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Enhancing the Sepsis Syndrome Understanding: A Bibliometric Analysis of the hundred most Cited Articles

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Abstract:

Background: This bibliometric analysis aimed to identify and evaluate the 100 most-cited articles (T100 articles) on Sepsis syndrome.

Method: The 100 most cited Sepsis syndrome-related articles were downloaded from Elsevier Scopus on 03.11.2020. Each article were evaluated and described with the core information, 100 Most cited documents, The 10 articles of our list with the highest citation per year (CY), Annual total citation per year, Most cited countries, Top10 Country-wise scientific production, Top 10 Authors Production Over time, Top 10 Most relevant source and impacts are main subjects of the study.

Results: The top 100 publications with highly cited articles are chosen for this analysis. The years 2003 and 2005 were the most productive and positive year during this research. Most of the best-cited papers have been published in the New England Journal of Medicine (NEJM) and in The Lancet. In the top 100 highly cited articles the title: *“Intensive insulin therapy in critically ill*

patients” got the highest citation with 7663 and published in 2001 followed by the title "*COVID-19: consider cytokine storm syndromes and immunosuppression*" written by Mehta P published in 2020, got the highest total Citation per Year with 1744. The highest number of total citations per article was 5972 from the year 2016.

Conclusion: A comprehensive list of the most cited studies on Sepsis syndrome disorders can be found in this review. This current approach is a way to acknowledge the classic Septic disease articles, provide insight into international leaders, and explain patterns in research on Septic disease syndrome.

Keywords: Sepsis, Blood Poisoning, Pyaemia, Septicemia, Severe sepsis, Bibliometric Analysis

INTRODUCTION:

The septic disorder is a life-threatening illness due to the host's exaggeration of inflammation. Sepsis is one of the important drivers of illness and death in the hospital, affecting about half of all admissions to critical care and over a third of all US hospital deaths(Rhee et al. 2017). Since their immune systems are not yet mature or compromised due to other bacterial, viral, and fungal diseases, sepsis impacted the lives of five million children every year¹ Sepsis-lead to acute kidney injury (S-AKI) occurs in up to 47% of hospitalized patients and is associated with poor clinical studies(Xu et al. 2015). Third international consensus definitions for sepsis and septic shock have been reviewed. In brief, sepsis has now been revolutionized as life-threatening organ failure due to the host's dysregulated reaction to infection(Hattori et al. 2017). However, the pathophysiological pathway in the development of sepsis-associated multiple organ dysfunction remains incompletely understood and the lack of adequate treatment for sepsis-key organ failure is a major obstacle in its clinical management. Although after years of the extensive clinical and laboratory study, there is still no effective cure for sepsis.

Sepsis requires prompt treatment with intravenous fluids and antimicrobials. In an intensive care unit, continuing care often continues (Naghavi et al. 2017; Deutschman and Tracey 2014). If an appropriate fluid replacement test is not sufficient to control blood pressure, it is important to use drugs that improve blood pressure. Mechanical ventilation and blood dialysis may be required to maintain the operation of the lungs and kidneys. For access to the bloodstream and to direct care, a central venous catheter and an arterial catheter can be positioned (Vos et al. 2017). Cardiac production and superior vena cava oxygen saturation are other helpful measurements. Unless other conditions prohibit such treatments, people with sepsis need preventative measures for deep vein thrombosis, stress ulcers, and pressure ulcers. Some people can benefit from strict insulin regulation of blood sugar levels. It is controversial to use corticosteroids, with some reports finding benefits and others, not (Annane et al. 2019).

This article intended to find the usefulness of sepsis syndrome research over a period and their scholarly communication pattern among the highly cited articles of sepsis syndrome, the detailed analysis and results were discussed.

SEARCH STRATEGY:

The search method was designed to collect all applicable indexed articles published relevant to Sepsis. We performed our electronic search in Scopus on 3rd November 2020. Therefore, the required search terms were collected and combined to ensure the identification of all applicable manuscripts as follows: TITLE-ABS-KEY (sepsis OR "Blood Poisoning" OR pyaemia* OR pyemia* OR pyohemia* OR septicemia OR "Severe Sepsis" OR "Sepsis syndrome" OR "Septic shock" OR "Septic infection" OR "Septic shock syndrome" OR "Sepsis spectrum syndrome")

SELECTION CRITERIA AND DATA EXTRACTION:

The research included all studies whose main subject was sepsis. Publications were sorted based on the Scopus rank feature according to the highest citation number, and the top 100 were chosen. Further analysis was made to obtain the following items: Most cited documents, top 10

highest citation articles, year-wise Annual total citation, most cited countries, Country-wise scientific production, Authors Production Over time, Most relevant source and impacts. The data was downloaded from the Scopus database as a RIS file and proceeded for further analysis. All tables and data were analyzed using the R studio Bibliometrix (Biblioshiny) software. Bibliometrix has developed open-source software for quantitative research in Scientometric and Bibliometric analysis.

THE LATEST EVOLUTION OF SEPSIS:

According to the Lawson Health Research Institute, the best available solution to the treatment of sepsis works approximately six percent of the time, although preliminary findings indicate that potential developmental treatment in London, Ontario, could be successful in 40 percent of cases. Sepsis is caused by an infection with microbial pathogens such as a virus or bacterium and entails a runaway infection that spreads across the body, causes death to organ failure, and has been described as a complication of COV(Jacquelyn LeBel 2020). Researchers have shown that extracellular DNA, one of the factors responsible for the development of COVID-19, can serve as a likely target for the treatment of sepsis-induced SARS-CoV-2 virus(Aradhana Subramanian 2020). The Center for Molecular Immunology (CIM) of Cuba has announced the launch of a new phase I and II study to determine the safety and effect of the Itolizumab therapeutic antibody in sepsis patients(Agencia Informativa Latinoamericana Prensa Latina 2020).

RESULTS:

The total outcome results in our search are $n=2,39,922$. We selected the top 100 highest cited articles for analysis between 1976 and 3rd November 2020. The total number of citations was $n=273306$ between 7663 and 1487. All articles were published between 1976 and 2020. The average citation number per document $n=2733$. Total Number of Authors contributed to the top 100 highly cited articles $n=4381$, single-author $n=6$, multi authors $n=4375$ (Table No.1). The most-cited article was "*Intensive insulin therapy in critically ill patients*" which was published in 2001(Table No.2). The oldest article on the list was ranked number 39 (cited 2467 times) and was published in 1976 entitled "*Radiological demarcation of cemented sockets in total hip replacement*". The highest citation per year article was ranked with (cited 1744 times) and was

published in 2020 entitled "*COVID-19: consider cytokine storm syndromes and immunosuppression*" published by Mehta.P, Lancet (Table.No 3.) The year with the highest number of articles was 2003($n = 8$), followed by 2003, 2004, 2006, 2008 each ($n = 6$). The highest number of total citations accounted for in 2001 with 5 articles ($n = 27518$).(Table No.4) The USA got a high number of total citations with $n=149177$ and average article citations ($n=2869$) (Table.5). Out of all countries, the USA is the highest number of articles published in the hole analysis($n =628$) followed by the UK ($n=159$).(table No.6) The first authors with the most occurrences were listed in table 7, Vincent JL (Université libre de Bruxelles ULB, Brussels, Belgium) has acted as the first authorship with 11 articles, citation ($n=38502$). (Table No.7)

The Top 100 Cited Papers were published from 1976 to 2020 with citation numbers varying from 7663 to 1487. The necessary information for the top 100 highest citations as shown in table no 1. Out of 100 papers, 42 numbers of sources such as Journals, Books, etc., are contributed. In the top 100 articles, a total of 2703 keywords will be used in the article. Out of a total of 100 highest cited publication Articles $n=65$, conference paper $n=5$, letter $n=1$, Review $n=29$ is included.

TABLE 1. MAIN INFORMATION

Description	Results	Document types	No
Documents	100	Article	65
Sources (Journals, Books, etc.)	42	Conference Paper	5
Keywords (ID)	2703	Letter	1
Author's Keywords (DE)	108	Review	29
Period	1976 - 2020	Total	100
Average citations per documents	2733		
Total Authors	4381		
Authors of single-authored documents	6		
Authors of multi-authored documents	4375		
Documents per Author	0.0228		
Authors per Document	43.8		

TABLE 2. LIST OF 100 MOST CITED DOCUMENTS.

Rank	Source	Title	Year	Cited by	Cite. per year
1.	New England Journal of Medicine	“Intensive insulin therapy in critically ill patients”	2001	7663	403.32
2.	New England Journal of Medicine	“Early goal-directed therapy in the treatment of severe sepsis and septic shock”	2001	7204	379.16
3.	Chest	“Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis”	1992	6575	234.82
4.	Critical Care Medicine	“Epidemiology of severe sepsis in the United States: Analysis of incidence, outcome, and associated costs of care”	2001	6017	316.68
5.	Science	“Defective LPS signaling in C3H/HeJ and C57BL/10ScCr mice: Mutations in Tlr4 gene”	1998	5994	272.45
6.	JAMA - Journal of the American Medical Association	“The third international consensus definitions for sepsis and septic shock (sepsis-3)”	2016	5972	1493
7.	Intensive Care Medicine	“The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure”	1996	5445	226.88
8.	New England Journal of Medicine	“The L-Arginine-Nitric Oxide Pathway”	1993	5403	200.11
9.	AJIC: American Journal of Infection Control	“CDC definitions for nosocomial infections, 1988”	1988	4855	151.72
10.	New England Journal of Medicine	“Efficacy and safety of recombinant human activated protein C for severe sepsis”	2001	4849	255.21
11.	New England Journal of Medicine	“The effect of cardiac resynchronization on morbidity and mortality in heart failure”	2005	4752	316.8
12.	Annual Review of Immunology	“Function and activation of NF-κB in the immune system”	1994	4443	170.88
13.	New England Journal of Medicine	“Nivolumab versus docetaxel in advanced squamous-cell non-small-cell lung cancer”	2015	4432	886.4
14.	New England Journal of Medicine	“The epidemiology of sepsis in the United States from 1979 through 2000”	2003	4361	256.53
15.	Critical care medicine	“American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure	1992	4248	151.71

		and guidelines for the use of innovative therapies in sepsis”.			
16.	Clinical Infectious Diseases	“Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the management of community-acquired pneumonia in adults”	2007	4125	317.31
17.	Cell	“Pattern Recognition Receptors and Inflammation”	2010	4124	412.4
18.	Critical Care Medicine	“2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference”	2003	4099	241.12
19.	The Lancet	“Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013”	2015	4019	803.8
20.	New England Journal of Medicine	“Medical progress: Staphylococcus aureus infections”	1998	3980	180.91
21.	Journal of the American Medical Association	“Actual Causes of Death in the United States, 2000”	2004	3972	248.25
22.	Critical Care Medicine	“Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2012”	2013	3911	558.71
23.	Critical Care Medicine	“Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2008”	2008	3740	311.67
24.	American Journal of Infection Control	“CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting”	2008	3615	301.25
25.	Critical Care Medicine	“Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock”	2006	3381	241.5
26.	New England Journal of Medicine	“Intensive versus conventional glucose control in critically ill patients	2009	3232	293.82
27.	Science	“CD14, a receptor for complexes of lipopolysaccharide (LPS) and LPS binding protein”	1990	3178	105.93
28.	Clinical Infectious Diseases	“Bad bugs, no drugs: No ESKAPE! An update from the Infectious Diseases Society of America”	2009	3056	277.82
29.	Clinical Infectious Diseases	“Nosocomial bloodstream infections in US hospitals: Analysis of 24,179 cases	2004	2991	186.94

		from a prospective nationwide surveillance study”			
30.	New England Journal of Medicine	“The pathophysiology and treatment of sepsis”	2003	2921	171.82
31.	New England Journal of Medicine	“Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine”	2013	2854	407.71
32.	Intensive Care Medicine	“Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock, 2012”	2013	2824	403.43
33.	Journal of Clinical Oncology	“Erlotinib plus gemcitabine compared with gemcitabine alone in patients with advanced pancreatic cancer: A phase III trial of the National Cancer Institute of Canada Clinical Trials Group”	2007	2796	215.08
34.	Journal of Clinical Investigation	“Macrophage plasticity and polarization: In vivo veritas”	2012	2773	346.63
35.	Science	“HMG-1 as a late mediator of endotoxin lethality in mice”	1999	2660	126.67
36.	Nature Reviews Microbiology	“Pathogenic Escherichia coli”	2004	2636	164.75
37.	Journal of the American Medical Association	“Acute renal failure in critically ill patients: A multinational, multicenter study”	2005	2633	175.53
38.	Nature Biotechnology	“Antimicrobial and host-defense peptides as new anti-infective therapeutic strategies”	2006	2542	181.57
39.	Clinical Orthopaedics and Related Research	“Radiological demarcation of cemented sockets in total hip replacement”	1976	2464	56
40.	Critical Care Medicine	“Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock”	2004	2384	149
41.	Journal of the American Medical Association	“Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock”	2002	2358	131
42.	New England Journal of Medicine	“Antiinflammatory therapy with canakinumab for atherosclerotic disease”	2017	2310	770
43.	Nature	“Cloning of a new cytokine that induces IFN- γ production by T cells”	1995	2275	91
44.	The Lancet	“Global, regional, and national causes of child mortality: An updated systematic analysis for 2010 with time trends since 2000”	2012	2217	277.13
45.	Circulation	“Percutaneous transcatheter implantation of an aortic valve	2002	2209	122.72

		prosthesis for calcific aortic stenosis: First human case description”			
46.	New England Journal of Medicine	“A comparison of continuous intravenous epoprostenol (prostacyclin) with conventional therapy for primary pulmonary hypertension”	1996	2202	91.75
47.	Lancet	“WHO analysis of causes of maternal death: a systematic review”	2006	2190	156.43
48.	Microbiological Reviews	“Listeria monocytogenes, a food-borne pathogen”	1991	2180	75.17
49.	The Lancet	“Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: A randomised open-label trial”	2010	2174	217.4
50.	New England Journal of Medicine	“Intensive insulin therapy and pentastarch resuscitation in severe sepsis”	2008	2157	179.75
51.	Science	“The crisis in antibiotic resistance”	1992	2134	76.21
52.	Blood	“Interleukin-1 and interleukin-1 antagonism”	1991	2079	71.69
53.	New England Journal of Medicine	“Bortezomib or high-dose dexamethasone for relapsed multiple myeloma”	2005	2059	137.27
54.	New England Journal of Medicine	“Infliximab, azathioprine, or combination therapy for Crohn's disease”	2010	2021	202.1
55.	Nature	“Nicotinic acetylcholine receptor $\alpha 7$ subunit is an essential regulator of inflammation”	2003	2016	118.59
56.	New England Journal of Medicine	“Efficacy of B-cell-targeted therapy with rituximab in patients with rheumatoid arthritis”	2004	1989	124.31
57.	New England Journal of Medicine	“Platinum-based chemotherapy plus cetuximab in head and neck cancer”	2008	1985	165.42
58.	Pediatrics	Breastfeeding and the use of human milk”	2005	1982	132.13
59.	Clinical Microbiology Reviews	“Acinetobacter baumannii: Emergence of a successful pathogen”	2008	1981	165.08
60.	Nature	“The immunopathogenesis of sepsis”	2002	1950	108.33
61.	Nature	“Anti-cachectin/TNF monoclonal antibodies prevent septic shock during lethal bacteraemia”	1987	1938	58.73

62.	Annual Review of Immunology	“The host defense of <i>Drosophila melanogaster</i> ”	2007	1934	148.77
63.	Intensive Care Medicine	“Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016”	2017	1916	638.67
64.	The Lancet	“Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016”	2017	1889	629.67
65.	Nature Reviews Immunology	“Signalling pathways of the TNF superfamily: A double-edged sword”	2003	1876	110.35
66.	Nature	“Circulating mitochondrial DAMPs cause inflammatory responses to injury”	2010	1867	186.7
67.	American Journal of Physiology - Cell Physiology	“Physiological roles and properties of potassium channels in arterial smooth muscle”	1995	1863	74.52
68.	The Lancet	“Global, regional, and national causes of child mortality in 2008: a systematic analysis”	2010	1860	186
69.	Lancet	“Randomised double-blind placebo-controlled study of interferon β -1a in relapsing/remitting multiple sclerosis”	1998	1834	83.36
70.	New England Journal of Medicine	“Sildenafil citrate therapy for pulmonary arterial hypertension”	2005	1827	121.8
71.	Critical Care Medicine	“Multiple organ dysfunction score: A reliable descriptor of a complex clinical outcome”	1995	1819	72.76
72.	Osteoarthritis and Cartilage	“OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines”	2008	1809	150.75
73.	Cellular Signalling	“LPS induction of gene expression in human monocytes”	2001	1785	93.95
74.	The Lancet	“COVID-19: consider cytokine storm syndromes and immunosuppression”	2020	1744	1744
75.	Nature Reviews Immunology	“High-mobility group box 1 protein (HMGB1): Nuclear weapon in the immune arsenal”	2005	1741	116.07
76.	Critical Care Medicine	“Sepsis in European intensive care units: Results of the SOAP study”	2006	1736	124
77.	Pediatric Critical Care Medicine	“International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics”	2005	1728	115.2

78.	Proceedings of the National Academy of Sciences of the United States of America	“Genomic responses in mouse models poorly mimic human inflammatory diseases”	2013	1683	240.43
79.	The Lancet	“Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial”	2009	1677	152.45
80.	New England Journal of Medicine	“Human infection with a novel avian-origin”	2013	1676	239.43
81.	European Heart Journal	“Nitric oxide synthases: Regulation and function”	2012	1659	207.38
82.	Physiological Reviews	“Heme oxygenase-1/carbon monoxide: From basic science to therapeutic applications”	2006	1640	117.14
83.	New England Journal of Medicine	“A Semiquantitative Culture Method for Identifying Intravenous-Catheter-Related Infection”	1977	1628	37.86
84.	Intensive Care Medicine	“2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference”	2003	1626	95.65
85.	JAMA: The Journal of the American Medical Association	“The Natural History of the Systemic Inflammatory Response Syndrome (SIRS): A Prospective Study”	1995	1611	64.44
86.	Lancet Infectious Diseases	“The global burden of group A streptococcal diseases”	2005	1609	107.27
87.	The Lancet Global Health	“Global causes of maternal death: A WHO systematic analysis”	2014	1606	267.67
88.	The Lancet	“Burden of disease caused by Streptococcus pneumoniae in children younger than 5 years: global estimates”	2009	1599	145.36
89.	Gastroenterology	“Adalimumab for Maintenance of Clinical Response and Remission in Patients With Crohn's Disease: The CHARM Trial”	2007	1599	123
90.	The Lancet	“Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: A systematic analysis for the Global Burden of Disease Study 2016”	2017	1597	532.33
91.	Pharmacological Reviews	“The sympathetic nerve - An integrative interface between two supersystems: The brain and the immune system”	2000	1574	78.7

92.	New England Journal of Medicine	“Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries”	1994	1565	60.19
93.	Nature Immunology	“Autophagy proteins regulate innate immune responses by inhibiting the release of mitochondrial DNA mediated by the NALP3 inflammasome”	2011	1548	172
94.	Journal of Clinical Oncology	“Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin, and cisplatin in advanced or metastatic bladder cancer: Results of a large, randomized, multinational, multicenter, phase III study”	2000	1548	77.4
95.	Journal of Trauma - Injury, Infection and Critical Care	“Problems in the management of type III (Severe) open fractures: A new classification of type III open fractures”	1984	1544	42.89
96.	New England Journal of Medicine	“Nurse-staffing levels and the quality of care in hospitals”	2002	1541	85.61
97.	Hepatology	“Diagnosis, Management, and Treatment of Hepatitis C”	2004	1522	95.13
98.	Lancet Oncology	“CHOP-like chemotherapy plus rituximab versus CHOP-like chemotherapy alone in young patients with good-prognosis diffuse large-B-cell lymphoma: a randomised controlled trial by the MabThera International Trial (MInT) Group”	2006	1512	108
99.	New England Journal of Medicine	“Pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer”	2018	1498	749
100.	The Lancet	“High serum procalcitonin concentrations in patients with sepsis and infection”	1993	1487	55.07

Based on the number of citations in Table 2, the 100 top-cited on sepsis-related articles are listed by ranking order. It also indicates the number of citations per year. The most-cited article in this review is the one entitled "Intensive insulin therapy in critically ill patients" (2001)(Van Den Berghe et al. 2001), according to the overall citation count. The decade between 2001 and 2020 was the most productive with 73 articles remaining 27 articles are published in before 2000. The articles were published in 42 different journals, more than four quarters of the articles ($n=24$) being published in the journal of New England Journal of Medicine (NEJM) followed by The Lancet $n=10$, Both of them accounted for 34 articles out of 100 (Table 2). A total of 4381 authors were

involved in the authorships, 6 were responsible for single-authored documents and 4375 were responsible for multi-authored documents. (Table No.1) The greatest count of top-cited publications was published in 2008 ($n=8$), 2003,2004,2006,2008 each ($n=6$). By the date of our search, these 100 articles were cited 273306 times in total, and the average citation per document was 2733 (Table No.1). Table No.2 shows that 2 articles with more than 7000 citation times cited in the journal of the New England Journal of Medicine in 2001.

TABLE.3 THE 10 ARTICLES ON OUR LIST WITH THE HIGHEST CITATION PER YEAR (CY).

Paper	Year	Total Citations	TC per Year
Mehta P, Covid-19: “Consider Cytokine Storm Syndromes and Immunosuppression”, LANCET(Mehta et al. 2020)	2020	1744	1744
Singer M, “The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)”, JAMA(Singer et al. 2016)	2016	5972	1194.4
Brahmer J, “Nivolumab Versus Docetaxel in Advanced Squamous-Cell Non-Small-Cell Lung Cancer”, NEW ENGL J MED(Brahmer et al. 2015)	2015	4432	738.7
Naghavi M, Global, “Regional, And National Age-Sex Specific All-Cause and Cause-Specific Mortality For 240 Causes of Death, 1990-2013: A Systematic Analysis for The Global Burden of Disease Study”, LANCET(Naghavi et al. 2015)	2015	4019	669.8
Ridker Pm, “Anti-inflammatory Therapy with Canakinumab for Atherosclerotic Disease”, NEW ENGL J MED(Ridker et al. 2017)	2017	2310	577.5
Gandhi L, “Pembrolizumab Plus Chemotherapy In Metastatic Non-Small-Cell Lung Cancer”, NEW ENGL J MED(Gandhi et al. 2018)	2018	1498	499.3
Dellinger Rp, “Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock”: CRIT CARE MED(Dellinger et al. 2013)	2013	3911	488.9
Rhodes A, “Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock”: INTENSIVE CARE MED(Rhodes et al. 2017)	2017	1916	479
Vos T, “Global, Regional, And National Incidence, Prevalence, And Years Lived with Disability For 328 Diseases and Injuries For 195 Countries, 1990-2016: A Systematic Analysis for The Global Burden of Disease Study”, LANCET(Vos et al. 2017)	2017	1889	472.2
Naghavi M, “Global, Regional, And National Age-Sex Specific Mortality For 264 Causes of Death, 1980-2016: A Systematic	2017	1597	399.2

Table 3 indicates the top 10 highly cited articles, the highest citation per year, record titles with citations. Mehta P et al, entitled “*Covid-19: Consider Cytokine Storm Syndromes and Immunosuppression*” published in 2020 in Lancet Journal and earned 1744 citations, preceded by Singer M, published in 2016 at Journal of the American Medical Association (JAMA), received 1194.4 citations with the article title “*The Third International Consensus Concepts for Sepsis and Septic Shock*” (Sepsis-3).

TABLE 4. YEAR-WISE ANNUAL TOTAL CITATION PER YEAR

Year	N	TC	Mean TCperArt	Mean TCperYear	Citable Years
1976	1	2464	2464	56	44
1977	1	1628	1628	37.86	43
1978	0	0	0	0	0
1979	0	0	0	0	0
1980	0	0	0	0	0
1981	0	0	0	0	0
1982	0	0	0	0	0
1983	0	0	0	0	0
1984	1	1544	1544	42.89	36
1985	0	0	0	0	0
1986	0	0	0	0	0
1987	1	1938	1938	58.73	33
1988	1	4855	4855	151.72	32
1989	0	0	0	0	0
1990	1	3178	3178	105.93	30
1991	2	4259	2129.5	73.43	29
1992	3	12957	4319	154.25	28
1993	2	6890	3445	127.59	27
1994	2	6008	3004	115.54	26

1995	4	7568	1892	75.68	25
1996	2	7647	3823.5	159.31	24
1997	0	0	0	0	0
1998	3	11808	3936	178.91	22
1999	1	2660	2660	126.67	21
2000	2	3122	1561	78.05	20
2001	5	27518	5503.6	289.66	19
2002	4	8058	2014.5	111.92	18
2003	6	16899	2816.5	165.68	17
2004	6	15494	2582.333333	161.4	16
2005	8	18331	2291.375	152.76	15
2006	6	13001	2166.833333	154.77	14
2007	4	10454	2613.5	201.04	13
2008	6	15287	2547.833333	212.32	12
2009	4	9564	2391	217.36	11
2010	5	12046	2409.2	240.92	10
2011	1	1548	1548	172	9
2012	3	6649	2216.333333	277.04	8
2013	5	12948	2589.6	369.94	7
2014	1	1606	1606	267.67	6
2015	2	8451	4225.5	845.1	5
2016	1	5972	5972	1493	4
2017	4	7712	1928	642.67	3
2018	1	1498	1498	749	2
2019	0	0	0	0	0
2020	1	1744	1744	1744	1
Total	100	273306			

Table 4 indicates the published year-wise citation of publications, the largest number of the citation ($n=27518$) for articles ($n=5$) published in 2001 accompanied by ($n=18331$) citations for articles ($n=8$) published in 2005. The highest number of citations per article for the year 2016 ($n=5972$) followed by ($n=5503.6$) for the year 2001. The largest number of total quotations per year in 2020 was ($n=1744$) followed by 2016 ($n=1493$). There are no publications were present in the highly cited category from the year of 1978-1983, 1985 and 1986, 1989,1997,2019.

TABLE 5. MOST CITED COUNTRIES

Country	continent	Total Citations	Average Article Citations
USA	N. America	149177	2869
Canada	N. America	18677	2668
UK	Europe	17152	2450
Belgium	Europe	15093	5031
France	Europe	13417	1917
Germany	Europe	9771	2443
Japan	Asia	6399	3200
Australia	Oceania	4841	2420
Italy	Europe	4600	2300
Israel	Asia	3848	1924

TABLE 6. TOP10 COUNTRY WISE SCIENTIFIC PRODUCTION

region	continent	Freq	percent
USA	N. America	628	26.55
UK	Europe	159	6.72
Australia	Oceania	143	6.05
Germany	Europe	107	4.52
Canada	N. America	99	4.19
India	Asia	85	3.59
Iran	Asia	68	2.88
France	Europe	64	2.71
Italy	Europe	59	2.49
Ethiopia	Africa	52	2.2

Tables 5 and 6 show the most cited countries and country-wise scientific productions. The top three countries by publication citation counts were the USA (n=149177) Canada (n=18677) UK (n=17152) in table no.5. In the scientific production table.6 USA (n=625) got the highest number of author's country production followed by the UK (n=159). European countries occupy the most numbers and are at the top of both tables 5 & 6. Countries in North America and Asia are second place in each table (Fig.1).

Country Scientific Production

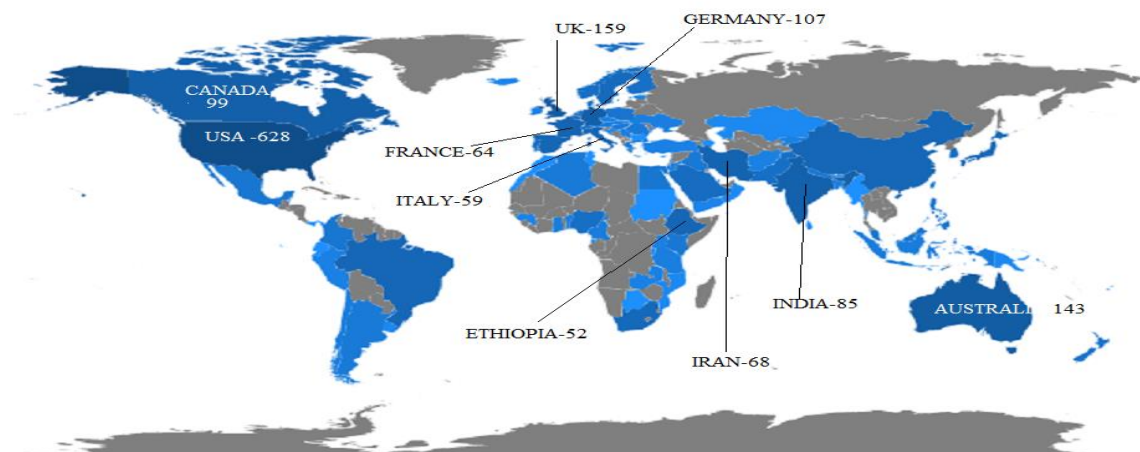


Figure 1: country wise distribution of number of authors involved in the highly cited sepsis articles

The journal with the highest number of top 100 cited articles was New England Journal of Medicine ($n=2422$), followed by The Lancet ($n=10$) while their total citations is ($n=76109$) and ($n=20263$) respectively (Table 7). Since the New England Journal of Medicine sepsis-related articles are published from 1977, It is one of the reasons for getting the highest number of citations. Cite score, SRJ, SNIP values are taken from Scopus. The Science journal got the highest number of Citations per article ($n=3491.50$)

Table 7. Top 10 Most relevant sources and impacts.

Source	Cite score 2019	SJR 2019	SNIP 2019	TC	NP	C/A	PY Start
New England Journal of Medicine	66.1	18.291	13.212	76109	24	3171.21	1977
The Lancet	73.4	14.554	21.313	20263	10	2026.30	1993
Critical Care Medicine	10.6	2.994	2.310	31335	9	3481.67	1992
Nature	51.0	14.047	8.820	10046	5	2009.20	1987
Intensive Care Medicine	14.0	3.473	2.986	11811	4	2952.75	1996
Science	45.3	13.110	7.521	13966	4	3491.50	1990
Clinical Infectious Diseases	12.5	4.226	2.888	10172	3	3390.67	2004
Journal of The American Medical Association	26.3	5.913	11.131	8963	3	2987.67	2002
Annual Review of Immunology	35.1	13.842	4.425	6377	2	3188.50	1994
Journal of Clinical Oncology	35.4	10.054	5.568	4344	2	2172.00	2000

*TC-Total Citation, NP-Number of Publication, C/A-Citation Per Article

TABLE .8 TOP 10 AUTHORS PRODUCTION OVERTIME

Author	Affiliation	h-index	TC	NP	PY_start
Vincent JL	Université libre de Bruxelles (ULB), Brussels, Belgium	139	38502	11	1996
Levy MM	Rhode Island Hospital, Providence, United States	68	26472	8	2003
Marshall JC	Ottawa Hospital Research Institute, Ottawa, Canada	93	24551	8	1995

Angus DC	University of Pittsburgh, Pittsburgh, United States	100	24380	6	2001
Bernard GR	Vanderbilt University Medical Center, Nashville, United State	100	21291	6	1995
Dellinger RP	Cooper Medical School of Rowan University, Camden, United States	54	21350	6	1992
Gerlach H	Vivantes Klinikum Neukölln, Berlin, Germany	51	16511	6	2004
Li, Yongmei	Francisco Veterans Affairs Health Care System, San Francisco, United States	38	9815	4	2015
Annane, Djillali	Hospital Raymond Poincare, Garches, France	77	16981	5	2002
Gupta R	Indian Institute of Technology Kanpur, Kanpur, India	90	7505	3	2015

A total of 4381 authors (Authors of single-authored documents 6, Authors of multi-authored documents 4375) (Table No.8) wrote these common articles, and their work laid the foundation for further study. The number of documents per author was 0.0228 and authors per document was 43.8. The most frequently mentioned author in all articles was Vincent JL working in Université libre de Bruxelles (ULB), Brussels, Belgium with 11 articles. More than half of the authors are in the United States (Fig.2).

Top Author's production over the Time

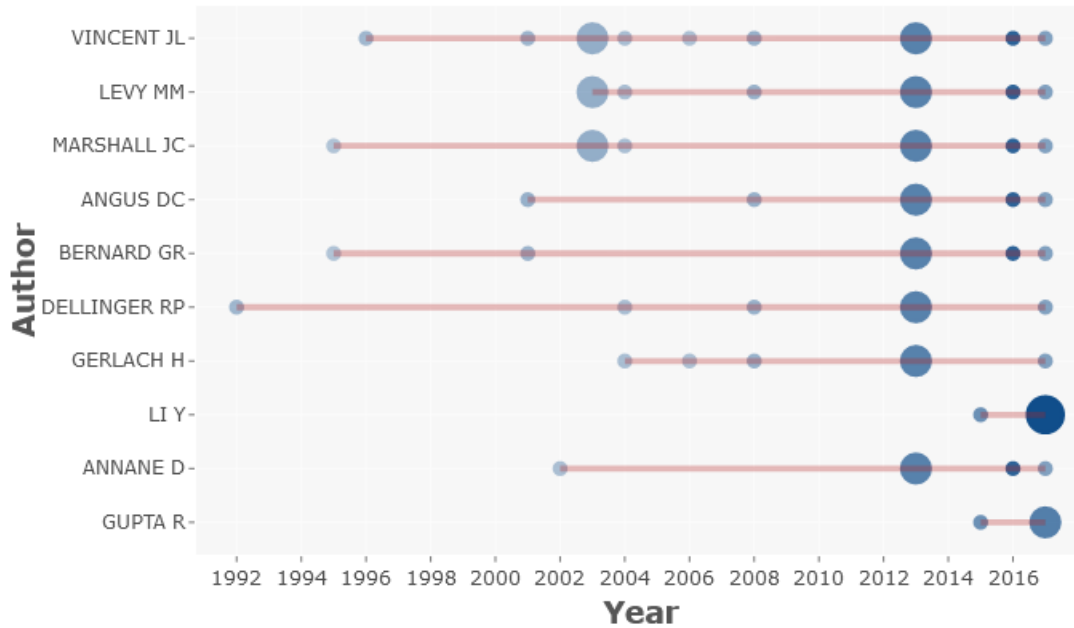


Figure 2: Top Authors production over the time

DISCUSSION:

Sepsis is an inflammatory immune reaction caused by bacteria. In most cases, fungal, bacterial, and protozoan infections spread sepsis (Deutschman and Tracey 2014). The lungs, brain, urinary tract, skin, and abdominal organs are common locations for the main infection. In this study, we evaluate the 100 most influential papers related to sepsis. The USA is the dominant country in terms of contribution to the developments of Sepsis research with the largest numbers of T100 articles. The journal *New England Journal of Medicine* published the T100 articles from 1976 to 2020. This is held in our study in terms of the numbers of T100 articles, most cited countries, and Country wise scientific production demonstrating that the USA has made the greatest contribution to the development of sepsis research. (Table 5 & 6). Interestingly, the top two scientists, namely, Vincent JL and Levy MM, who published the most T100 articles as the first author, were from Belgium and the US, respectively. The author with the third-highest number of T100 articles in this study is the well-known Marshall JC from Ottawa Hospital Research Institute, Ottawa, Canada. The largest number of the citation (Table No.4) for articles published in 2001 followed by 2005. The highest number of citations per article for the year 2016 followed

for the year 2001. This study also clearly indicates that all the highly cited articles are directly involved in diagnosis and treatment oriented as well from reviews category.

CONCLUSION:

In recent decades, the standard treatment of Sepsis diseases has been affected and updated by the results of important studies. An internationally relevant clinical study aims to improve the use of antibiotics in sepsis risk patients with Covid-19(University 2020). This research shows that the developed countries, the United States, and European Countries are constantly advancing in the development of Sepsis research. There has been news that the care of sepsis patients is being delayed due to corona causes. There is a very high chance that the number of research publications will decrease due to such reasons. Research articles with the highest citations are written by western countries, developing countries like India, China, should pay more attention to the publication of research articles with high citations.

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