Oxidative Stress in Pre-Eclampsia: Bibliometric Visualization Studies and Analysis

Endang Sri Wahyuni[1], Nanang Wiyono[2], Maryatun Maryatun[3], Irvina Nurul Mahmudah[4], Juleha Duwi Handayani[5], Safella Lutfatul Jannah[6]

[1] Bachelor of Midwifery Program, Faculty of Health Sciences, Universitas 'Aisyiyah Surakarta, Indonesia. Jalan Ki Hajar Dewantara No.11 Surakarta, Jawa Tengah, Indonesia 57126.

[2] Department of Anatomy, Faculty of Medicine, Universitas Sebelas Maret, Indonesia. Jalan Ir. Sutami 36A Surakarta, Jawa Tengah, Indonesia 57126.

[3] Nursing Study Program, Faculty of Health Sciences, Universitas 'Aisyiyah Surakarta, Indonesia. Jalan Ki Hajar Dewantara No.11 Surakarta, Jawa Tengah, Indonesia 57126.

[4] Student Bachelor of Midwifery, Faculty of Health Sciences, Universitas 'Aisyiyah Surakarta, Indonesia. Jalan Ki Hajar Dewantara No.11 Surakarta, Jawa Tengah, Indonesia 57126.

[5] Student National Taipei University of Nursing and Health Science, Taiwan. No. 365, Mingde Rd, Beitou District, Taipei City, Taiwan 112.

[1*]endang@aiska-university.ac.id , [2]nanang.wiyono@staff.uns.ac.id, [3]tunmarya@aiska-university.ac.id, [4]vinaa.nurul25@gmail.com, [5]julehaduwihandayani@gmail.com, [6]safellas4@gmail.com

Abstract

Background*: Preeclampsia is a major cause of death and maternal health problems in the world. Preeclampsia can be triggered by an increase in free radicals which cause oxidative stress.* ***Aim****: This study aimed to visually map research publications on the mechanisms of oxidative stress in preeclampsia based on bibliometric analysis.* ***Methods****: Systematic Literature Review research design with bibliometric analysis. VOSviewer, Publish or Perish (PoP), and Microsoft Excel resources were used. The database was retrieved from Scopus using the keywords: preeclampsia AND "oxidative stress" AND mechanism as input.* ***Results****: The Scopus database revealed a total of 685 published publications on the effects of oxidative stress on preeclampsia from 1996 to 2022. Annual publishing growth is on rising, with 2022 showing the greatest growth rate at 11.68%. The United States has the highest percentage of articles in the world, with a total of 25.8%. The most prolific author is Davidge, ST, with 14 documents. "The effects of oxidative stress on female reproduction: a review", is the most influential article with 928 citations. The International Journal of Molecular Sciences is the most successful journal, with 30 publications and a total link strength of 3988. The University of Mississippi Medical Center is the main institution's research site, with 26 publication documents. The most extensively explored terms are preeclampsia and oxidative stress.* ***Conclusion****: The mechanisms of oxidative stress in preeclampsia in the network map were categorized into 5 clusters based on co-occurrence, and "oxidative stress" was the most highlighted term not only in cluster 1 but throughout the network.*

Keywords*: Preeclampsia; oxidative stress; bibliometric analysis*

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Abstrak

Latar Belakang: Preeklamsia merupakan penyebab utama kematian dan masalah kesehatan ibu di dunia. Preeklamsia dapat dipicu oleh peningkatan radikal bebas yang menyebabkan stres oksidatif. **Tujuan:** Penelitian ini bertujuan untuk memetakan secara visual publikasi penelitian tentang mekanisme stres oksidatif pada preeklamsia berdasarkan analisis bibliometrik. **Metode:** Desain penelitian Tinjauan Pustaka Sistematis dengan analisis bibliometrik. Sumber daya yang digunakan adalah VOSviewer, Publish or Perish (PoP), dan Microsoft Excel. Basis data diambil dari Scopus dengan menggunakan kata kunci: preeklamsia DAN "stres oksidatif" DAN mekanisme sebagai input. **Hasil:** Basis data Scopus mengungkapkan total 685 publikasi yang diterbitkan tentang efek stres oksidatif pada preeklamsia dari tahun 1996 hingga 2022. Pertumbuhan penerbitan tahunan terus meningkat, dengan tahun 2022 menunjukkan tingkat pertumbuhan terbesar sebesar 11,68%. Amerika Serikat memiliki persentase artikel tertinggi di dunia, dengan total 25,8%. Penulis yang paling produktif adalah Davidge, ST, dengan 14 dokumen. "Dampak stres oksidatif pada reproduksi wanita: tinjauan", adalah artikel yang paling berpengaruh dengan 928 kutipan. Jurnal Internasional Ilmu Molekuler adalah jurnal yang paling sukses, dengan 30 publikasi dan total kekuatan tautan 3988. Pusat Medis Universitas Mississippi adalah situs penelitian lembaga utama, dengan 26 dokumen publikasi. Istilah yang paling banyak dieksplorasi adalah preeklamsia dan stres oksidatif. **Kesimpulan:** Mekanisme stres oksidatif pada preeklamsia dalam peta jaringan dikategorikan menjadi 5 kelompok berdasarkan ko-kemunculan, dan "stres oksidatif" adalah istilah yang paling disorot tidak hanya di kelompok 1 tetapi di seluruh jaringan.

Kata kunci: Preeklamsia; stres oksidatif; analisis bibliometrik

INTRODUCTION

Numerous countries are focusing their efforts on reducing maternal mortality since it is still the main problem of poor health status. Preeclampsia is a major resulted of maternal and fetal morbidity and mortality. Preeclampsia impact approximately 2–8% of pregnancies worldwide, causing maternal health concerns such as eclampsia, hemolysis, hemorrhagic stroke, and the development of HELLP syndrome (Amaral et al., 2015; Rana et al., 2019; Taylor & George, 2022; Vaka et al., 2018).

The pathogenesis of preeclampsia is not known with certainty (theory of disease), the beginning of the course of preeclampsia cannot be predicted properly, and the condition of preeclampsia affects the fetus directly due to placental insufficiency or complications during delivery. Preeclampsia can be caused by an increase in free radicals, which causes oxidative stress and, as a result, an inflammatory reaction with systemic inflammation (Alam et al., 2023; Brenneisen et al., 2022; Yang et al., 2023; Zhang et al., 2023). Preeclampsia is a proinflammatory state, syncytiotrophoblastic microvesicles activate peripheral blood mononuclear cells which cause the release of proinflammatory cytokines (Cornelius, 2018; Rana et al., 2019). Preeclampsia is believed to be an inflammatory illness caused by poor placentation, with oxidative stress leading to the development of clinical symptoms (Cao et al., 2022; Medjedovic et al., 2022;

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Possomato-Vieira & Khalil, 2016; Rana et al., 2019). TNFα levels were discovered to be relatively high in preeclampsia; previously, TNFα was shown to promote mitochondrial oxidative stress in pregnant rats (Brenneisen et al., 2022; Collier et al., 2021; Dai & Piquette-Miller, 2022; Ren et al., 2021). Increased free radical generation and lower levels of certain trace elements disrupt antioxidant defense systems, contributing to increased oxidative stress (Graf et al., 2021; Possomato-Vieira & Khalil, 2016; Tesfa et al., 2021).

An important condition the course of preeclampsia is the increase in free radicals originating from oxygen and nitrogen (reactive oxygen species/reactive nitrogen species (ROS/RNS), which appear to be central players regulating the development and incidence of preeclampsia linkage communication between cells is probably going to suffer. Connexins (Cxs), a family of transmembrane proteins that form hemichannels and gap junction channels (GJCs), are critical in paracrine and autocrine cell communication, enabling the movement of signaling molecules between cells as well as between the cytoplasm and media of GJCs. endothelial and smooth muscle, thereby deep impact controlling the contraction and relaxation of blood vessels. In systemic blood vessels, the activity of GJCs and hemichannels is modulated by ROS and RNS. Cxs participates during the formation of the placenta and is expressed in the placental blood vessels (Graf et al., 2021; Rozas-Villanueva et al., 2020; Vaka et al., 2018).

Numerous studies on oxidative stress in preeclampsia have been conducted and published in international journals with indexes, but limited bibliometric analysis of the research's findings has been done. The Scopus database was chosen for the bibliometric analysis since it was regarded as the best and Qualified by the VOSviewer program. VOSviewer software was taken as a bibliometric analysis tool to visualize the network of articles, countries, institution, journals, authors, and keywords. The objective of this study is to visually map research on oxidative stress mechanisms in preeclampsia based on bibliometric analysis.

Methods

Research design

This research used a bibliometric-based systematic review as its methodology. The researchers employed the programs VOSviewer, Publish or Perish (PoP), and Microsoft Excel. Preeclampsia AND "oxidative stress" AND mechanism were the search terms used to extract the database from Scopus. The research question is: “What is the bibliographical map of research publication articles on the mechanisms of oxidative stress in preeclampsia?”

Data source

The databases Scopus were used to conduct a literature search. Scopus was chosen as the research data source. Scopus was employed for this research considering it is the biggest database for citations and abstracts of peer-reviewed scientific literature, with over 24,000 titles from 11,000 publishers. Scopus was chosen as an information source since it comprises all MEDLINE documents, which are the most frequently used free citation databases (Hernández-Vásquez et al., 2020).

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Search methods

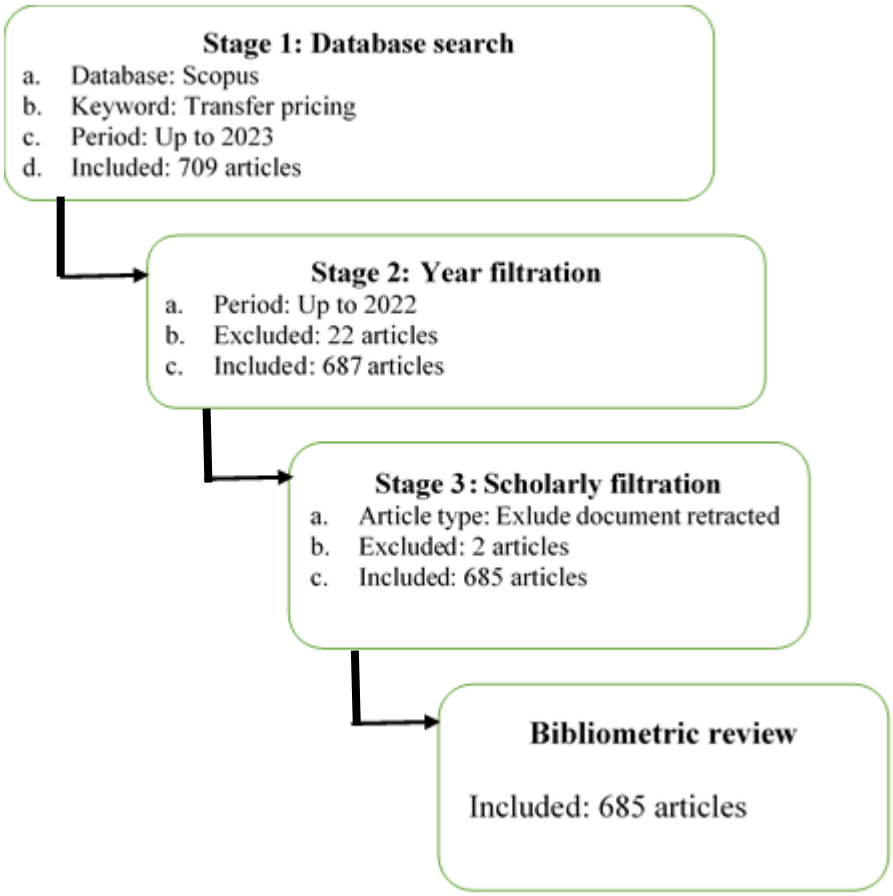

Figure 1. Research Data Search Strategies

Data collection

Data collection from the Scopus database was carried out on March 31, 2023. Complete record data from each publication is downloaded in CSV file format.

Bibliometric analysis

Bibliometrics employed VOSviewer software (version 1.6.17, Leiden University, Leiden, The Netherlands) for network build and describe based on co-authorship and co-occurrence. The bibliometric study also utilized the PoP application to obtain information on citations per year, number of articles, number of citations, citations per year, citations per article, and citations per author. The output of the study produced a map of publications, countries, authors, citations, journals, articles, and theme networks based on keywords.

Ethical considerations.

This study has received ethical approval with number 060/III/AUEC/2023, granted by the Research Ethics Commission of Universitas 'Aisyiyah Surakarta.

Result and discussion

Result

1. Publication

There were 685 research articles published from 1996 to 2022 that addressed the mechanism of oxidative stress in preeclampsia. There have been 33,015

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citations in total, with 1,222.78 on average for each year. Every article receives 48.20 citations on average.

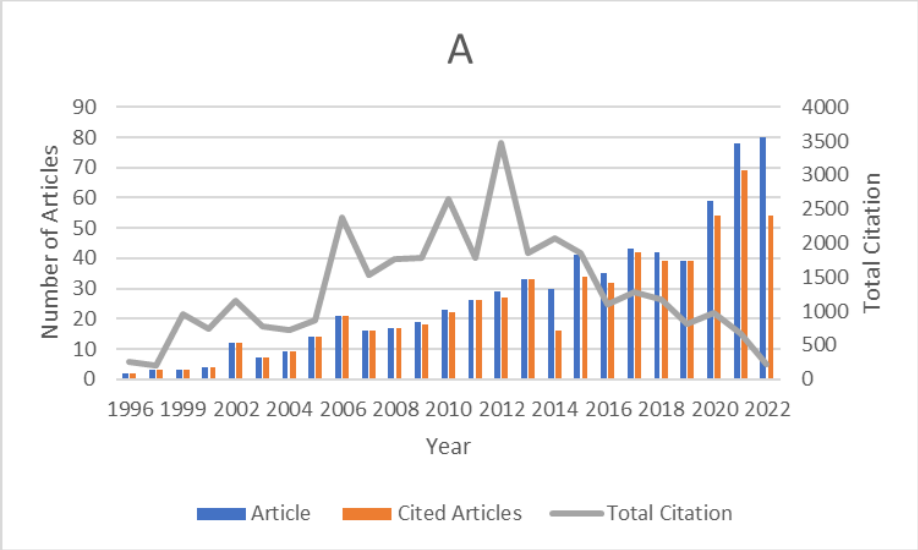

Figure 2. The growth trend in publications and the number of articles cited worldwide from 1996 to 2022. There was an increasing trend in the number of articles on the mechanism of oxidative stress in preeclampsia from 1996 to 2022, with articles being cited more frequently between 2006 and 2018, particularly in 2012.

2. Countries

The most productive country conducting research on the mechanism of oxidative stress in preeclampsia was the United States with a total of 25.8% of the total research publications, and had 12,535 citations, and a total link strength of 83.

Table 1. Top 10 productive countries in research related to the mechanism of oxidative stress in preeclampsia

Rank	Country	Quantity	Percentage	Citation	Average Citation	Total Link Strength
1	United States	177	25,8	12535	70.82	83
2	China	136	19,9	2056	15.12	36
3	United Kingdom	76	11,1	6006	79.03	61
4	Canada	45	6,6	3086	68.58	23
5	Australia	44	6,4	1208	27.45	54
6	Germany	34	5.0	1887	55.50	35
7	India	32	4,7	2136	66.75	7
8	Italy	28	4,1	1301	46.46	21
9	Brazil	26	3,8	365	14.04	22
10	Chile	25	3,6	669	26.76	31

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3. Institutes

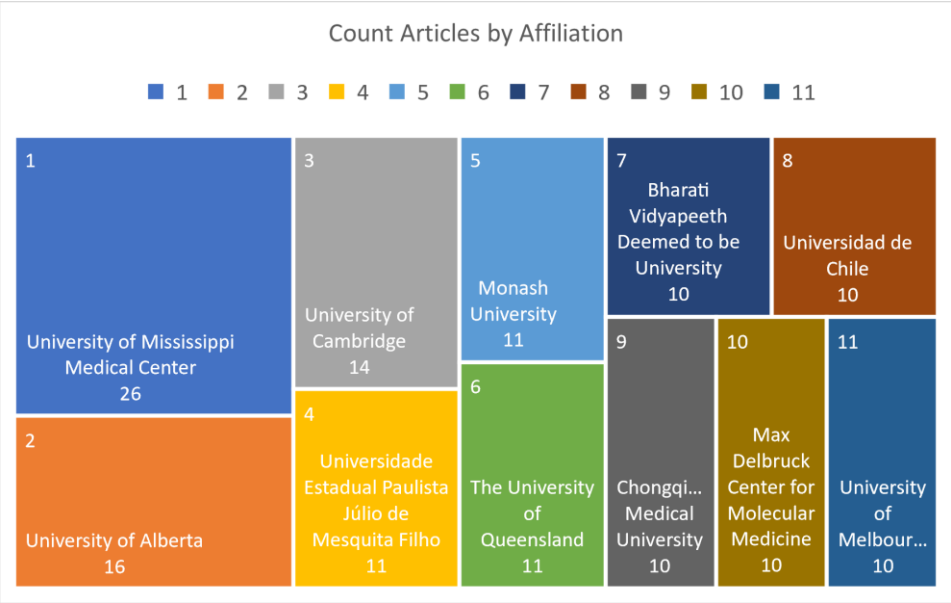

Figure 3. Top 11 productive affiliations in research related to the mechanism of oxidative stress in preeclampsia.

4. Journals

Table 2. Top 10 productive journals in research related to the mechanism of oxidative stress in preeclampsia.

Rank	Source	Quantity	SR 2022	Citation	Avg, Citation	Total Link Strength
1	International Journal of Molecular Sciences	30	Q1	820	27.33	3988
2	Placenta	28	Q1	1321	47.18	3278
3	Free Radical Biology and Medicine	13	Q1	1158	89.08	2194
4	Medical Hypotheses	11	Q2	494	44.91	2341
5	American Journal of Reproductive Immunology	10	Q2	813	81.30	1459
6	Oxidative Medicine and Cellular Longevity	10	Q1	109	10.90	1391
7	Pregnancy Hypertension	10	Q1	222	10:20 p.m	1536
8	Current Hypertension Reports	9	Q1	428	47.56	1539
9	Hypertension	9	Q1	317	35.22	1181
10	American Journal of Obstetrics and Gynecology	8	Q1	496	62.00	1146

5. Authors

Table 3. Top 10 active writer in research on the mechanisms of oxidative stress in preeclampsia.

Rank	First Author	Affiliation	Country	Count of Published	Citation	Avg. Citation Items	Total Link Strength
1	Davidge, ST	University of Alberta	United States	14	933	66.64	146

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2	LaMarca, B.	University of Mississippi Medical Center	United States	12	638	53.17	243
3	Chen, Y	Tianjin Medical University General Hospital	China	12	328	27.33	132
4	Zhang, L.	Zhejiang University School of Medicine	China	12	145	12.08	100
5	Cornelius, D.C	University of Mississippi Medical Center	United States	10	285	28.50	122
6	Zhang, Y.	School of Medicine, Tongji University	China	10	87	8.70	36
7	Decend, R.	University of Southern Denmark	Denmark	9	459	51.00	171
8	Qi, H.	Hospital of Chongqing Medical University	China	9	113	12.56	91
9	Burton, GJ	University of Cambridge	United Kingdom	8	1157	144.62	258
10	Roberts, JM	University of Pittsburgh	United States	8	961	120.12	95

6. Citation

Table 4. Top 10 documents cited in research related to the mechanism of oxidative stress in preeclampsia.

Rank	Title	Source	Subject	First Author	Year	Citation	TotalLink Strength	Country
1	The effects of oxidative stress on female reproduction: a review	Reproductive Biology and Endocrinology	Reviews	Agarwal A.	2012	928	205	United States
2	Pre-eclampsia part 1: current understanding of its pathophysiology	Nature Reviews Nephrology	Reviews	Chaiworapongsa T.	2014	667	161	United States
3	Vitamins C and E: Beneficial effects from a mechanical perspective	Free Radical Biology and Medicine	Reviews	Traber MG	2011	575	76	United States
4	Oxidative Stress in the Pathogenesis of Preeclampsia	Proceedings of the Society for Experimental Biology and Medicine	Conference	Hubel CA	1999	537	150	United States
5	Microparticles in cardiovascular disease	Cardiovascular Research	Reviews	Vanwijk MJ	2003	532	4	Netherlands
6	The Role of cellular reactive oxygen species, oxidative stress, and	The International Journal of	Reviews	Al-Gubory KH	2010	531	98	France

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	Antioxidants in pregnancy outcomes	Biochemistry & Cell Biology						
7	Immunology of Pre-Eclampsia	American Journal of Reproductive Immunology	Reviews	Redman CWG	2010	506	63	United Kingdom
8	Placental-related diseases of pregnancy: involvement of oxidative stress and implications in human evolution	Human Reproduction Update	Reviews	Jauniaux E.	2006	463	140	United Kingdom
9	Placental Stress and Pre-eclampsia: A Revised View	Placenta	Articles	Redman CWG	2009	439	74	United Kingdom
10	Association of maternal endothelial dysfunction with preeclampsia	Jama	Articles	Chambers JC	2001	432	83	United Kingdom

7. Keyword

Table 5. The top 30 keywords from research documents related to the mechanism of oxidative stress in preeclampsia.

No	Keywords	Count	No	Keywords	Count	No	Keywords	Count
1	Preeclampsia	292	11	Endothelium	19	21	Melatonin	10
2	Oxidative stress	187	12	Reactive oxygen species	19	22	Angiogenesis	10
3	Pregnancy	104	13	Apoptosis	17	23	sFlt-1	10
4	Placenta	81	14	Antioxidants	14	24	Eclampsia	10
5	Pre-eclampsia	62	15	Mitochondria	13	25	Fetal Growth Restriction	9
6	hypertension	59	16	Lipid peroxidation	13	26	Cytokines	9
7	inflammation	45	17	Cardiovascular disease	13	27	Biomarkers	9
8	Trophoblast	34	18	Intrauterine Growth Restriction	12	28	Preterm birth	9
9	hypoxia	29	19	Free radicals	11	29	Diabetes	9
10	Endothelial dysfunction	25	20	Autophagy	11	30	Pathogenesis	9

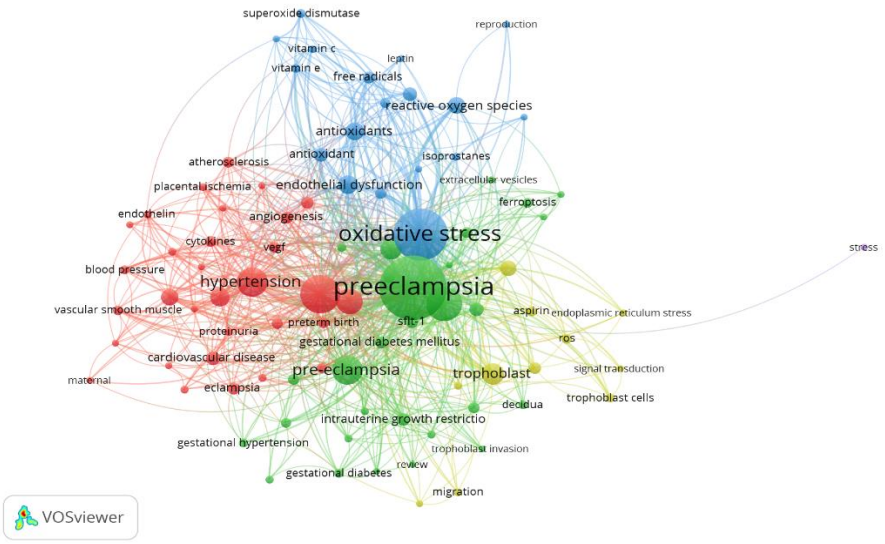

Figure 4. The Analysis of Network Visualization Co-Occurrences map.

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The number of keywords was 90 items divided into 5 clusters, 726 links, and the Total Link Strength of 1848. Different colors represent different clusters that cooperate closely, the size of the circle is equal to the number of articles on the theme, and the distance between the two themes illustrates the relationship between the two themes. There are five distinct clusters among them, however, some of them are closely related.

Table 6. The analysis of co-occurrence keywords.

No	Cluster 1 – Red (31 Items)	Total Link Strength	Occurrences	No	Cluster 2- Green (29 Items)	Total Link Strength	Occurrences
1	Pregnancy	257	104	1	Preeclampsia	595	292
2	Hypertension	164	59	2	Placenta	196	81
3	Inflammation	109	45	3	Pre-eclampsia	106	62
4	nitric oxide	74	24	4	hypoxia	72	29
5	Endothelium	62	19	5	Mitochondria	45	13
6	Cardiovascular disease	30	13	6	Intrauterine Growth Restriction	38	12
7	Angiogenesis	27	10	7	Gestational diabetes mellitus	28	11
8	Eclampsia	24	10	8	sFlt-1	27	10
9	Melatonin	28	10	9	Fetal Growth Restriction	31	9
10	Cytokines	27	9	10	Pathogenesis	19	9
11	Preterm birth	23	9	11	Diabetes	20	9
12	Angiotensin ii	9	4	12	NRF3	26	8
13	Atherosclerosis	29	8	13	Insulin resistances	16	7
14	Endothelial cells	18	8	14	Ferroptosis	14	7
15	VEGF	20	8	15	biomarkers	10	6
16	Vascular smooth muscles	27	7	16	Decidua	14	6
17	Vitamin D	14	7	17	Gestational diabetes	18	6
18	Blood Pressure	25	6	18	Gestational hypertension	15	6
19	Endothelin	21	5	19	Endothelial function	17	5
20	Placental ischemia	19	5	20	Fetal programming	19	5
21	Pregnancy-induced hypertension	13	5	21	Obesity	8	5
22	Proteinuria	12	5	22	Pregnancy complications	11	5
23	Treatment	10	5	23	Diagnosis	8	4
24	Cardiovascular diseases	11	5	24	Endoglin	13	4
25	Cardiovascular	14	4	25	Epigenetics	13	4
26	Maternal	7	4	26	Extracellular vesicles	7	4
27	Cancer	8	4	27	Reviews	7	4
28	Soluble fms-like tyrosine kinase-1	13	4	28	Therapy	13	4
29	Statins	15	4	29	Trophoblast invasion	10	4
30	Heme oxygenase-1	14	4				
31	Metformin	14	4				
No	**Cluster 3 – Blue (18 Items)**	**Total Link Strength**	**Occurrences**	**No**	**Cluster 4 – Yellow (11 Items)**	**Total Link Strength**	**Occurrences**
1	Oxidative stress	428	187	1	Trophoblast	75	34
2	Endothelial dysfunction	76	25	2	Apoptosis	41	17
3	Antioxidants	65	23	3	Autophagy	32	11
4	Reactive Oxygen Species	46	19	4	Aspirin	18	7
5	Antioxidants	32	14	5	ROS	11	7
6	Lipid peroxidation	35	13	6	Trophoblast cells	14	6
7	Free radicals	36	11	7	Enos	15	5
8	Biomarkers	24	9	8	Migration	10	5
9	Fetus	20	7	9	Endoplasmic reticulum stress	10	4

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10	Superoxide dismutase	20	6	10	invasion	9	4
11	Vitamin E	27	6	11	signal transduction	9	4
12	Isoprostanes	13	5				
13	Vitamin C	24	5				
14	Free radicals	10	4				
15	Glutathione peroxidase	15	4				
16	PE	12	4				
17	Leptin	8	4				
18	Reproduction	6	4				

No	Cluster 5 – Purple (1 Item)	Total Link Strength	Occurrences
1	stress	1	4

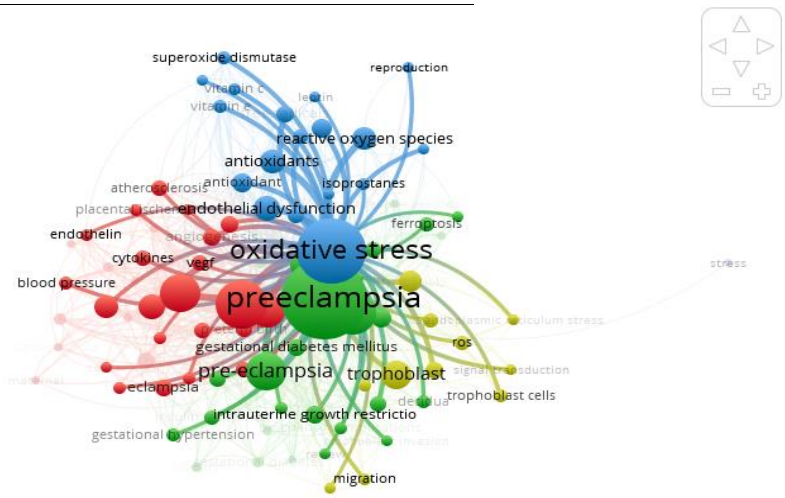

Figure 5. Network Visualization Co-Occurrences oxidative stress map.
These terms were keywords that appear most often not only in cluster 1 but throughout the network.

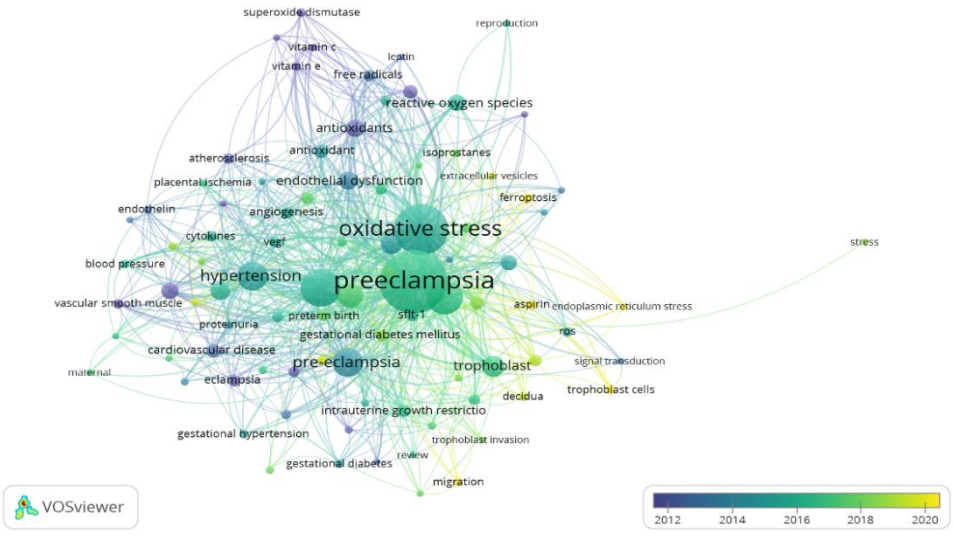

Figure 6. The Analysis of Overlay Visualization Co-Occurrences map.
The number of keywords was 90 items which are divided into 5 clusters, 726 links, and the Total Link Strength of 1848. The lighter color (yellow) is the theme that was researched more recently, namely above 2020. Meanwhile, the darker color (dark blue) is the theme that was researched in earlier years.

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Discussion

A search of the Scopus database revealed literature from 1996 that discussed the mechanisms of oxidative stress in preeclampsia. A total of 685 articles were discovered till 2022 (Figure 2). Total index and number of published publications have an increasing trend from year to year and the highest peak is the number of publications in 2022 at 11.68%. Document types were dominated by original articles at 53%, followed by review articles at 41%. Considering that the researches focus on the analysis of the mechanism of oxidative stress in preeclampsia, there are many different forms of review articles to be discovered. This type of review evaluates research findings in order to discover new phenomena or theories. Starting in 2006, the number of citations to published publications increased from 859 (2005) to 2370 (2006), with the peak occurring in 2012, specifically 3479. According to the data, there has been a significant increase in the number of studies referencing article references that have been published in the recent ten years. This is due to the existence of the Sustainable Development Goals (SDGs) policy, one of the targets of which is to reduce the Maternal Mortality Rate. Preeclampsia is one of the main causes of maternal death in the world, however, the etiology of preeclampsia is not known with certainty. Several theories are considered as the cause, one of which is the hypothesis of an imbalance between the number of free radicals and antioxidants that cause oxidative stress (Alam, 2022; Gao, 2021; Gao et al., 2021; Klran et al., 2023; Rana et al., 2019; Schoots et al., 2018; Wu et al., 2018). Therefore, research on preeclampsia still needs to be developed.

This research finds 76 countries that participated in the publication, the country that dominated the publication of the mechanism of oxidative stress in preeclampsia was the United States, namely 25.8%, followed by China, 19.9%, and the United Kingdom, 11.1% (Table 1). The affiliations discovered in this analysis were 160 institutions, which dominated publications, namely the University of Mississippi Medical Center with 3.8% of the total articles, followed by the University of Alberta with 2.3%, and the University of Cambridge with 2% (Figure 3). There were 157 identified journal sources, publications dominated by the International Journal of Molecular Sciences 4.4%, followed by Placenta 4.1%, and Free Radical Biology and Medicine 1.9% (Table 2). For journals that are included in the top 10 are Scopus journals with Q1 and Q2, this illustrates the quality of research published.

A total of 2836 authors were identified in this study, but only 54 authors had more than 5 documents. The author who has the most documents is Davidge, ST with 14 documents from the University of Alberta, United States. Followed by LaMarca B, Chen, Y, and Zhang, L each with 12 documents (Table 3). The United States is the most productive developed country in producing research publications, and Davidge, ST is the country's largest contributor to publications.

Based on the 685 identified documents, the publication entitled "The effects of oxidative stress on female reproduction: a review" is the article most cited by other researchers (Table 4). Citations were subjected to bibliometric analysis to measure the impact of the research as a reflection of the number of references the article received from time to time. The results of the citation analysis were able to evaluate research performance, as well as find the most influential papers. "The effects of oxidative stress on female reproduction: a review" is the title of a paper that

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discusses the mechanism of oxidative stress in preeclampsia, and is the most influential with a total of 928 citations, and a total link strength of 205. The paper was published in the journal "Reproductive Biology and Endocrinology" in 2012 The paper was written by Ashok Agarwal from the United States, which is the country with the most research on the mechanism of oxidative stress in preeclampsia. The paper is a type of review article that describes it in full and broadly so that many authors quote the paper. This article generally discusses the role of reactive species and oxidative stress in the physiological processes of normal and abnormal reproduction. The article explains how this cycle of chaos due to the number of pro-oxidants and antioxidants that are not balanced, causing several reproductive diseases, as well as pregnancy complications. This article also discusses how weight and extreme lifestyle factors such as smoking, alcohol use, and drug use can increase the production of excess free radicals, which can affect health. Exposure to environmental pollutants was also found to induce an oxidative state, possibly contributing to female infertility (Agarwal et al., 2012; Aski et al., 2020; Schoenaker et al., 2015; Zhang et al., 2023).

Occurrences of 685 documents identified 1434 keywords in titles and abstracts, the most frequently found keywords can be seen in Table 5. The research revealed merely 90 keywords with at least four keyword occurrences. Links linkages between keywords were divided into five clusters, it can be seen in Figure 4 which presents a map of the keyword co-occurrence network. The thicker the connection between the nodes, the more often the two keywords appear together. The size of the circles indicates the number of occurrences (the larger the circle size, the direct proportion to the number of occurrences by keyword), and the proximity of circles indicates close cooperation or association (Tantengco et al., 2021). The most highlighted terms in cluster 1 are: nitric oxide, endothelium, cardiovascular disease, angiogenesis, eclampsia, cytokines, preterm birth, atherosclerosis, VEGF, endothelin, blood pressure, placental ischemia, vascular smooth muscle, cardiovascular, proteinuria, maternal. The most highlighted cluster 2 are: preeclampsia, pre-eclampsia, Intrauterine Growth Restriction, gestational diabetes mellitus, sFlt-1, insulin resistances, feroptosis, decidua, Gestational diabetes, Gestational hypertension, obesity, endoglin, Extracellular vesicles, Trophoblast invasion. The most highlighted cluster 3 are: Oxidative stress, Endothelial dysfunction, Antioxidants, Reactive Oxygen Species, Antioxidant, Superoxide dismutase, Vitamin e, Isoprostanes, Vitamin C, Free radicals, Leptin, and Reproduction. The most highlighted cluster 4 is: Trophoblast, Apoptosis, Aspirin, Trophoblast cells, Migration, Endoplasmic reticulum stress, and Signal transduction. Cluster 5 only has 1 occurrence, namely stress. More details for the size of the occurrences of each cluster can be found in the order of the number of keywords based on the number of documents which can be seen in Table 6. For the keyword oxidative stress, the occurrence is the most highlighted and has a link connected to all clusters (Figure 5). This is because preeclampsia cases show an imbalance in enzymes that produce reactive oxygen species (ROS) and antioxidants (Gathiram & Moodley, 2016; Klran et al., 2023; Liao et al., 2023; Tinnakorn Chaiworapongsa et al., 2014; Vaka et al., 2018). An imbalance of pro-oxidants and antioxidants can trigger conditions of oxidative stress that affect all body systems

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(Possomato-Vieira & Khalil, 2016; Wahyuni, Maryatun, Prabasari, et al., 2023). Oxidative stress can also promote the transcription of mastiogenic factors such as sFlt1 (Castro et al., 2022; Maebayashi et al., 2014). The antioxidant mechanism is disrupted in patients with preeclampsia, indicated by decreased expression of superoxide dismutase and glutathione peroxidase compared to women with normal pregnancies (Agarwal et al., 2012; Rana et al., 2019; Schoots et al., 2018; Tenório et al., 2019; Wahyuni, Maryatun, Veri, et al., 2023; Wu et al., 2018).

The analysis of the Overlay Visualization Co-Occurrences map (Figure 6), reflects the novelty of the occurrences studied. The colors in the overlay depiction represent the average publication year of the keywords found (Hernández-Vásquez et al., 2020; Shen et al., 2022). Most keywords, with a greener or yellower hue, were released after 2018, whereas yellow was released after 2020. Yellow appeared at random in all clusters. Occurrences with a dark blue color representing years less than 2012 are almost dominant in all clusters 1, 2, and 3. For occurrences published for more than 2020, they describe the trend of occurrences being studied and their novelty value is high. Whereas for occurrences published less than 2012, further study is required to update the most recent theory. Both are equally interesting to study therefore they complement each other in discussing the mechanisms of oxidative stress in preeclampsia. With this overview of the overlay network, it can provide a basic description for conducting further research according to the needs of researchers (Miao et al., 2022; Stasi et al., 2023).

This bibliometric analysis of the literature can provide objective directions for researchers (Brandt et al., 2019; Ercan & Yildirim, 2020; Gao, 2021; Handayani et al., 2022; Li et al., 2022; Saputro, 2022; Shen et al., 2022; Wang et al., 2019; Zheng et al., 2022), however, some limitations must be acknowledged. The limitation is to only select journal studies from one database, namely Scopus. The joint word analysis used to calculate the frequency of related words may ignore topics that arise with low frequency and attention. Therefore, to expand the scope of the research database, it can be done by using various types of databases in order to focus more on future research directions.

Conclusion

The number of studies on oxidative stress in preeclampsia was increasing and developing. The mechanisms of oxidative stress in preeclampsia in the network map were categorized into 5 clusters based on co-occurrence, and “oxidative stress” was the most highlighted term not only in cluster 1 but throughout the network.

Suggestion

It is recommended for future researchers to carry out bibliometric analysis using several databases other than Scopus. Further research could focus on analyzing long-term publication trends regarding oxidative stress in preeclampsia.

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