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SCIENTOMETRICS

Trends in iron deficiency anemia research 2001-2020: A bibliometric analysis

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Abstract

BACKGROUND

Iron deficiency anemia has a worldwide impact on individual health and national and international economies, with an estimated one-third of the world population being iron deficient.

AIM

To evaluate the iron deficiency literature published between 2001-2020 with an emphasis on: (1) Identification of collaborative research networks most active in this field; (2) Research topics of greatest importance; and (3) Analysis of the most-cited papers published between 2001-2020 and the most cited papers in 5-year intervals during this period to assess for emerging trends in research in this area.

METHODS

A search of Clarivate Analytics World of Science Core Collection was performed for the topic "iron deficiency anemia", limited to document type (article or review), language (English), and time span (2001-2020). The following data were extracted from these articles: Year of publication, journal, study design, country of first author, and number of citations. The metadata derived from the search were used to identify publication trends in iron deficiency anemia research and their distribution in countries/regions and institutions. Network visualization by VOSviewer (Leiden University) was performed to identify international collaborative groups and research hotspots.

RESULTS

The search identified 4828 publications. Three international collaborative networks were identified: United States, Canada, and India; Turkey, China, and Japan; and England and other European countries. Five research areas were hotspots: Epidemiologic aspects of iron deficiency anemia, biochemical aspects of iron deficiency anemia, clinical evaluation of causes of iron deficiency anemia, causes of iron deficiency anemia, and bioavailability of dietary iron. Subset analysis of the top-10 overall cited papers, and the top-10 cited papers for each 5-

and experimental

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year increment beginning in 2001 showed that the largest number of highly cited papers were from the field of epidemiology, the smallest number from the field of bioavailability of dietary iron.

CONCLUSION
The literature on iron deficiency anemia has a high citation rate compared to studies of other topics using similar methodology and is heavily biased toward studies from the United States and epidemiologic studies.

Key Words: Iron deficiency anemia; Bibliometrics; VOSviewer; Trends

Core Tip: Iron deficiency is a common micronutrient deficiency with a worldwide impact. This bibliometric analysis was performed to analyze the literature on iron deficiency published between 2001-2020. Three international collaborative networks based in North America/India, Europe, and Asia were identified. There are 5 areas of greatest focus: Epidemiologic aspects of iron deficiency anemia, biochemical aspects of iron deficiency anemia, clinical evaluation of iron deficiency anemia, causes of iron deficiency anemia, and bioavailability of dietary iron. Evaluation of the papers published during this period identified epidemiology as the most cited area, and bioavailability of iron as the least cited.

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INTRODUCTION

Iron deficiency and iron deficiency anemia

Iron deficiency and iron deficiency anemia are health conditions with a worldwide effect on individual health and an impact on national and international economies. An estimated one-third of the world population is affected by iron deficiency, and deficiency of this micronutrient has effects on multiple systems of the body, including the central nervous system and reticuloendothelial systems[1,2]. Health consequences of iron deficiency are widespread and include impaired intellectual function and decreased immunity[3,4].

Anemia is a common consequence of iron deficiency. The degree of severity of anemia is variable, and it is microcytic and hypochromic as demonstrated by routine laboratory testing, which identifies a moderate to severe decrease in red blood cell count, hemoglobin, and hematocrit, accompanied by a moderately decreased mean corpuscular volume and moderate to marked elevation of red blood cell distribution width[1].

The bibliometric method as a research tool

Bibliometric methods are useful to evaluate trends in research activities over time[5]. Bibliometrics take advantage of literature databasing technology, including literature metrology, and is an increasingly important method of providing insight into research in specific fields. This format has been used to evaluate the impact of articles in many areas of study. It is valuable to identify the most cited studies that have influenced the evolution of a given scientific field[6].

Rationale

In this study, the research trends in the field of iron deficiency anemia in the past 20 years were considered. The aims of this study were to: (1) Identify and analyze scientific publications in this field; and (2) Compare the contribution of this research in different countries and institutions. Bibliometric analysis was performed using the functions of the Web of Science Core Collection and further analysis of the metadata

was performed using VOSviewer software (Leiden University). Using the features of VOSviewer, a network visualization of international collaborations and a keyword-based visualization of research fields was performed. This study provides a refined understanding of global trends in iron deficiency anemia research.

MATERIALS AND METHODS

This bibliometric analysis was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) principles (see PRISMA 2009 checklist statement for PRISMA checklist) according to a methodology similar to that described in earlier studies[6-10], which is detailed below.

Data collection and bibliometric analysis

All articles were searched using the Clarivate Analytics World of Science Core Collection (WOSCC) on August 30, 2020. The study used publicly available data, and thus ethical approval was not required. The search criteria were topic ("iron deficiency anemia"), limited to document type (article or review), language (English), and time span (2001-2020). A topic search includes a search of the following fields: The title of the article or review; the abstract, the keywords; and the keywords plus©, which is a proprietary algorithm using expanded terms from an article's cited references or bibliography. The following data were extracted from these articles: Year of publication, journal, study design, country of first author, and number of citations. The metadata derived from the search were used to identify publication trends in iron deficiency anemia research and their distribution in countries/regions and institutions. This protocol has not been registered.

VOSviewer bibliometric software (Van Eck and Waltman, Leiden University, Leiden, The Netherlands) was used to perform data mining, mapping, and clustering of the retrieved articles[11]. Keywords and countries were labeled with colored circles, the size of which correlated with the occurrence of the keyword or countries in the title and abstract.

Subset analysis of abstracts/full-text

Because of the large number of search results, the title, abstract and full text of the top 200 cited articles were reviewed for appropriateness to the topic. The entire list of retrieved articles was analyzed, and an additional subset analysis of the articles grouped by publication in 5-year increments (2001-2005; 2006-2010; 2011-2015; 2016-2020) was performed. The top 25 keywords identified in the title and abstract of each publication in each time interval was compiled[12]. In addition, the top 10 articles published in each time interval was identified, along with their number of citations.

RESULTS

The search returned 4828 references. Review of the titles, abstracts, and full texts of the top 200 cited papers in this group was performed to assess the quality of the search, and all papers in this group were appropriate to the topic of iron deficiency anemia.

These publications had an h-index of 137 with an average of 25.42 citations *per* item. The number of papers published *per* year in this study has varied from 124 to 402. The year with the largest number of papers published in this study was 2019. The rate of publication of papers in this study has varied from 2.568% to 8.326% (Figure 1).

Of 4163 papers were classified as articles, 695 as reviews. 4569 papers (94.6% of the total) were published in English. Based on WOSCC metadata, the papers were published in 97 different research areas, of which the most common were nutrition and dietetics (n = 672, 13.919% of total), gastroenterology (n = 610, 12.635%), hematology (n = 570, 11.806%), pediatrics (n = 566, 11.723%), and general internal medicine (n = 522, 10.812%).

Country of publication

In total, publications were contributed by 157 countries, with the top ten publishing countries listed in Figure 2.

The United States has contributed the largest number of the papers. Other nations in the top 5 countries of publication were Turkey, China, Italy, and England. The authors in this study represented 4840 institutions. The institutions contributing the most

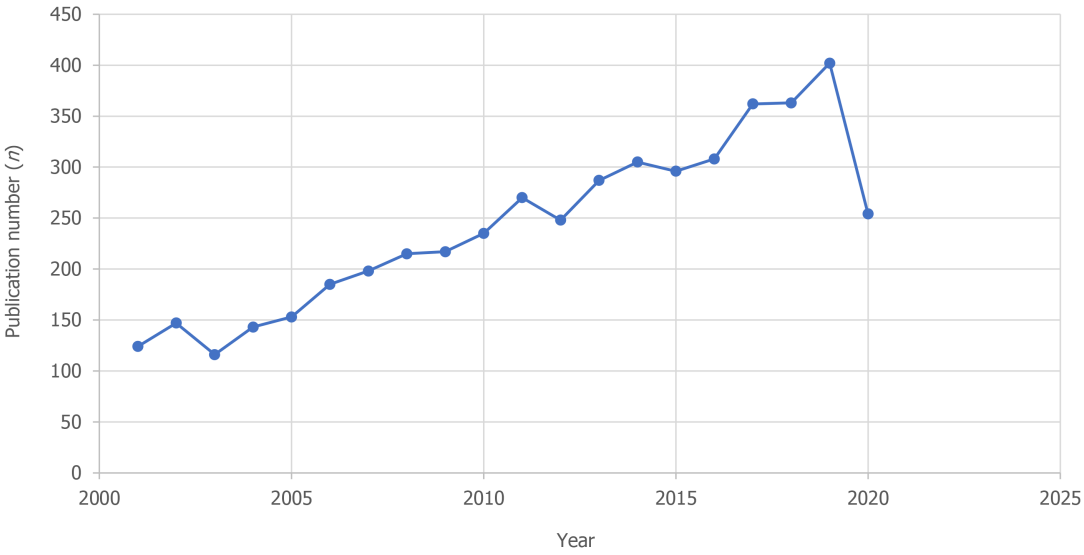

Figure 1 Number of publications (*n*) *per* year, 2001-2020.

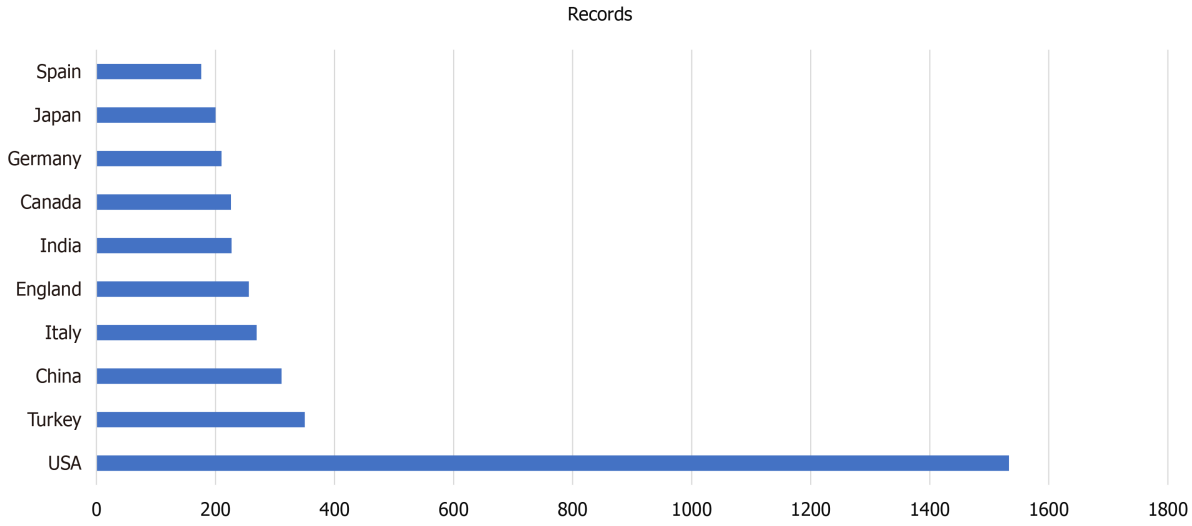

Figure 2 Number of records (*n*) *per* country for the top 10 countries contributing papers to this study.

papers to this study were the University of California system (n = 179 records) and Harvard University (n = 126 records). 2411 funding agencies were listed in these publications, of which the largest number of studies were funded by the United States Department of Health and Human Services (n = 448), the National Institutes of Health (United States, n = 431), and the National Natural Science Foundation of China (n = 119).

Collaborations

The collaboration network analysis is illustrated in Figure 3 and includes countries contributing at least 10 papers. Using this criterion, 64 countries are included in the analysis. There are 3 nodes identified using international collaboration data. The largest, illustrated in red, includes the United States, Canada, and India as the largest contributors. The second, illustrated in blue, includes Turkey, China, and Japan as the most prominent contributing members. The third, illustrated in green, includes England and many European countries.

Journals

The papers in this study were published by 1365 journals. 659 journals published ≥ 1 paper; the remaining journals published 1 paper apiece. The top 15 journals, with the number of articles published and the journal's impact factor (IF), drawn from the 2020

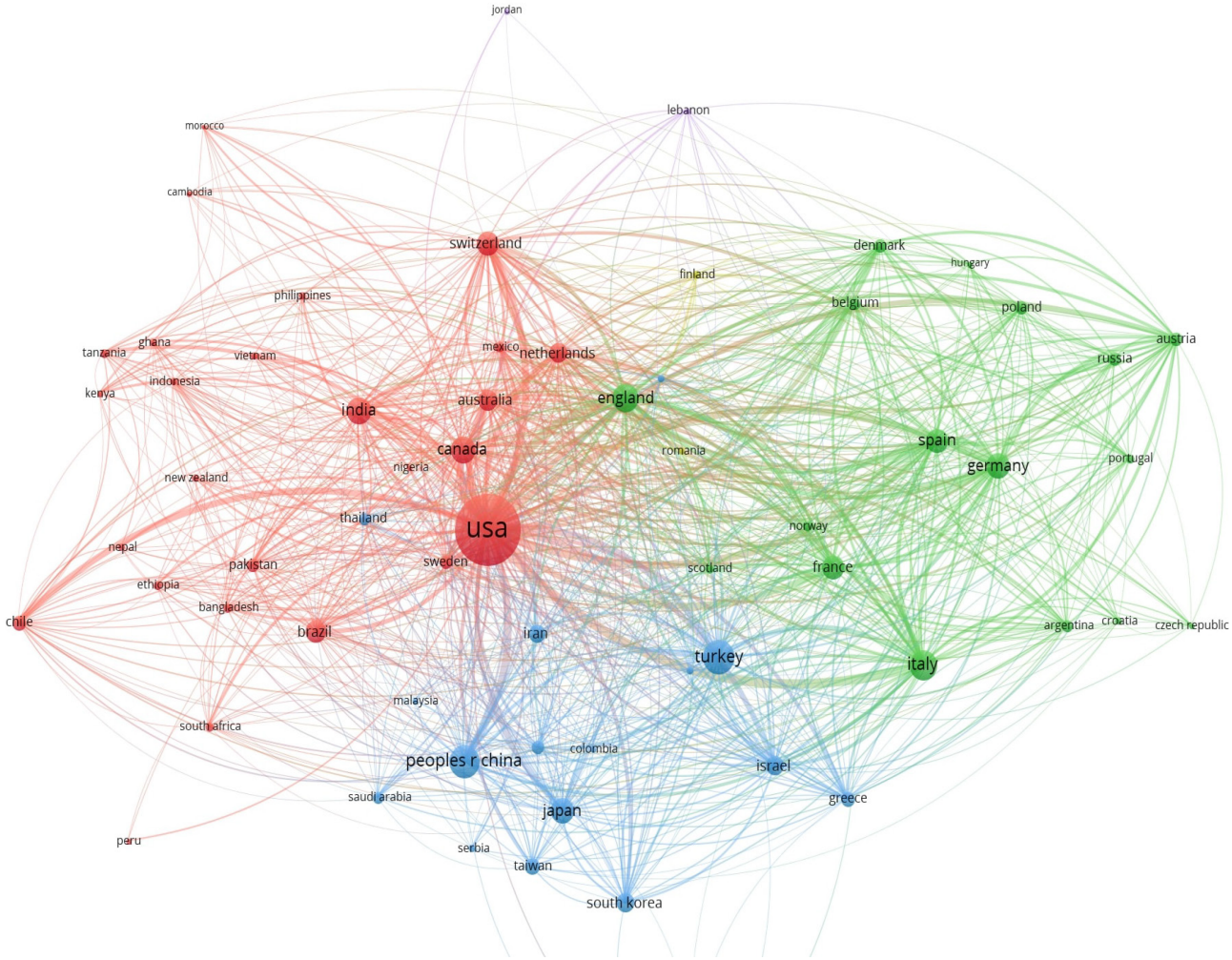

Figure 3 Collaboration network analysis of the 64 countries contributing ≥ 10 papers.

Journal Citation Reports of Clarivate Analytics) are shown in Table 1. The IF for the journals in this group ranged from 17.543 (*Blood*) to 1.016 (*Journal of Pediatric Hematology Oncology*). The largest number of papers were published by *Journal of Nutrition* (n = 107), *PLOS One* (n = 81), and *World Journal of Gastroenterology* (n = 76).

Co-occurrence of keywords

Overall, 123 terms appeared 50 times or more in the titles or abstracts of the papers in this study (Figure 4). For example, "iron deficiency anemia" appeared 1533 times, "anemia" appeared 1252 times, "children" appeared 726 times, "iron deficiency" appeared 627 times, and "prevalence" appeared 608 times. Based on the VOSviewer keyword mapping, the terms or phrases associated with iron deficiency anemia were divided into 5 clusters, represented by 5 colors (red, green, blue, yellow, and purple). From the results of co-occurrences, current iron deficiency anemia research was shown to be mainly focused on 5 major areas. These are: (1) Epidemiologic aspects of iron deficiency anemia (red); (2) Bioavailability of dietary iron (purple); (3) Clinical evaluation of causes of iron deficiency anemia (blue); (4) Causes of iron deficiency anemia (yellow); and (5) Biochemical aspects of iron deficiency anemia (green). These 5 topics may thus be regarded as the research hotspots in the field of iron deficiency anemia between 2001-2020.

A subset analysis of the top 25 author-selected keywords of each 5-year interval between 2001-2020 and coded to the 5 areas presented in Figure 4 is presented in Table 2[12]. The distribution of keywords was relatively unchanged over the years. The largest number of keywords mapped to the epidemiologic aspects of iron deficiency anemia (red) cluster (11-12 keywords in each interval), with smaller numbers of keywords mapping to the other clusters.

Table 1 Top 15 journals ranked by number of papers published, and corresponding impact factors

Journal	Records	Impact factor
Journal of nutrition	107	4.281
PLoS One	81	2.740
World Journal of Gastroenterology	76	3.665
American Journal of Clinical Nutrition	75	6.766
Nutrients	67	4.546
Pediatrics	50	5.359
Food	48	1.485
Journal of Pediatric Hematology Oncology	48	1.016
Helicobacter	44	4.000
American	39	6.973
Blood	39	17.543
Digestive Diseases and Sciences	35	2.751
Pediatric Hematology and Oncology	34	1.232
Biological	33	2.639
Journal of Pediatric Gastroenterology and Nutrition	33	2.937

Top 10 cited papers

The top 10 cited papers published for the entire period 2001-2020, and the top 10 cited papers published in each 5-year interval are listed in Table 3. The total number of citations *per* paper for the top 10 cited papers published from 2001-2020 ranged from 752 to 4084.

DISCUSSION

This bibliometric analysis was performed to evaluate the research trends in the field of iron deficiency anemia between 2001-2020. The purpose of this study was: (1) To identify and analyze scientific publications in this field; and (2) To compare the contribution of this research in different countries and institutions. The main findings were (1) That the most common topic areas were nutrition and dietetics, gastroenterology, hematology, pediatrics, and general internal medicine; (2) United States-based researchers contributed to the vast majority of papers, although researchers from Turkey, China, Italy, and England also made significant contributions to the literature; (3) Keyword analysis revealed that 5 research areas have developed as current hotspots: Epidemiologic aspects of iron deficiency anemia, biochemical aspects of iron deficiency anemia, clinical evaluation of causes of iron deficiency anemia, causes of iron deficiency anemia, and bioavailability of dietary iron; and (4) Evaluation of the top keywords in 5 year intervals showed that the relative contributions of each research area to the total number of papers has remained static, with the largest contribution to the area of epidemiologic aspects of iron deficiency anemia. The citation rate of the top cited papers in this study is high compared to studies on other research areas using similar methodology[13].

Epidemiologic aspects of iron deficiency anemia

The topic of iron deficiency anemia has been the subject of numerous epidemiologic studies, including the Global Burden of Disease Study, a large-scale observational epidemiologic survey which was published as a 4-paper series[14-17]. This includes the top-cited paper identified in the current study[14]. Approximately a third of the world population is iron-deficient[18], though there are clear disparities in the distribution of iron deficiency. Darmon *et al*[19] established that iron deficiency anemia was more prevalent in individuals from low socioeconomic backgrounds, possibly due to diet quality[19]. Guralnik *et al*[20]'s 2005 paper identified that iron deficiency anemia contributes to a high percentage of cases of anemia in the elderly[20]. Although at-risk

Table 2 Top 25 keywords of each 5-year interval between 2001-2020 color coded to the clusters identified in Figure 4

2001	2006	2011	2016
Iron-deficiency anemia[3]	Iron-deficiency anemia[3]	Iron-deficiency anemia[3]	Iron-deficiency anemia[3]
Anemia[1]	Anemia[1]	Anemia[1]	Anemia[1]
Children[1]	Iron deficiency anemia[1]	Iron deficiency anemia[1]	Iron deficiency anemia[1]
Iron deficiency anemia[1]	Children[1]	Children[1]	Prevalence[1]
Iron deficiency[2]	Iron deficiency[2]	Iron deficiency[2]	Children[1]
Iron[5]	Prevalence[1]	Prevalence[1]	Iron deficiency[2]
Prevalence[1]	Diagnosis[3]	Iron[5]	Diagnosis[3]
Serum ferritin[5]	Iron[5]	Diagnosis[3]	Management[3]
Ferritin[5]	Supplementation[1]	Supplementation[1]	Iron[5]
Supplementation[1]	Infants[1]	Hepcidin[5]	Supplementation[1]
Diagnosis[3]	Serum ferritin[5]	Management[3]	Pregnancy[1]
Absorption[2]	Women[1]	Hemoglobin[1]	Hepcidin[5]
Deficiency[5]	Hemoglobin[1]	Pregnancy[1]	Hemoglobin[1]
Infants[1]	Absorption[2]	Ferritin[5]	Risk[3]
Erythropoietin[4]	Deficiency[5]	Intravenous iron[4]	Intravenous iron[4]
Pregnancy[1]	Hepcidin[5]	Women[1]	Women[1]
Women[1]	Therapy[4]	Deficiency anemia[1]	Ferritin[5]
Therapy[4]	Iron-deficiency[1]	Disease[3]	Oral iron[4]
Hemoglobin[1]	Growth[1]	Inflammation[5]	Health[1]
Eradication[3]	Helicobacter pylori[3]	Risk[3]	Disease[3]
Serum transferrin receptor[5]	Pregnancy[1]	Association[3]	Infants[1]
Helicobacter pylori[3]	Disease[3]	Metabolism[1]	Deficiency[5]
Iron-deficiency[1]	Risk[3]	Infants[1]	Iron-deficiency[1]
Deficiency anemia[1]	Celiac disease[3]	Serum ferritin[5]	Deficiency anemia[1]
Disease[3]	Expression[5]	Deficiency[5]	Ferric carboxymaltose[4]
Number of keywords			
Red			
11	12	11	12
Purple			
2	2	1	1
Blue			
5	5	6	5
Yellow			
2	1	1	3
Green			
5	5	6	4
New items in each quartile			
(None)	Serum ferritin[5]	Management[3]	Oral iron[4]
	Hepcidin[5]	Intravenous iron[4]	Health[1]
	Growth[1]	Inflammation[5]	Ferric carboxymaltose[4]
	Risk[3]	Association[3]	

	Celiac disease[3]	Metabolism[1]
	Expression[5]	Infants[1]

[1]Red.
[2]Purple.
[3]Blue.
[4]Yellow.
[5]Green.
Summary shows the number of keywords in each 5-year quartile by cluster and a list of the keywords appearing for the first time in the top-25 list for each quartile.

populations are particularly prevalent in the developing world[21], residents of industrialized national are also impacted, as noted by Dubé *et al*[22].

Additional highly cited papers in this study addressed the neurologic implications of iron deficiency and iron deficiency anemia. These include Grantham-McGregor *et al*[23]'s review of the long-term effects of iron deficiency on neurological functioning in children[23] and Beard and Connor's seminal paper on iron status and its correlation with neural functioning[24]. The work of Lozoff and colleagues, including their 2006 paper which is highlighted in the current study, detailed that the neurological defects in patients in iron-deficient children may extend into adulthood, even after correction of the underlying nutritional issue[25].

An important consequence of iron deficiency and iron deficiency anemia is decreased work output, which may have long-term impact on affected individuals and has an established societal effect. These features were described in highly-cited work by Haas and Brownlie[2].

Bioavailability of dietary iron

Although iron deficiency is a widespread international public health issue, few high-impact studies have been dedicated to the critical issue of iron bioavailability, as evidenced from the survey of top 10-cited papers. Two review papers have discussed features of iron bioavailability. The first, by Plum *et al*[26], examines the role of zinc in iron metabolism[26]. The second, by Xie *et al*[27], examines the physiologic role of polysaccharides derived from medicinal plants, some of which have been identified as having iron-chelating properties[27].

Biochemical aspects of iron deficiency anemia

Though none of the top-10 cited studies had iron metabolism as a main topic, 4 studies in the quartile analysis were focused on biochemical aspects of iron anemia. Three of these had a particular focus on hepcidin. Hepcidin, a protein produced by the liver and cleared by the kidneys, plays a central role in iron uptake by the duodenum and spleen. Its regulation was described in a highly cited paper identified in this study [28], which showed that hepcidin expression is upregulated in response to anemia and hypoxia and downregulated by increased hematopoiesis. An immunoassay for hepcidin was described by Ganz *et al*[29] and Girelli *et al*[30]. Laboratory testing for serum hepcidin levels can be used to distinguish iron deficiency anemia from anemia of chronic disease (inflammation)[1].

Another important step in iron metabolism highlighted by the current study is the action of ferroreductase, which acts on ferric (3+) iron-containing molecules in the cytoplasm of phagocytes to produce bioavailable ferrous (2+) iron[31,32].

Causes of iron deficiency anemia

Numerous health conditions have been implicated in the etiology of iron deficiency anemia. Among these are chronic inflammatory conditions, chronic gastritis (in particular gastritis secondary to *Helicobacter pylori*), chronic use/abuse of non-steroidal anti-inflammatory drugs (NSAID), and celiac disease. Iron deficiency may also follow gastrointestinal procedures such as bariatric surgery and capsule endoscopy[33]. The role of *Helicobacter pylori* gastritis and celiac disease were the subjects of 2 papers from the overall top 10-cited group[34-36]. In addition, Graham *et al*[37] identified the mucosal lesions in the gastrointestinal tracts of chronic NSAID users, many of whom developed iron deficiency anemia[37]. In patients with chronic kidney disease, decreased renal clearance of hepcidin may result in chronic kidney disease, as described by Levin and Rocco[38].

Table 3 The top 10 cited papers published for the entire period 2001-2020, and the top 10 cited papers published in each 5-year interval within the study period

Ref.	Title	Journal	Year	Volume	Start page	End page	Times cited	Topic
2001-2020								
Vos *et al*[14], 2012	Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010	*Lancet*	2012	380	2163	2196	4084	1
Malfertheiner *et al*[34], 2007	Current concepts in the management of Helicobacter pylori infection: the maastricht III consensus report	*Gut*	2007	56	772	781	1481	3
Bhutta *et al*[44], 2008	Maternal and Child Undernutrition 3 - What works? Interventions for maternal and child undernutrition and survival	*Lancet*	2008	371	417	440	1147	4
Darmon and Drewnowski[19], 2008	Does social class predict diet quality?	*American Journal of Clinical Nutrition*	2008	87	1107	1117	1061	1
Walker *et al*[45], 2007	Child development in developing countries 2 - Child development: risk factors for adverse outcomes in developing countries	*Lancet*	2007	369	145	157	1033	4
Chey and Wong[39], 2007	American college of gastroenterology guideline on the management of *Helicobacter pylori* infection	*American Journal of Gastroenterology*	2007	102	1808	1825	830	3
Guralnik *et al*[20], 2004	Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia	*Blood*	2004	104	2263	2268	793	1
Ludvigsson *et al*[40], 2013	The Oslo definitions for coeliac disease and related terms	*Gut*	2013	62	43	52	790	3
Rubio-Tapia *et al*[41], 2013	ACG Clinical Guidelines: Diagnosis and Management of Celiac Disease	*American Journal of Gastroenterology*	2013	108	656	676	788	3
Hill *et al*[35], 2005	Guideline for the diagnosis and treatment of celiac disease in children: Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition	*Journal of Pediatric Gastroenterology and Nutrition*	2005	40	1	19	752	4
2001-2005								
Guralnik *et al*[20], 2004	Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia	*Blood*	2004	104	2263	2268	793	1
Hill *et al*[35], 2005	Guideline for the diagnosis and treatment of celiac disease in children: Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition	*Journal of Pediatric Gastroenterology and Nutrition*	2005	40	1	19	752	4
Grantham-McGregor and Ani[23], 2001	A review of studies on the effect of iron deficiency on cognitive development in children	*Journal of Nutrition*	2001	131	649S	666S	736	1
Pennazio *et al*[33], 2004	Outcome of patients with obscure gastrointestinal bleeding after capsule endoscopy: Report of 100 consecutive cases	*Gastroenterology*	2004	126	643	653	688	3
Nicolas *et al*[28], 2002	Severe iron deficiency anemia in transgenic mice expressing liver hepcidin	*Proceedings of The National Academy of Sciences of The United States of America*	2002	99	4596	4601	694	2
Haas and Brownlie[2], 2001	Iron deficiency and reduced work capacity: A critical review of the research to determine a causal relationship	*Journal of nutrition*	2001	131	676S	688S	573	1
Dubé *et al*[22], 2005	The prevalence of celiac disease in average-risk and at-risk Western European populations: A systematic review	*Gastroenterology*	2005	128	S57	S67	427	1
Ohgami *et al*[31], 2005	Identification of a ferrireductase required for efficient transferrin-dependent iron uptake in erythroid cells	*Nature Genetics*	2005	37	1264	1269	394	2

Beard and Connor[24], 2003	Iron status and neural functioning	*Annual Review of Nutrition*	2003	23	41	58	383	1
Graham *et al*[37], 2005	Visible small-intestinal mucosal injury in chronic NSAID users	*Clinical Gastroenterology and Hepatology*	2005	3	55	59	391	4
2006-2010								
Malfertheiner *et al*[34], 2007	Current concepts in the management of Helicobacter pylori infection: the maastricht III consensus report	*Gut*	2007	56	772	781	1481	3
Bhutta *et al*[44], 2008	Maternal and Child Undernutrition 3 - What works? Interventions for maternal and child undernutrition and survival	*Lancet*	2008	371	417	440	1147	4
Darmon and Drewnowski[19], 2008	Does social class predict diet quality?	*American Journal of Clinical Nutrition*	2008	87	1107	1117	1061	1
Walker *et al*[45], 2007	Child development in developing countries 2 - Child development: risk factors for adverse outcomes in developing countries	*Lancet*	2007	369	145	157	1033	4
Chey and Wong [39], 2007	American college of gastroenterology guideline on the management of Helicobacter pylori infection	*American Journal of Gastroenterology*	2007	102	1808	1825	830	3
Levin and Rocco [38], 2006	KDOQI clinical practice guidelines and clinical practice recommendations for anemia in chronic kidney disease - Foreword	*American Journal of Kidney Diseases*	2006	47	S9	S145	565	4
Lozoff *et al*[25], 2006	Long-lasting neural and behavioral effects of iron deficiency in infancy	*Nutrition Reviews*	2006	64	S34	S43	532	1
Rostom *et al*[46], 2006	American Gastroenterological Association (AGA) Institute Technical Review on the Diagnosis and Management of Celiac Disease	*Gastroenterology*	2006	131	1981	2002	514	3
Ganz *et al*[29], 2008	Immunoassay for Human Serum Hepcidin	*Blood*	2008	112	4292	4297	502	2
Plum *et al*[26], 2010	The Essential Toxin: Impact of Zinc on Human Health	*International Journal of Environmental Research and Public Health*	2010	7	1342	1365	484	5
2011-2015								
Vos *et al*[14], 2012	Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010	*Lancet*	2012	380	2163	2196	4084	1
Ludvigsson *et al* [40], 2013	The Oslo definitions for coeliac disease and related terms	*Gut*	2013	62	43	52	790	3
Rubio-Tapia *et al* [41], 2013	ACG Clinical Guidelines: Diagnosis and Management of Celiac Disease	*American Journal of Gastroenterology*	2013	108	656	676	788	3
Kassebaum *et al* [18], 2014	A systematic analysis of global anemia burden from 1990 to 2010	*Blood*	2014	123	615	624	623	1
Walker *et al*[47], 2011	Child Development 1 Inequality in early childhood: risk and protective factors for early child development	*Lancet*	2011	378	1325	1338	621	1
Camaschella[48], 2015	Iron-Deficiency Anemia	*New England Journal of Medicine*	2015	372	1832	1843	402	Multiple
Chey *et al*[49], 2015	Irritable Bowel Syndrome A Clinical Review	*Jama-journal of The American Medical Association*	2015	313	949	958	378	3
Balarajan *et al* [21], 2011	Anaemia in low-income and middle-income countries	*Lancet*	2011	378	2123	2135	353	1
Pennazio *et al* [33], 2004	Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline	*Endoscopy*	2015	47	352	376	317	3
Goodnough *et al* [42], 2011	Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines	*British Journal of Anaesthesia*	2011	106	13	22	303	3

2016-2020								
Chey *et al*[50], 2017	ACG Clinical Guideline: Treatment of Helicobacter pylori Infection	*American Journal of Gastroenterology*	2017	112	212	239	324	3
Amieva and Peek [51], 2016	Pathobiology of Helicobacter pylori-Induced Gastric Cancer	*Gastroenterology*	2016	150	64	78	224	4
Kyu *et al*[52], 2016	Global and National Burden of Diseases and Injuries Among Children and Adolescents Between 1990 and 2013 Findings From the Global Burden of Disease 2013 Study	*Jama Pediatrics*	2016	170	267	287	214	1
Girelli *et al*[30], 2005	Hepcidin in the diagnosis of iron disorders	*Blood*	2016	127	2809	2813	147	2
Kassebaum[53], 2016	The Global Burden of Anemia	*Hematology-oncology Clinics of North America*	2016	30	247	308	141	1
Trenkwalder *et al* [54], 2016	Restless legs syndrome associated with major diseases A systematic review and new concept	*Neurology*	2016	86	1336	1343	117	4
Xie *et al*[27], 2016	Advances on Bioactive Polysaccharides from Medicinal Plants	*Critical Reviews in Food Science and Nutrition*	2016	56	S60	S84	112	5
Enns *et al*[55], 2017	Clinical Practice Guidelines for the Use of Video Capsule Endoscopy	*Gastroenterology*	2017	152	497	514	111	3
Froessler *et al*[36], 2018	The Important Role for Intravenous Iron in Perioperative Patient Blood Management in Major Abdominal Surgery A Randomized Controlled Trial	*Annals of Surgery*	2016	264	41	46	98	4
Vasanawala *et al* [56], 2016	Safety and technique of ferumoxytol administration for MRI	*Magnetic Resonance in Medicine*	2016	75	2107	2111	93	3 and 4

For the Topic column, the following numbers correspond to these topics: (1) Epidemiologic aspects of iron deficiency anemia; (2) Biochemical aspects of iron deficiency anemia; (3) Clinical evaluation of causes of iron deficiency anemia; (4) Causes of iron deficiency anemia; and (5) Bioavailability of dietary iron.

Clinical evaluation and management of causes of iron deficiency anemia

Several of the papers in the current study that detailed the causes of iron deficiency anemia were consensus papers that also recommended protocols for the clinical evaluation of patients. These include the American college of Gastroenterology guidelines and the Maastricht III report, which provided guidance on the management of *Helicobacter pylori* infection[34,39], and the Oslo and American College of Gastroenterology guidelines for celiac disease[40,41]. Presurgical workup of anemias was also a highly-cited topic: An example is the NATA guidelines for the evaluation of anemia in preoperative orthopedic patients[42]. The use of perioperative intravenous iron after abdominal surgery has been an important recent contribution to the list of highly-cited papers[36].

Limitations

Bibliometric analysis, although a potent means for highlighting the research hotspots of a given field, has some limitations. First, the bibliometric data are best accessed using the Web of Science database, and currently are not as widely available in other databases. This may cause problems with the search, since checklists for systematic reviews such as PRISMA generally recommend the use of 2 or more databases for searches[43]. Another limitation is that since the number of citations of a given paper would be expected to increase over time, it would be expected that older papers would have a higher citation rate than more recently published papers.In the current study, dividing the study period into 5-year quartiles was an attempt to identify papers which had a high citation rate within their cohort.

CONCLUSION

This study was a bibliometric analysis of the medical literature on iron deficiency anemia published over the last 20 years. Five research hotspots were identified; the area of epidemiology had the largest number of highly cited papers, and the area of bioavailability of dietary iron had the lowest. These relative contributions have been

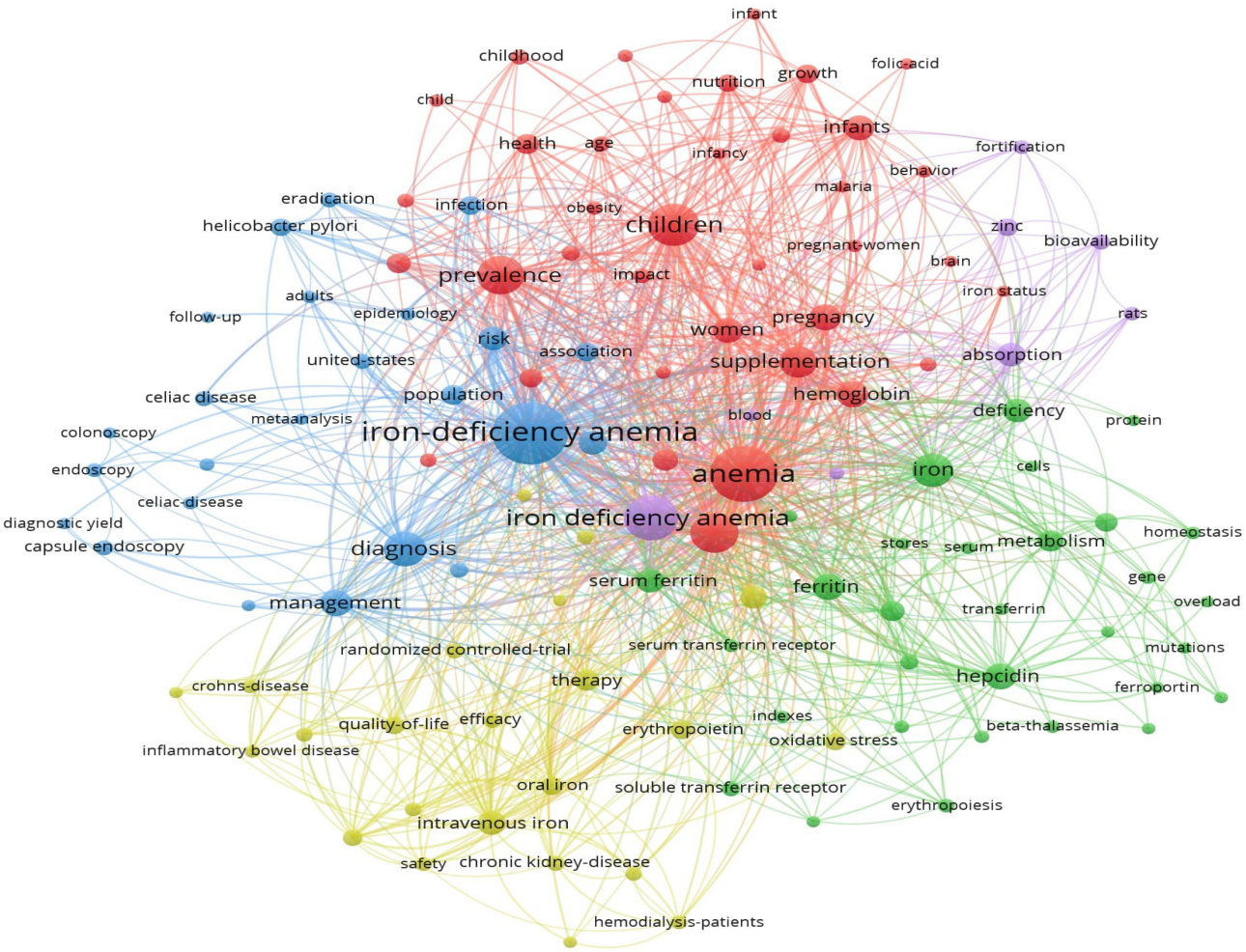

Figure 4 123 terms appearing 50 times or more in the titles or abstracts of the papers in this study.

apparently unchanged over the course of the study period. Although iron deficiency anemia has a worldwide impact, the published research of this period was highly influenced by studies from the United States.

ARTICLE HIGHLIGHTS

Research background

Iron deficiency is the most common micronutrient deficiency and has a worldwide impact. A bibliometric analysis focused on research trends on the topic of iron deficiency anemia has not been performed.

Research motivation

Analyzing the iron deficiency anemia research published between 2001-2020 what collaborative research networks are most active in this field? What subfields are of greatest importance? Are there any emerging research trends in this area?

Research objectives

The objectives of this study were to evaluate the literature published over the last 2 decades, focusing on: (1) The extent of collaborative research networks in this field; (2) The research topics of greatest prominence; and (3) A subset analysis of the most-cited papers published between 2001-2020 and the most-cited papers in 5-year intervals during this period to assess for emerging trends in research in this area.

Research methods

This study was conducted as a bibliometric analysis using Preferred Reporting Items

for Systematic Reviews and Meta-analysis guidelines. A search of the medical literature published between 2001-2020 and related to iron deficiency anemia was performed and data from the search were used to identify publication trends in iron deficiency anemia research. Network visualization by VOSviewer (Leiden University) was performed to identify international collaborative groups and research hotspots in works published during this period.

Research results

Of 4828 publications were included in the study. Network visualization identified 3 international collaborative networks: United States, Canada, and India; Turkey, China, and Japan; and England and other European countries. Five research hotspots were highlighted: (1) Epidemiology of iron deficiency anemia; (2) Biochemistry of iron deficiency anemia; (3) Clinical evaluation of iron deficiency anemia; (4) Causes of iron deficiency anemia; and (5) Bioavailability of iron in the diet. An additional analysis of the top-10 overall cited papers, and the top-10 cited papers for each 5-year increment starting in 2001 showed that the largest number of highly cited papers were from the field of epidemiology, the smallest number from the field of bioavailability of dietary iron.

Research conclusions

Iron deficiency anemia has a high citation rate compared to studies of other topics using similar methodology. Studies from the United States and epidemiologic studies dominate the field.

Research perspectives

Future studies directed from relatively underrepresented areas of the world, and studies directed at less prominently featured areas such as bioavailability of dietary iron may be welcome additions to this already well-developed research area.

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