi-Stakeholder Dialogue to develop the 2030 Global Agenda for Sepsis” the GSA proposed five pillars (see Table) to structure such agenda in the pursue of a “world free of sepsis” (Couball, 2024). There is common consensus among GSA leaders that political leadership play a pivotal role in facilitating strategic cooperation among stakeholders at different levels of decision making. Cooperation and political action are fundamental to prepare health systems to be ready not only for sepsis response but also for future pandemics, humanitarian crisis and other emergencies. There is no doubt that society, patient and public involvement are an essential component of such response. Societal awareness of the burden of sepsis will push political action and multilateral cooperation. To tailor an integrated public health response to sepsis, decision making at all levels must be led by evidence. Therefore, research and innovation become underlying conditions for data driven actions against sepsis.

Table

Pillars of the 2030 Global Agenda for Sepsis

1. Political Leadership and Multilateral Cooperation Strategic
2. Health System Readiness for Sepsis and Its Sequelae Strategic
3. Whole-of-Society Response to Sepsis Strategic
4. Sepsis Research and Innovations, and Strategic
5. Sepsis in Pandemics and Other Emergencies

Source: Couball (2024).

The future sepsis agenda shows promise to address perennial disparities in the access to sepsis care. Sepsis is a medical emergency, and it is preventable. When a patient is admitted to the ICU with septic shock, preventive measures have failed. The health system has failed.

However, sometimes ICU care is unavailable in countries with limited health resources. It is likely that a global advocacy for sepsis may help our brothers and sisters from regions in the world where there is poor sanitation, limited access to clean water, vaccination and safe delivery, to improve infection prevention and access to essential sepsis care. These problems are not new; however, the global advocacy is giving momentum and hope for a sustainable global response to sepsis. Like in the ancient times, we have reached a decisive point. To achieve a “world free of sepsis,” it is time for critical care nurses to play a pivotal role beyond the ICU, in the global health arena.

REFERENCES

- Bahar I, Oksuz H, Senoglu N, Demirkiran H, Aydogan M, Tomak Y, Comez M, Bayrakci S, Gonullu E & Berktaş M. Compliance with the surviving sepsis campaign bundle: a multicenter study from Turkey. *Cureus*. 2021;13(5):e14989. doi: 10.7759/cureus.14989
- Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, Schein RMH & Sibbald WJ. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *CHEST*. 1992;101(6):1644-1655. doi: 10.1378/chest.101.6.1644
- Breasted JH. The Edwin Smith Surgical Papyrus: published in facsimile and hieroglyphic transliteration with translation and commentary in two volumes. University of Chicago Press: Chicago. 1930
- Cassini A, Allegranzi B, Fleischmann-Struzek C, Kortz T, Markwart R, Saito H, Bonet M, Brizuela V, Mehrtash H, Tuncalp Mingard Ö. Global Report on the epidemiology and burden on sepsis: current evidence, identifying gaps and future directions. Geneva: World Health Organization. 2020.
- Couball K. 2030 Global Agenda for Sepsis – Geneva Dialogue and Next Steps [Online]. Global Sepsis Alliance. Available: 2030 Global Agenda for Sepsis – Geneva Dialogue and Next Steps, 2024. [Accessed August 2, 2024].
- Cuthbertson BH, Elders A, Hall S, Taylor J, MacLennan G, Mackirdy F, Mackenzie SJ. Mortality and quality of life in the five years after severe sepsis. *Critical Care*. 2013;17(2):R70. doi: 10.1186/cc12616
- Ehlenbach WJ, Gilmore-Bykovskiy A, Replinger MD, Westergaard RP, Jacobs EA, Kind AJH, Smith M. Sepsis survivors admitted to skilled nursing facilities: cognitive impairment, activities of daily living dependence, and survival. *Critical Care Medicine*. 2018;46(1):37-44. doi: 10.1097/CCM.0000000000002755

- Elsberg CA. The Edwin Smith surgical papyrus: and the diagnosis and treatment of injuries to the skull and spine 5000 years ago. *Annals of Medical History*. 1931;3(3):271-279
- Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, Machado FR, Mcintyre L, Ostermann M, Prescott HC, Schorr C, Simpson S, Wiersinga WJ, Alshamsi F, Angus DC, Arabi Y, Azevedo L, Beale R, Beilman G, Belley-Cote E, Burry L, Cecconi M, Centofanti J, Coz Yataco A, De Waele J, Dellinger RP, Doi K, Du B, Estenssoro E, Ferrer R, Gomersall C, Hodgson C, Hylander Moller M, Iwashyna T, Jacob S, Kleinpell R, Klompas M, Koh Y, Kumar A, Kwizera A, Lobo S, Masur H, Mcgloughlin S, Mehta S, Mehta Y, Mer M, Nunnally M, Oczkowski S, Osborn T, Papathanassoglou E, Perner A, Puskarich M, Roberts J, Schweickert W, Seckel M, Sevransky J, Sprung CL, Welte T, Zimmerman J & Levy M. Surviving Sepsis Campaign: International guidelines for management of sepsis and septic shock 2021. *Critical Care Medicine*. 2021;49(11):e1063-e1143. doi: 10.1097/CCM.0000000000005337
- Fleischmann C, Scherag A, Adhikari NK, Hartog CS, Tsaganos T, Schlattmann P, Angus DC & Reinhart K. Assessment of global incidence and mortality of hospital-treated sepsis. Current estimates and limitations. *American Journal of Respiratory and Critical Care Medicine*, 2016;193(3):259-272. doi: 10.1164/rccm.201504-0781OC
- Levy MM, Rhodes A, Phillips GS, Townsend SR, Schorr CA, Beale R, Osborn T, Lemeshow S, Chiche JD, Artigas A & Dellinger RP. Surviving Sepsis Campaign: association between performance metrics and outcomes in a 7.5-year study. *Intensive Care Medicine*. 2014;40(11):1623-33. doi: 10.1007/s00134-014-3496-0
- Li A, Ling L, Qin H, Arabi YM, Myatra SN, Egi M, Kim JH, Mat Nor MB, Son DN, Fang WF, Wahyuprajitno B, Hashmi M, Faruq MO, Patjanasontorn B, Al Bahrani MJ, Shrestha BR, Shrestha U, Nafees KMK, Sann KK, Palo JEM, Mendsaikhan N, Konkayev A, Detleuxay K, Chan YH, Du B, Divatia JV, Koh Y, Gomersall CD & Phua J. Epidemiology, management, and outcomes of sepsis in icus among countries of differing national wealth across Asia. *American Journal of Respiratory and Critical Care Medicine*. 2022;206(9):1107-1116. doi: 10.1164/rccm.202112-2743OC
- Mostel Z, Perl A, Marck M, Mehdi SF, Lowell B, Bathija S, Santosh R, Pavlov VA, Chavan SS & Roth J. Post-sepsis syndrome - an evolving entity that afflicts survivors of sepsis. *Molecular Medicine*. 2019;26(1):6. doi: 10.1186/s10020-019-0132-z

- Prescott HC, Osterholzer JJ, Langa KM, Angus DC, Iwashyna TJ. Late mortality after sepsis: propensity matched cohort study. *British Medical Journal*. 2016;353,i2375. doi: 10.1136/bmj.i2375
- Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, Colombara DV, Ikuta KS, Kissoon N, Finfer S, Fleischmann-Struzek C, Machado FR, Reinhart KK, Rowan K, Seymour CW, Watson RS, West TE, Marinho F, Hay SI, Lozano R, Lopez AD, Angus DC, Murray CJL & Naghavi M. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. *Lancet*, 2020;395(10219):200-211. doi: 10.1016/s0140-6736(19)32989-7
- Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, Van Der Poll T, Vincent JL & Angus DC. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *Journal of American Medical Association*, 2016;315(8):801-810. doi: 10.1001/jama.2016.0287