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# Global research trends on the links between insulin resistance and obesity: a visualization analysis

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## Abstract

**Background:** Obesity increases the chance of developing insulin resistance. Numerous inflammatory markers have been linked to an increased risk of insulin resistance in obese individuals. Therefore, we performed a bibliometric analysis to determine global research activity and current trends in the field of obesity and insulin resistance.

**Methods:** Scopus was used between 2002 and 2021 to retrieve publications related to terms related to obesity and insulin resistance. Data were exported to Microsoft Excel. Additionally, we use VOSviewer software to create visualization maps that describe international collaborations and research hotspots.

**Results:** We identified 6626 publications, including 5754 journal articles, 498 review articles, and 109 letters to the editor. The most productive countries were the United States ( $n = 995$ , 30.11%), followed by China ( $n = 650$ , 9.81%), Italy ( $n = 412$ , 6.22%) and Spain ( $n = 386$ , 5.83%). Previously to 2012, this field was mainly focused on 'adipocyte dysfunctions that link obesity with insulin resistance'; and 'relationship between obesity, insulin resistance, and risk of cardiovascular disease'. 'Supplements improve insulin sensitivity', and 'obesity-induced inflammation and insulin resistance' were found more recently (after 2014), indicating that research in this field has acquired significant interest and emphasis in recent years.

**Conclusions:** This is the first bibliometric study to focus on publications related to insulin resistance and obesity at the global level. Our reporting of quantifiable knowledge in this field may be useful in providing evidence and direction for future research, clinical practice, and educational initiatives.

**Keywords:** Insulin Resistance, Obesity, Global, VOSviewer, Scopus

## Background

Insulin is a hormone secreted by  $\beta$  cells of the pancreas regularly and in response to food. Its main function is to regulate the metabolism of carbohydrates, fats and proteins by enhancing the absorption of blood glucose from

the circulation into adipose tissue, skeletal muscle, and the liver to be used as a source of energy [1, 2]. However, an excess blood glucose level results in a decrease in cell absorption, which eventually leads to insulin resistance, and affects the cellular insulin response [3, 4]. Many factors play a role in stimulating insulin resistance, such as oxidative stress and reticulum stress, genetic factors, oxygen insufficiency, and lipodystrophy, which can lead to several diseases [5–7].

Insulin resistance has long been associated with obesity that is directly related to cardiovascular diseases,

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including dyslipidemia, atherosclerosis, type 2 diabetes mellitus (T2DM), and hypertension [8, 9]. The percentage of obesity worldwide has reached epidemic proportions, where almost 30% of the population is considered overweight or obese [10, 11]. The obesity and overweight categories are classified according to body mass index (BMI). Obesity is defined as a body mass index of  $30 \text{ kg} / \text{m}^2$  and above, while overweight represents a BMI of  $25 \text{ kg} / \text{m}^2$  and above [12].

Overweight and obesity are the consequences of excess fat accumulation in adipose tissues (AT) due to an imbalance between nutrient intake and energy expenditure [10]. On the other hand, central obesity, which is a consequence of the accumulation of intraabdominal fat, is associated with a higher risk of cardiovascular disease [13] and metabolic diseases such as insulin resistance, T2DM, dyslipidemia, and hypertension in overweight and moderately obese patients ( $\text{BMI} < 35$ ). Central obesity is defined as an increase in waist circumference (WC) measured in the mid-horizontal plane between the superior iliac crest and the lower margin of the last rib to WC 94 or 102 cm and above for men and 80 or 88 cm and above for women according to European and US guidelines [13–16]. Furthermore, several studies found that adipose tissue remodeling in obese people shows an inflammatory response and activates the secretion of pro-inflammatory cytokines and chemokine; which can induce systemic inflammation and insulin resistance [17–19].

This is also supported by evidence that expanded adipose tissue, characterized by activating pro-inflammatory responses, is significantly associated with excess body fat mass that increases infiltration of AT macrophages [20]. Recent studies have also shown that almost 80% of patients with T2DM are obese [21]. By 2025, 100 million adults worldwide are expected to have T2DM as a consequence of obesity [22]. Insulin resistance is the main cause of expanded adipose tissue inflammation accompanied by impaired insulin secretion by pancreatic cells [23].

Furthermore, cardiovascular diseases are strongly associated with obesity and T2DM, with higher morbidity and mortality [24–27]. For this purpose, it is important to understand the mechanisms that link obesity with insulin resistance to improve the knowledge of T2DM and cardiovascular disease and control obesity-related diseases.

The literature on insulin resistance and obesity has not yet been published using bibliometric tools. Furthermore, only a small number of study has been conducted to predict obesity hotspots [28–31] or insulin hotspots [32, 33]. Therefore, we performed a bibliometric analysis to determine global research activity and current trends in the area of obesity and insulin resistance interaction.

Furthermore, we hoped to visualize bibliometric hotspots for research on insulin resistance and obesity during the last two decades. This study provides a quick overview of current insulin resistance and obesity and forecasted future development trends in this area. This analysis will give researchers a holistic view of the entire knowledge area's macroscopic and microscopic properties.

## Methods

### Sources of literature data

The data of this study were derived from the Scopus database. For numerous reasons, the current analysis was performed using the SciVerse Scopus database [34–36]. First, compared to other databases such as PubMed or Web of Science, Scopus has a much larger number and diversity of indexed publications. For example, Scopus has more than the number of journals indexed in PubMed and Web of Science [37]. Second, because all publications listed in PubMed are also indexed in Scopus, PubMed is completely included in Scopus [37]. Third, Scopus publishes publications in various disciplines, including medical, health, mathematics, computer science, and social sciences. Fourth, Scopus enables researchers to create sophisticated and extensive search queries by combining various Boolean operators. Fifth, Scopus enables the researcher to export and examine the data that have been retrieved. This comprises mapping and statistical analysis. Finally, Scopus is the database most commonly used to search for bibliometric studies and obtain articles on various scientific topics [35, 38–42]. The literature data search was conducted on February 18, 2022.

### Search strategy

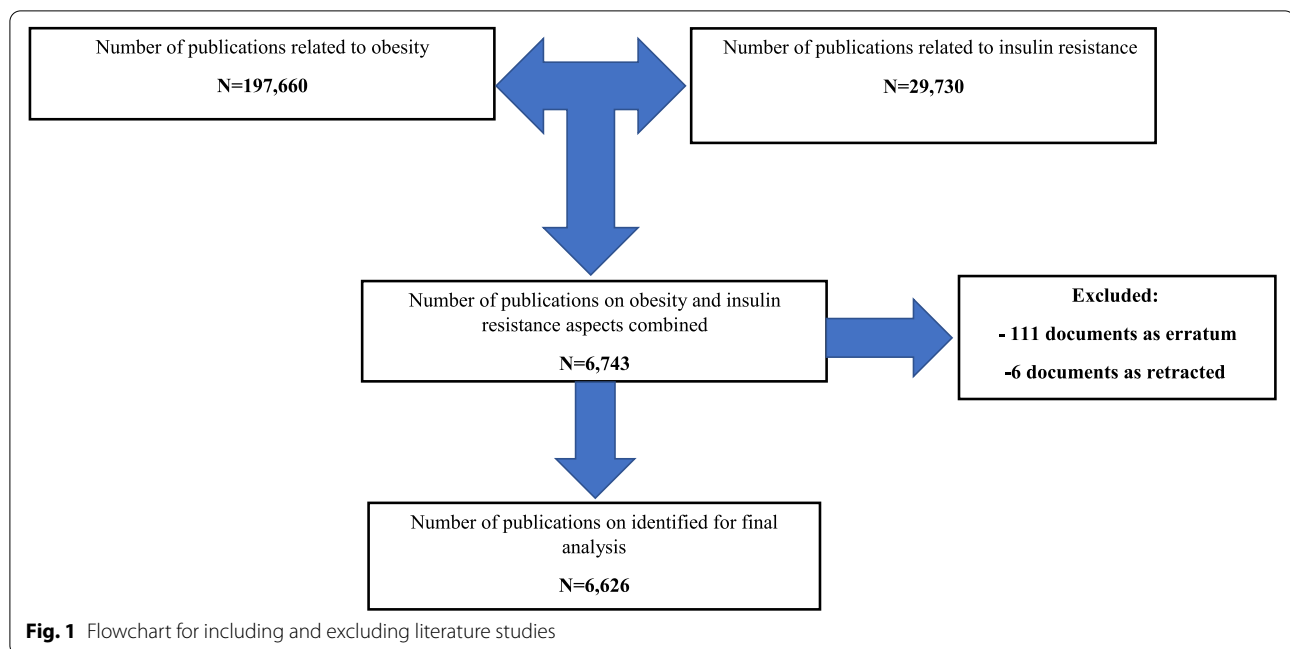
After using the “Advanced search” tool of the Scopus online database and entering relevant keywords, we located the relevant literature on insulin resistance and obesity over the previous two decades (from January 2002 to December 31, 2021). Detailed selective procedures of the enrollment publications are illustrated as a flowchart in Fig. 1. The following search steps included the use of synonyms for insulin resistance and obesity.

#### Step 1

The terms related to insulin resistance entered into the Scopus engine were selected from several previous systematic reviews and meta-analyses of insulin resistance [43–45]. As a result, the following terms were used in the Article Title: “insulin resistance” or “insulin sensitivity”.

#### Step 2

The publications revealed in Step 1 were narrowed down to only those with the terms “obesity and linked terms” in their titles. Several previous systematic reviews and



meta-analyses on obesity [46–50] were used to generate keywords entered into the Scopus search engine to achieve the objective of this study. The “Article Title” was filled out using these “terms”: *obes\* OR corpulence OR fatness OR overweight OR over weight OR adipose tissue OR body mass index OR body composition OR BMI OR waist circumference OR skinfold thickness OR waist to hip ratio OR percentage body fat OR adiposity*.

As a result, keywords were used instead of a title/abstract search in the title search. Since the title search will result in a small number of false positive documents, it is a reliable technique [51–55]. Alternatively, a title/abstract search will provide many false positives in which the primary focus is not insulin resistance and obesity per se but rather on other topics.

#### Bibliometric analysis

The results of insulin resistance and obesity were analyzed with the type of publications, the distribution of publication years, countries, organizations, journals, funding agencies, and citations.

#### Visualization analysis

The search approach was applied, and the obtained data were exported to Microsoft Excel as a “CSV” file. VOSviewer 1.6.18 (Leiden University, Leiden, The Netherlands) was applied to present the network characteristics for countries and the co-occurrence terms in titles and to present the results visually. VOSviewer may be used to build scientifically based knowledge networks that depict the progress of research areas to predict future

research hotspots and inter-country collaborations. VOSviewer’s co-occurrence analysis may group terms into various clusters, with each cluster denoted by a distinctive color. Through a term co-occurrence network, cluster analysis of research hotspots may be enhanced to display and detect the development trend.

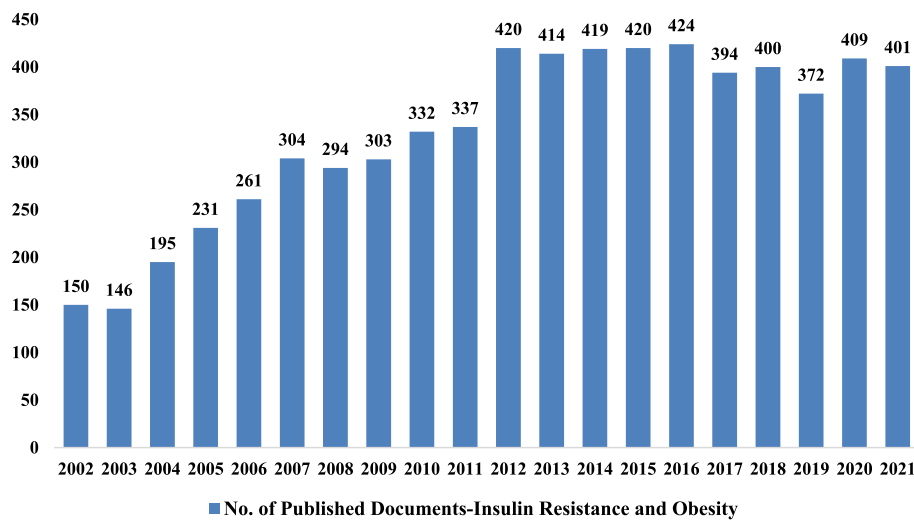
#### Statistical analysis

Data were exported from Scopus to Microsoft Office Excel® and subsequently transferred to Microsoft Word. Figures were created using Microsoft Excel 2013 and VOSviewer version 1.6.18. The descriptive statistics were reported in the form of frequencies and percentages. The bibliometric analysis (such as countries, cited publications, journals, and institutions) were transformed into a ranking. Consideration was given to the top ten orders in each category. If the bibliometric analysis have the same ranking number, there will be a gap between the subsequent ranking numbers.

#### Results

##### Distribution of publications by year

In total, we identified 6626 publications, including 5754 journal articles, 498 review articles, and 109 letters to the editor. Figure 2 shows the trend of publications related to insulin resistance and obesity from 2002 to 2021. During the last two decades, the growth trajectory has been divided into two phases: the first (2002–2011), which experienced rapid growth, and the second (2012–2021), which revealed that research output grew steadily during those years. As a result, the publication annual average



**Fig. 2** Distribution of publications on insulin resistance and obesity according to the year (2002–2021)

production climbed from 25.53 in the first period to 40.73 in the steady growth period.

#### Contributed Countries

According to Scopus, the retrieved publications on insulin resistance and obesity were contributed by 106 countries. The most productive countries were the United States ( $n=1995$ , 30.11%), followed by China ( $n=650$ , 9.81%), Italy ( $n=412$ , 6.22%), and Spain ( $n=386$ , 5.83%) (Fig. 3). Figure 4 illustrates the network of national collaborations for the research of insulin resistance and obesity. Centrality analysis revealed that the United States was at the center of the network, followed by China.

#### Contributed Institutions

Table 1 shows the top 10 institutions in terms of publication number. These ten institutions produced 13.66% ( $n=905$ ) of all the publications analyzed in this study. Among them, *INSERM* has published the highest number of papers related to insulin resistance and obesity ( $n=162$ ), followed by *Harvard Medical School* ( $n=127$ ) and *Karolinska Institutet* ( $n=97$ ).

#### Contributed funding agencies

The top ten funding agencies in terms of production are shown in Table 2. The *National Institute of Diabetes and Digestive and Kidney Diseases* (NIDDK) ( $n=761$ , 11.49%), the *National Institutes of Health* (NIH) ( $n=630$ , 9.51%), and the *National Center for Research Resources* (NCRR) ( $n=364$ , 5.49%) were the top three most productive funding agencies.

#### Contributed journals

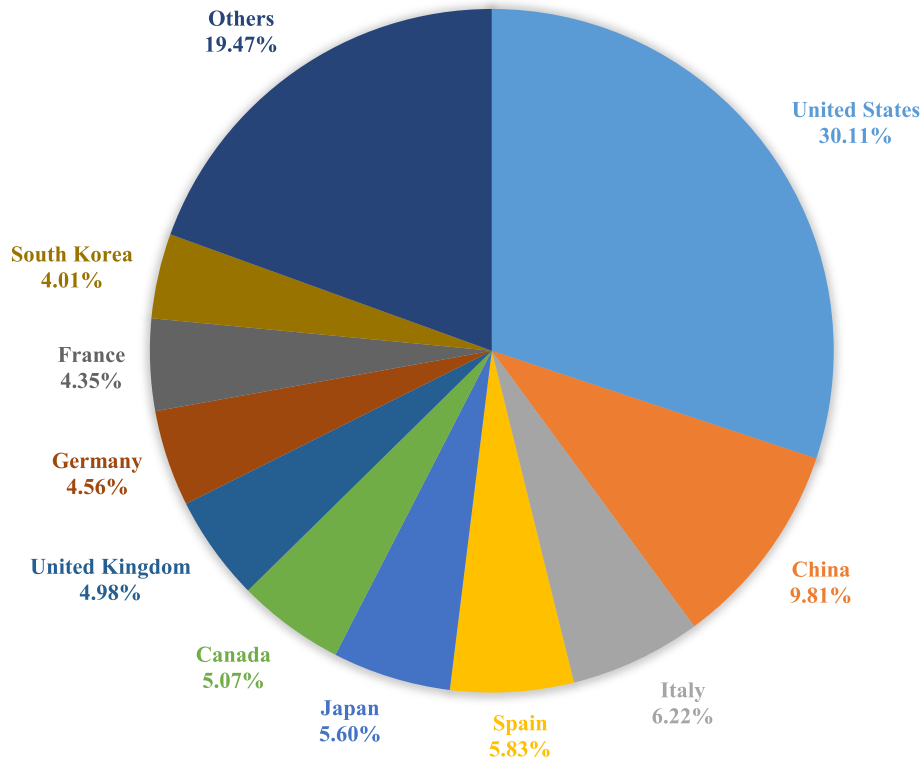
Table 3 summarizes the top ten journals by total number of publications. These ten journals accounted for 22.14% ( $n=1467$ ) of all publications analyzed in this study. *Diabetes* published the most publications ( $n=269$ ) on insulin resistance and obesity, followed by the *Journal of Clinical Endocrinology and Metabolism* ( $n=206$ ) and *Plos One* ( $n=154$ ).

#### Highly Cited Publications

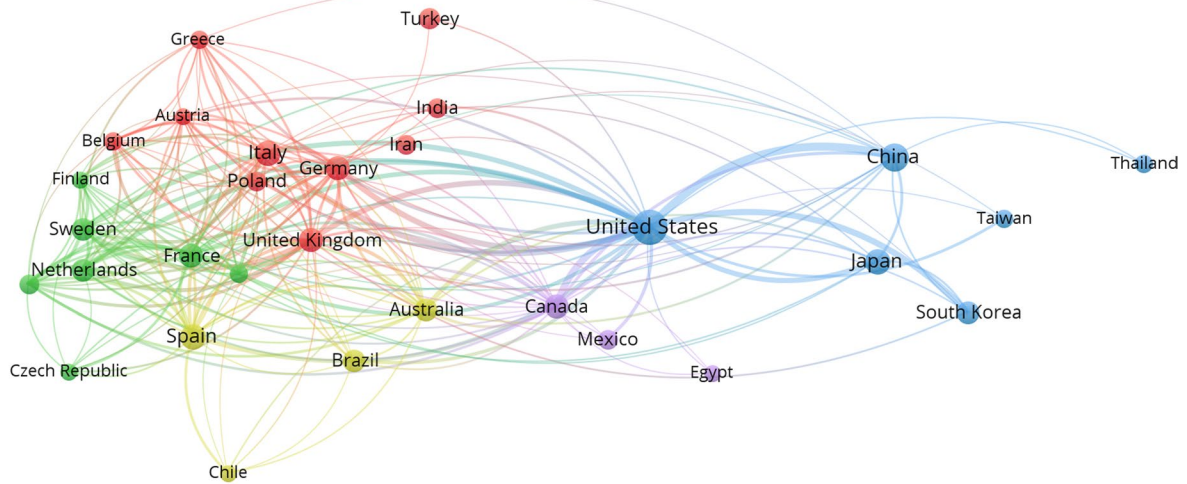
The 10 articles with the most citations from 2002 to 2021 were cited 24,248 times, ranging from 1551 to 4925, as listed in Table 4 [56–65]. The article most frequently cited by Xu et al. [56], which received 4.925 citations, was published in the *Journal of Clinical Investigation* in 2003. The second most cited article, with 3679 citations, is Cani et al. [57], published in 2007 in *Diabetes*.

#### Hot spots related to insulin resistance and obesity research

Figure 5 shows the main hot spots related to insulin resistance and obesity in the past 20 years. For the 6626 documents retrieved, VOSviewer analysis was used to search the titles for terms. The map was then created with 225 terms (12,343 in total), categorized into four clusters with at least ten appearances per term. The most frequent terms on the map include ones related to (a) obesity-induced inflammation and insulin resistance (green cluster); (b) adipocyte dysfunctions linking obesity to insulin resistance (blue cluster); (c) relationship between obesity, insulin resistance, and cardiovascular



**Fig. 3** Distribution of the top ten countries that published research on insulin resistance and obesity from 2002 to 2021



**Fig. 4** Network visualization map of international research collaboration between countries with a minimum research output of 50 documents ( $n = 30$  countries) on insulin resistance and obesity. The map was created using VOSviewer software version 1.6.18

**Table 1** A list of the top ten institutions that published research on insulin resistance and obesity from 2002 to 2021

Ranking	Institute	Country	n	%
1st	INSERM	France	162	2.44
2nd	Harvard Medical School	USA	127	1.92
3rd	Karolinska Institutet	Sweden	97	1.46
4th	Instituto de Salud Carlos III	Spain	88	1.33
5th	Universidade de São Paulo	Brazil	80	1.21
6th	Københavns Universitet	Denmark	77	1.16
7th	National Institutes of Health NIH	USA	74	1.12
8th	Consiglio Nazionale delle Ricerche	Italy	68	1.03
9th	VA Medical Center	USA	67	1.01
10th	Universidade Estadual de Campinas	Brazil	65	0.98
10th	University of California, San Diego	USA	65	0.98

disease risk (red cluster); and finally, (d) supplements improve insulin sensitivity (yellow cluster).

#### Future research direction analysis

VOSviewer colored each term differently in Fig. 6 based on the average number of times it appeared in all retrieved publications. Blue denotes the earliest occurrences of the terms, while yellow denotes the most recent occurrences. Previously to 2012, this field was mainly focused on ‘adipocyte dysfunctions that link obesity with insulin resistance’; and ‘relationship between obesity, insulin resistance, and the risk of cardiovascular disease’. ‘Supplements improve insulin sensitivity’, and ‘obesity-induced inflammation and insulin resistance’ were found more recently (after 2014), reflecting the latest research trends.

#### Discussion

In this study, we performed a bibliometric analysis of publications on insulin resistance and obesity in the past two decades to identify the main hotspots and trends. This type of bibliometric seeks to fill the gaps

**Table 2** The top ten funding agencies having the most publications on insulin resistance and obesity from 2002 to 2021

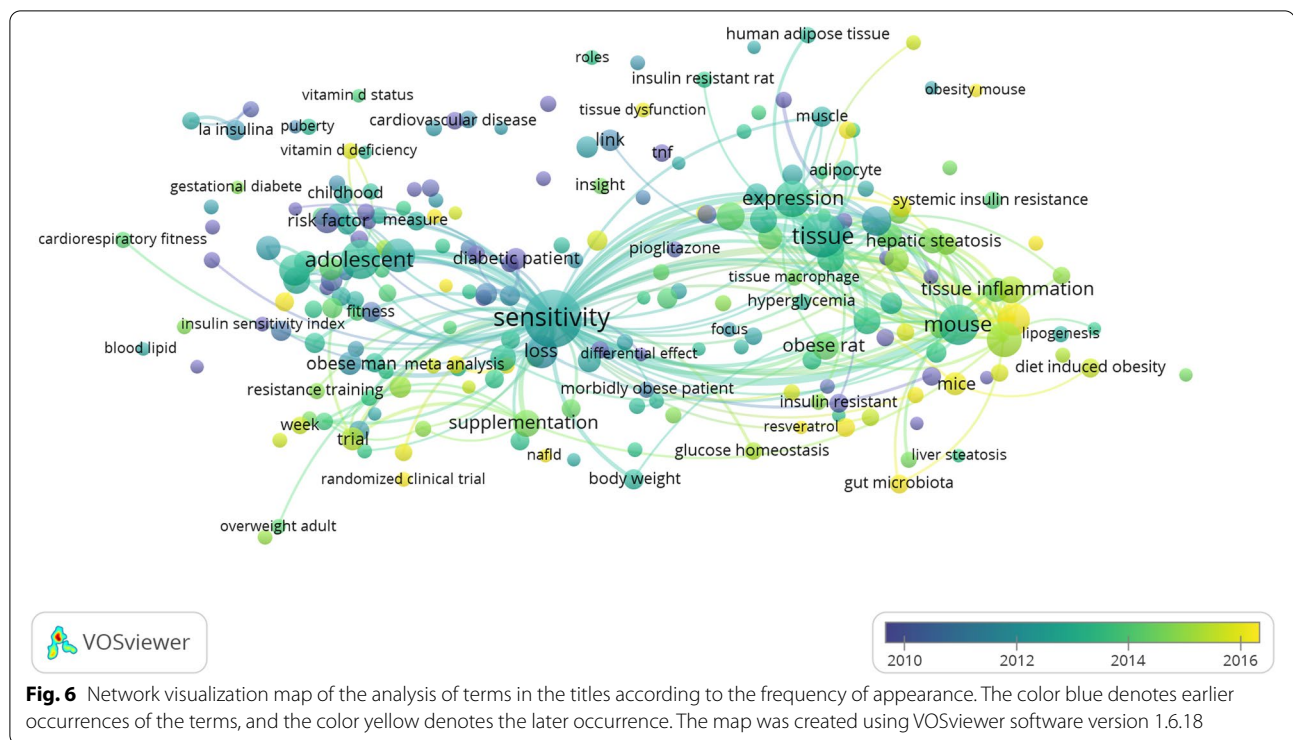
Ranking	Institute	Country	N	%
1st	National Institute of Diabetes and Digestive and Kidney Diseases	USA	761	11.49
2nd	National Institutes of Health	USA	630	9.51
3rd	National Center for Research Resources	USA	364	5.49
4th	National Heart, Lung, and Blood Institute	USA	350	5.28
5th	National Natural Science Foundation of China	China	243	3.67
6th	U.S. Department of Health and Human Services	USA	174	2.63
7th	National Center for Advancing Translational Sciences	USA	162	2.44
8th	Eunice Kennedy Shriver National Institute of Child Health and Human Development	USA	155	2.34
9th	National Institute on Aging	Canada	125	1.89
10th	Japan Society for the Promotion of Science	Japan	121	1.83

**Table 3** A list of the top ten journals that published research on insulin resistance and obesity from 2002 to 2021

Ranking	Journal	n	%	IF <sup>a</sup>
1st	<i>Diabetes</i>	269	4.06	9.461
2nd	<i>Journal of Clinical Endocrinology and Metabolism</i>	206	3.11	5.958
3rd	<i>Plos One</i>	154	2.32	3.34
4th	<i>Diabetologia</i>	141	2.13	10.122
5th	<i>Diabetes Care</i>	134	2.02	19.112
6th	<i>International Journal of Obesity</i>	133	2.01	5.095
7th	<i>Obesity</i>	132	1.99	5.002
8th	<i>Metabolism Clinical and Experimental</i>	122	1.84	8.694
9th	<i>American Journal of Physiology Endocrinology and Metabolism</i>	104	1.57	4.310
10th	<i>Scientific Reports</i>	72	1.09	4.379

<sup>a</sup> 2020 Journal Citation Reports® Science Edition (Clarivate Analytics, 2021)





published during this period [56–61, 72–75], presenting unique theories and generating new study fields. Several studies have shown that inflammation plays an important role in obesity-induced insulin resistance. Most of these studies examined the connections between adipose tissue in obesity and the control of inflammation and insulin resistance [62, 64, 65, 76], as well as the processes through which dietary anti-inflammatory components/functional nutrients may be beneficial [77–79]. A more recent study showed that multidisciplinary research collaboration was prevalent in the field of insulin resistance [33]. However, most of the articles originated in high-income countries. More studies should be promoted in poorer nations where insulin resistance is still a major problem. Identification, investigation of the underlying molecular processes and evaluation of insulin resistance's function in the pathogenesis of a plethora of metabolic diseases are the current research foci for insulin resistance publications [33].

The United States, Europe, and China are the world leaders in scientific research output on insulin resistance and obesity. In fact, this finding is surprising considering the long history of research and health funding agencies and institutions in the United States [80–82], China [83, 84], and France [65, 85]. According to the current study, the United States has the highest publication rate for insulin resistance and obesity, which is consistent with other approaches to obesity [28, 30, 86–91].

Numerous organizations and funding agencies that have made significant contributions in this field are also based in the United States. The United States is ahead of other countries in terms of advanced technology, a high-quality experimental environment, favorable clinical trial settings, and professional personnel [92].

The current study identified the terms that occur most frequently in the scientific literature and demonstrated how they appeared in several publications. Four research hotspots on insulin resistance and obesity were identified, visualized, and expounded. Of these, the theme of 'relationship between obesity, insulin resistance, and cardiovascular disease risk' was among the main hot topics in the current study and received more attention to insulin resistance and obesity. Several studies have shown a considerable relationship between obesity, insulin resistance, and the risk of cardiovascular disease [93, 94]. Metabolic disorders such as hyperinsulinemia, glucose intolerance, high triglycerides, and low HDL cholesterol levels found in most insulin-resistant individuals increase the risk of coronary heart disease [95–98].

Although most people with higher BMI can be considered more insulin resistant [99], several studies have shown that a person of normal weight can be insulin resistant. On the contrary, obese people could have a high insulin sensitivity. Importantly, previous data confirm that visceral fat mass is associated with insulin resistance and is considered an independent risk factor for adverse



health outcomes regardless of BMI [100–103]. Therefore, insulin resistance at any BMI significantly increases the risk of cardiovascular disease in diabetic and non-diabetic patients [8, 94, 98, 104].

Another theme that has received much attention is ‘supplements improve insulin sensitivity’. Supplements to improve insulin sensitivity have become a new idea. However, consistent evidence was found by taking magnesium, berberine, resveratrol, and chromium picolinate supplements. They may effectively improve the body’s response to insulin and reduce sugar in diabetic patients [105–109]. Previous results provide significant evidence that oral Mg supplementation, for example, improves insulin sensitivity in hypomagnesemic, overweight, diabetic and non-diabetic individuals [110, 111] and decreases the consequence risk of cardiovascular disease [112]. In randomized clinical trials, olive leaf polyphenol supplementation has been shown to be an independent factor in improving insulin secretion and sensitivity [113, 114].

Inflammation is one factor that increases insulin resistance. Therefore, the treatment with vitamin C, vitamin E, lycopene, and vitamin D 3 have been suggested to improve insulin sensitivity through antioxidant and anti-inflammatory effects [77, 115]. However, it should be mentioned that although the association between vitamin D deficiency and central obesity with its related diseases has been confirmed by numerous studies [116, 117], inconsistent results were found regarding the management of obesity and associated conditions, including insulin resistance with vitamin D supplementation [117–119]. Therefore, to improve the inflammatory phenotype and insulin sensitivity, diet and the weight loss programs and assessment of vitamin deviancies are key to providing balanced healthy nutrition and vitamin supplementation [77, 120].

Another hot topic is ‘obesity-induced inflammation and insulin resistance’. In 1993, Spiegelman’s group sparked the idea of the impact of certain inflammatory markers on the development of insulin resistance and, eventually, T2DM [18]. Nowadays, this concept has become widely passable [121]. Obesity and inflammation have shown a marked association with haptoglobin and CCN3, and both were found to be elevated in T2DM [122, 123]. A recent study found that patients with T2DM had a significantly higher expression rate of some interleukin-36 subtypes than healthy individuals [124]. Some suggested that the implementation of the strategic measure to control inflammation may reduce the incidence of T2DM [125]. So far, researchers have tested an anti-inflammatory drug, IL-1 $\beta$  inhibitor, in patients with cardiac diseases and showed that the occurrence of diabetes mellitus did not decrease [126]. Although progress in

this proposition is evident, 20–30% of obese patients are considered metabolically healthy and have a high level of insulin sensitivity [77]. Thus, multiple types of research must be conducted [121].

Another subject that has attracted a lot of interest is “adipocyte dysfunctions associated with obesity and insulin resistance”. Adipocytes are cells with the capacity to store excess energy in the form of lipids; the total number of these cells seems constant after the age of the child [127]. Although these cells can also renew every eight years, it is suggested that dysfunctions in the renewal capacity of fat cells are associated with T2DM [128]. In fact, ways to increase adipogenesis instead of fat cell hypertrophy are supposed to combat the negative impact of obesity on metabolic disorders, such as insulin resistance [127]. In addition, adipocyte size was found to be linked with insulin resistance, in which adults with high insulin resistance had a larger adipocyte size and interleukin-6 receptor [129]. For example, data suggested that manipulation in specific molecules, such as Ant2 adipocyte [130] and phosphatidylinositol 4-phosphate 5-kinase [131] can reduce insulin resistance.

In recent years, the ‘relationship between obesity, insulin resistance, and cardiovascular disease risk’ and ‘supplements improve insulin sensitivity’ have become the main hotspots in the field of insulin resistance and obesity, with a high centrality. The findings of our analysis show that the most widely cited publications on insulin resistance and obesity [56–65] emphasized a variety of subtopics close to the study hotspots in co-occurring terms. These findings show that research in this field has gained significant attention and emphasis in recent years.

### Strengths and limitations

The current study is the first of its kind and provides baseline data on research activities related to the connection between insulin resistance and obesity. However, there are certain limitations to the current study. First, the fact that we used Scopus to retrieve documents might have led to the loss of certain documents published in local unindexed journals. However, Scopus is a large database and numerous unindexed health-related publications are from many countries. These findings resulted in a bias that favors countries with Scopus-indexed journals or English-language articles. As a result, research productivity may be underestimated. Second, the analysis is based on publications retrieved from the Scopus database, so it may not be comprehensive. On the other hand, Scopus continues to be the most accessible database for analyzing research activity and locating research hotspots on a specific topic. Another limitation is that the current study was limited to the search terms ‘insulin resistance

and obesity' and related terms only in the title search. Therefore, this analysis may have missed any publications that used "insulin resistance and obesity" as a keyword or within the publication.

## Conclusions

This is the first bibliometric study to focus on publications related to insulin resistance and obesity at the global level. Detail information for various publications can be understood more intuitively via visual or cluster analysis. Within 20 years, we noticed that the number of publications on insulin resistance and obesity research had risen rapidly since 2003, then stabilized after 2012. The leading countries included the United States, China, Italy, and Spain. Furthermore, the themes 'Supplements improve insulin sensitivity' and 'obesity-induced inflammation and insulin resistance' were found more frequently in recent years (after 2014), indicating that research in this field has gained significant interest and emphasis in recent years. Our reporting of quantifiable knowledge in this field may be useful in providing evidence and direction for future research, clinical practice, and educational initiatives.

## Abbreviations

T2DM: Type 2 diabetes mellitus; BMI: Body mass index; AT: Adipose tissues; WC: Waist circumference.

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## Authors' contributions

Zyoud SH conceptualized and designed the research project, took care of data management and analysis, generated figures, made significant contributions to the manuscript's existing literature search and interpretation of the manuscript, and drafted the manuscript; Shakhshir M contributed to the conceptualisation and methodology of the study, involved in interpretation of the data, contributed to the manuscript writing, and made revisions to the initial draft. Abushanab AS, Al-Jabi SW, Jairoun AA, Shahwan WM, and Koni A were involved in interpretation of the data, contributed to the manuscript writing, and made revisions to the initial draft; all authors provided a critical review and approved the final manuscript before submission.

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No support was received for conducting this study.

## Availability of data and materials

All data generated or analyzed during this study are included in this published article. In addition, other data sets used during the current study are available from the corresponding authors on reasonable request.

## Declarations

### Ethics approval and consent to participate

Because the current study did not include any human interaction, it does not require the permission of the Ethics Committee.

### Consent for publication

Not applicable.

## Competing interests

The author declares that he has no competing interests.

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