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Mapping the global research landscape on insulin resistance: Visualization and bibliometric analysis

Zyoud SH *et al*. Global research landscape on insulin resistance

Abstract

BACKGROUND

Insulin resistance is a risk factor for metabolic syndromes and is associated with a wide variety of metabolic illnesses, including obesity, type 2 diabetes, and cardiovascular disease.

AIM

To investigate and map global insulin resistance studies.

METHODS

A bibliometric methodology was applied to the literature retrieved from the Scopus database and *Reference Citation Analysis* by using a validated search strategy. The study period was limited from 2002 to 2021. Bibliometric indicators and mapping were presented.

RESULTS

A total of 26808 articles on the topic of insulin resistance were included in the Scopus database. The articles included research articles (n = 21918; 81.76%), review articles (n = 2641; 9.85%), and letters (n = 653; 2.44%). During the study period, 136 countries contributed to the research on insulin resistance. The highest number of articles was from the United States (n = 7360; 27.45%), followed by China (n = 3713; 13.85%), Japan (n = 1730, 6.45%), Italy (n = 1545; 5.54%) and the United Kingdom (n = 1484; 5.54%). The retrieved articles identified two main research themes: "inflammatory mechanisms in the regulation of insulin resistance"; and "mechanisms linking obesity to insulin resistance".

CONCLUSION

Our data show that insulin resistance has steadily gained interest from researchers, as evidenced by the number of citations and yearly publications. Publications have grown

significantly in the last decade, while low-income countries with greater burdens continue to produce fewer publications in this field. This approach might assist researchers in choosing new research areas and recognizing research hotspots and frontiers. In the future, perhaps, high-quality clinical evidence will be acquired.

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Core Tip: Several bibliometric studies have been conducted in the field of diabetes research. However, no bibliometric study has been conducted on insulin resistance research. Therefore, the current study aims to investigate and mapping global research on insulin resistance. The retrieved articles identified two main research themes: "inflammatory mechanisms in the regulation of insulin resistance"; and "mechanisms linking obesity to insulin resistance". This approach might assist researchers in choosing new research areas and recognizing research hotspots and frontiers. In the future, perhaps, high-quality clinical evidence will be acquired.

INTRODUCTION

During the last two decades, the global prevalence of diabetes has increased dramatically. Diabetes is becoming increasingly worldwide, both in terms of prevalence and the number of affected[1]. For more than half a century, insulin resistance and type 2 diabetes have been associated. Insulin resistance is not only a powerful predictor of future type 2 diabetes development, but is also a therapeutic target in the presence of hyperglycemia[2]. Insulin resistance is defined as a reduced physiological response to insulin stimulation of target tissues, especially adipose tissue, liver, and muscle. Insulin resistance limits glucose disposal, leading to a compensatory increase in beta cell insulin

synthesis and hyperinsulinemia[3]. More than 30 years ago, hyperinsulinemia and insulin resistance were hypothesized to be key contributors to hypertension, hyperglycemia, dyslipidemia, hyperuricemia, visceral adiposity, elevated inflammatory markers, prothrombic state, and endothelial dysfunction related to obesity and the metabolic syndrome[4].

Several bibliometric studies have been conducted in diabetes research[5-10]. However, no bibliometric study has been conducted on insulin resistance research. As a scientific evaluation approach, bibliometrics can assess the research impact of organizations and individuals[11]. Similarly, bibliometrics provide evidence to promote the formation of future research hotspots[12,13]. As a result, this research aims to examine the scientific development in insulin resistance thoroughly. Therefore, this bibliometric analysis was designed to examine the research trend related to insulin resistance and identify future research hotspots. Furthermore, the study offers some important information by providing references and ideas for future studies on insulin resistance pathophysiology and clinical applications.

MATERIALS AND METHODS

Data acquisition

The documents in the current study were obtained and downloaded from the Scopus database on January 29, 2022, to prevent bias caused by the database's daily updates. With more than 36000 titles from around 11678 publishers, of which 34346 are peer-reviewed journals, Scopus is one of the most extensive and authoritative databases for collecting academic information[14,15]. Unfortunately, only one database may be utilized in bibliometric analyses because data from many databases cannot be integrated and analyzed. On the other hand, systematic reviews use multiple databases to retrieve a large number of documents for further analysis[16]. Furthermore, only one database was chosen on the topic's and objective's coverage and past research show that Web of Science and PubMed are included in the Scopus. Based on previous studies and findings, it was recommended to use Scopus (Elsevier database) because it was the most

comprehensive database on the subject, offering all the data needed for quantitative analysis[17,18].

Search strategy

Keywords used in the Scopus engine to achieve the aim of this study were chosen from previous systematic reviews and meta-analyses on insulin resistance[19-21]. "Insulin resistance" or "insulin sensitivity" was used as a search expression in the title search in the Scopus over the last two decades (January 2002 to December 2021). This study used the keywords "insulin resistance" or "insulin sensitivity" because we are more interested in these terms than related terminology. Therefore, keywords were used instead of a title/abstract search in the title search. Consequently, the search for the title will provide the fewest false positive documents, making it a trustworthy strategy[22-26]. A title/abstract search, on the other hand, will provide numerous false positives in which the main focus is not on insulin resistance *per se*.

Bibliometric analysis

As described in previous studies, the bibliometric technique was applied[27-30]. The following bibliometric indicators were generated when the refined findings were exported to Microsoft Excel: (1) Growth pattern; (2) Type of publications; (3) Core countries; (4) Core institutions; (5) Core funding agencies; (6) Prolific authors; (7) Core journals with their impact factors (IF); and (8) Top 10 cited articles. The *Impact Index per article* for the top 10 high-cited papers collected from *Reference Citation Analysis* (RCA), https://www.referencecitationanalysis.com, is presented. *RCA* is an open, multidisciplinary citation analysis database owned by Baishideng Publishing Group Inc. (Pleasanton, CA 94566, United States)[31].

Visualized analysis

VOSviewer 1.6.18 was used to perform a co-occurrence analysis and visualize the collaborative networks of the countries to determine a worldwide scientific cooperation

network across countries/regions, and keywords in the titles or/and abstracts to determine hotspots and research trends. VOSviewer maps have nodes or frames that are colored and scaled differently. The node or the frame size is proportional to the number of times it appears. The node's or the frame's color indicates its link to other nodes with similar colors[32].

RESULTS

Current status and annual trend

A total of 26808 articles on insulin resistance were included in the Scopus database. The articles included research articles (n = 21918; 81.76%), review articles (n = 2641; 9.85%), and letters (n = 653; 2.44%). After 2003, as shown in Figure 1, the number of publications on insulin resistance studies increased rapidly. In 2021, 1645 papers were published, the highest amount in two decades.

Analysis of countries

During the study period, 136 countries contributed to research on insulin resistance. The highest number of articles was from the United States (n = 7360; 27.45%), followed by China (n = 3713; 13.85%), Japan (n = 1730, 6.45%), Italy (n = 1545; 5.54%) and the United Kingdom (n = 1484; 5.54%), in Table 1. The country network map included 42 frames (Figure 2). The top three countries in terms of centrality were the United States, China, and the United Kingdom. The centrality proved that they had close relationships and substantial intellectual effects on other countries.

Analysis of institutions

The top ten active institutions are listed in Table 2. Harvard Medical School was first with 515 (1.92%) articles, followed by INSERM with 451 (1.68%) articles and the National Institutes of Health with 298 (1.11%). The top ten active institutions were mainly based in the United States.

Analysis of funding agencies

Table 3 lists the top 10 funding agencies with the highest output. Seven funding agencies are from the United States, and one each is from Japan, China, and Canada. These countries contributed 10459 (39.01%) documents. The three most productive funding agencies were the National Institute of Diabetes and Digestive and Kidney Diseases (n = 2548; 9.50%), the National Institutes of Health (n = 2094, 7.81%) and National Heart, Lung, and Blood (n = 1140, 4.25%).

Analysis of journals

Table 4 shows the top ten most active journals. Diabetes journal was first (n = 830; 3.10%), followed by Clinical Endocrinology and Metabolism (n = 692, 2.58%) and Diabetes Care (n = 623; 2.32%). Four of the journals on the active list were on the subject of diabetes. All the journals on the active list have a pretty high impact factor.

Analysis of citations

Table 5 lists the top ten articles that were the most cited in research related to insulin resistance from 2002 to 2021. The ten highest citations ranged from 4911 to 1827[33-42]. Furthermore, the ten most cited articles have an *impact index per article* of 101.5 to 241.2 (Table 5).

Term co-occurrence cluster analysis of research hotspots

The term co-occurrence analysis provides a complete summary of hot topics discussed in insulin resistance research. VOSviewer detected 456 keywords that appeared a minimum of 300 times in the titles and abstracts of the included articles by analyzing the contents of the titles and abstracts. All terms are sorted into clusters on the VOSviewer keyword co-occurrence visualization map, and various clusters are colored differently (Figure 3). There are two clusters: (1) Cluster #1, shown by green dots, contains phrases typically found in publications relating to "inflammatory mechanisms in the regulation of insulin resistance"; and (2) Cluster #2, shown by red dots, contains

phrases typically found in publications relating to "mechanisms linking obesity to insulin resistance". Hotspots in the field of insulin resistance were revealed *via* an overlay visualization map scaled by occurrences. The colored terms differ depending on when they appeared in the literature. The blue keywords were first shown, followed by the yellow keywords. After 2013, the most popular terms were related to inflammatory mechanisms in the regulation of insulin resistance.

Analysis of authorship

The total number of authors who participated in the publication of the retrieved documents was 80932, a mean of 3.1 authors per document. The list of the top ten active authors in insulin resistance research, ranked by the total number of publications in the last two decades (2002-2021), is shown in Table 6. The top ten list included four from the United States, three from Germany, two from Spain, and one from Italy.

DISCUSSION

Bibliometric analysis of insulin resistance publications in the last 20 years revealed that the number of articles published has gradually increased in recent years, indicating that more and more researchers are becoming involved in insulin resistance research. To our knowledge, this is the first bibliometric study that comprehensively examines worldwide trends in insulin resistance research over the last 20 years. The current study showed that research activity on insulin resistance was worldwide and involved countries in different world regions. The United States and China had a noticeable edge on this topic, probably due to a greater economy and investment in the scientific field. The research output from these countries may be related to a diverse spectrum of researchers interested in this topic and strong financial support for researchers. Another important reason for the contribution of different world regions is the high level of international collaboration, as evident from the thick lines coming out from most countries in the visualization map. This collaboration was initiated because different regions of the research groups in different regions of the world were involved in

different aspects of insulin resistance research or different complications of insulin resistance. Another area of relevance for the current study with regard to scientific publications on insulin resistance is the quality of research papers. It is worth noting that nine of the top ten cited articles were published in journals with IF larger than ten, implying that they have a large impact in medicine: Journal of Clinical Investigation, Cell Metabolism, and Nature. As shown, articles related to insulin resistance have been published both in endocrinology and non-endocrinology subject areas, such as medicine; biochemistry, genetics, and molecular biology; nursing; pharmacology, toxicology, and pharmaceutics; agricultural and biological sciences; neuroscience; and immunology and microbiology journals, revealing the contribution and collaboration of many researchers from different subject areas. Previous research has found that[43-45]. The findings of this study confirm the close association between IF and citations and the fact that the most cited articles are frequently published in journals at the top of the IF list, which helps these journals maintain their high IF.

Furthermore, the increase in insulin resistance publications can be attributed to the fact that numerous hot topics were published during this period[33-42], exposing novel hypotheses and establishing new research fields such as "inflammatory mechanisms in the regulation of insulin resistance" and "mechanisms linking obesity and insulin resistance". Several studies have shown that inflammation is a critical mediator in obesity-induced insulin resistance. Most of these investigations examined the links between adipose tissue in obesity and the regulation of inflammation and insulin resistance[46-49], and the mechanisms by which dietary anti-inflammatory components/functional nutrients may be helpful[50-52].

Publications with the highest citation frequencies have the greatest academic effect[53,54]. For example, the study published in the Journal of Clinical Investigation in 2003 by Xu *et al*[36] was ranked first. It was revealed that macrophages in white adipose tissue are involved in morbid obesity and that macrophage-associated inflammatory activities may contribute to the pathophysiology of obesity-induced insulin resistance[36]. On the second other hand, the article was published in Diabetes by Cani *et*

al[40]. Metabolic endotoxemia was found to alter the inflammatory tone of the body, causing weight gain and diabetes[40].

Strengths and limitations

This is the first bibliometric and visual analysis study to investigate research trends and hotspots in insulin resistance from 2002 to 2021. The current study reviewed linked papers on this issue from numerous perspectives, demonstrated a comprehensive view of understanding in this field during the last few years, and gave direction for future investigations. New researchers in this discipline may simply access meaningful and relevant material with the aid of this bibliometric study. However, certain limitations apply to the generalizability of these findings. For example, first, bibliometric analyzes used solely published material from the Scopus database. This may underestimate the amount of research done in South America, China, the Middle East, and other regions of the globe with non-English and unindexed publications. Second, because bibliometric data changes over time, indexing delays may have caused a slight (but not significant) in the number of documents or other metrics. Third, to avoid selection bias, the current study only searched the title for terms such as "insulin resistance" or "insulin sensitivity". As a result, the possibility of false positive or false-negative results should always be considered. Fourth, Scopus's results reflect the type and content of Scopus's database. As a result, if prolific authors have two or more Scopus profiles, their research output is likely to be dispersed, and their names may not appear in the active list. The same is true when alternative spellings of an institution's name are used in published documents. As a result, interpreting data about the most active authors, institutions, and nations should be limited to the Scopus findings produced using the described technique.

CONCLUSION

To our knowledge, this was the first research to conduct a comprehensive bibliometric analysis of insulin resistance publications from 2002 to 2021, covering the publication

year and the number of citations and current hot topics and trends projected from them. Our data show that insulin resistance has steadily gained interest from researchers, as evidenced by the number of citations and yearly publications. So far, the United States has been the undisputed leader in this topic, which cannot be divorced from adequate funding sources. Publications have grown significantly in the last decade, while low-income countries with greater burdens continue to produce fewer publications in this field. "Inflammatory mechanisms in the regulation of insulin resistance"; and 'mechanisms linking obesity to insulin resistance' were hotspots for insulin residence research in the past 20 years. This approach might assist researchers in choosing new research areas and recognizing research hotspots and frontiers. In the future, perhaps, high-quality clinical evidence will be acquired.

ARTICLE HIGHLIGHTS

Research background

Insulin resistance is a condition in which muscle cells to take up and store glucose and triglycerides, resulting in elevated amounts of glucose and triglycerides circulating in the bloodstream.

Research motivation

Several bibliometric studies have been carried out on the subject of diabetic investigation. However, no bibliometric study has been done on research into insulin resistance.

Research objectives

This bibliometric study aimed to identify and assess the current state and trends in insulin resistance research production worldwide and visually analyze research hotspots on this subject.

Research methods

The Scopus database and *Reference Citation Analysis* (RCA) were used to compile the literature on insulin resistance. In addition, VOSviewer software was used to assess data collected from relevant publications visually.

Research results

This is the first bibliometric analysis of trends in insulin resistance. The number of publications on insulin resistance has increased in the last decade. Our results indicated that the "Inflammatory mechanisms in the regulation of insulin resistance"; and "mechanisms linking obesity to insulin resistance" will remain research hotspots in the future.

Research conclusions

Our findings indicate that interest in insulin resistance has gradually increased among researchers, as shown by the increasing number of citations and annual publications. Moreover, publications in this field have increased significantly in the last decade, while low-income countries with higher burdens continue to produce fewer publications.

Research perspectives

This paper contributes essential information by providing references and suggestions for future research on pathophysiology and clinical uses of insulin resistance. This approach may aid researchers in identifying new topics of inquiry and identifying research hotspots and frontiers. Perhaps in the future, high-quality clinical evidence will be collected.

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