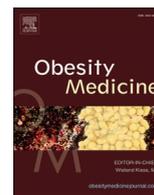


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A bibliometric analysis of highly cited insulin resistance publications in Science Citation Index Expanded

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ABSTRACT

Background: Bibliometrics methods are commonly used to analyse and compare scientific performance. At present there are no bibliometric analyses on insulin resistance (IR) publications. In this study, we analysed highly-cited IR publications.

Methods: The analysis presented is based on Web of Science (WoS): Science Citation Index Expanded. Total citations (TC), citation in latest year, citation per publication, number of authors, and collaborations were analysed. Most productive institutes and authors were also identified.

Results: Our search identified 103,742 documents including 72,909 articles related to IR. A total of 167 highly-cited documents (0.016% of 103,742 documents) with TC_{2019} of $\geq 1,000$ in IR research were identified inclusive of 124 highly-cited articles, which were all written in English. These highly-cited documents were mainly published in the journal Nature and for most of them, the WoS category was “multidisciplinary-sciences”. United States of America was the country which has published most number of the highly-cited publications. Harvard University held the highest rank with the most number of highly-cited papers.

Conclusions: Collaborative multidisciplinary research were common in the field of IR. Majority of the publications were arising from developed countries and highly-ranked institutions. More research should be encouraged in developing countries where IR remains a significant issue.

List of abbreviations

AB	Abstract
AK	Author keywords
APP	Authors per publication
C ₂₀₁₉	Citation received only in 2019
CP	Internationally collaborative publications
CPP	Citation per publications
FP	First-author highly cited articles
HOMA	Homeostatic model assessment
IF	Impact Factor
IFG	Impaired Fasting Glycaemia

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Hard copy of the highly cited articles were collected for checking authors' affiliation when it was missing in SCI-EXPANDED. Affiliation re-classification was done to ensure consistency regarding the origin of all publications, as per recommended standards (Chiu and Ho, 2005). For example, affiliations in England, Scotland, Northern Ireland, and Wales were reclassified as being from the United Kingdom (UK). A potential bias in analysis of institutions occur when authors use different spelling for the same institution, therefore, we merged these institutions during analysis (Fu et al., 2014). In the SCI-EXPANDED database, the corresponding-author is labelled as reprint author, but in this study, we used the term corresponding-author. Collaboration was evaluated by the affiliations of the authors in a publication, where 'internationally collaborative articles' were those articles co-authored by researchers from different countries.

3. Results and discussion

A total of 167 highly cited documents (0.016% of 103,742 documents) with TC_{2019} of 1,000 or more in insulin resistance research, all of which were written in English. A similar percentage of highly cited documents have also been found previously in topics such as *Helicobacter pylori* (0.037%) (Suk et al., 2019).

3.1. Document type

Previously Hsieh et al. proposed a relationship between document types and citations per publication (CPP) (Hsieh et al., 2004). In 2015, CPP was further improved by using the citation indicator CPP_{year} which gives more accurate and reproducible values (H.-C. Ho and Ho, 2015). Furthermore, recently the number of authors per publication (APP) has also been identified as being related to document types (Monge Nájera and Ho, 2017). Table 1 shows characteristics of six document types of the identified highly cited documents, including 124 highly cited articles (74.2% of 167 highly cited documents) with an APP of 20. It should be appreciated that a single document could be classified in two document types in the Web of Science Core Collection, for example, 3 highly cited documents have been classified as both reviews and book chapters; and therefore the total percentages represented in Table 1 is higher than 100% (Usman and Ho, 2020). Document type of notes had the highest CPP_{2019} of 2,811. With a single note entitled "An anti-diabetic thiazolidinedione is a high affinity ligand for peroxisome proliferator-activated receptor γ (PPAR γ)" (Lehmann et al., 1995) having a TC_{2019} of 3,143. The average APP was 16 with the maximum being number of authors in a single publication being 936. Ten highly cited publications (6.0% of 167 highly cited publications) were published by a single author, while 26 (15.6%) were published by two authors, 16 (9.6%) by three authors, and 15 (9.0%) by four authors. Only document type of articles were considered for further analysis because they included complete research projects, inclusive of complete publication of methods, results, discussions, and conclusions (Y.-S. Ho, Satoh and Lin, 2010).

3.2. Publication years

A relationship between number of annual highly cited articles (TP) and their citations per publication ($CPP_{year} = TC_{year}/TP$) by decades in a Web of Science category as an indicator has been applied previously in medical-related research fields, such as Web of Science categories of surgery (Long et al., 2014), psychology (Y.-S. Ho and Hartley, 2016), neurosciences (Yeung and Ho, 2018), and orthopedics (Li, Xu, Long and Ho, 2019a). A total of 124 highly cited insulin resistance articles in SCI-EXPANDED were published between 1963 and 2013. The average value of TC_{2019} 1,945 with a minimum and maximum of 1,005 and 20,459 respectively. Fig. 1 shows the distribution of these 124 highly cited articles over the different decades, and their citations per publication (CPP_{2019}). The 124 highly cited articles had a TC_{2019} of 241,208 in the Web of Science Core Collection.

The earliest highly cited article entitled "Glucose fatty-acid cycle: Its role in insulin sensitivity and metabolic disturbances of diabetes mellitus" (Randle et al., 1963) was published in Lancet in 1963 with TC_{2019} of 4,196 (overall rank 6th). This paper presents evidence on the higher rate of release of fatty acids and ketone bodies for oxidation, which is postulated to be responsible for abnormalities of carbohydrate metabolism in muscle in diabetes (Randle et al., 1963). Philip Randle and his colleagues developed the fundamental concept of interplay between carbohydrate and lipid fuels in relation to the requirement for energy utilisation and storage, which fashioned current understanding of the regulation of metabolism in health and disease (Sugden, 2007). The latest highly cited articles were published in 2013, including "Richness of human gut microbiome correlates with metabolic markers" (Le Chatelier et al., 2013) and "Cross talk between *Akkermansia muciniphila* and intestinal epithelium controls diet-induced obesity" (Everard et al., 2013) with TC_{2019} of 1,443 and 1,291 respectively. Citations of these articles has been increased since their publication. Breakthrough metagenomic studies are providing a profile of the microbial communities in the human gut and revealing an association

Table 1
Citations and authors according to document type.

Document type	TP	%	AU	APP	TC_{2019}	CPP_{2019}
Article	124	74.2	2,454	20	241,208	1,945
Review	39	23.4	107	2.7	64,378	1,651
Book chapter	3	1.8	6	2.0	4,372	1,457
Editorial material	2	1.2	26	13	2,314	1,157
Note	2	1.2	11	5.5	5,621	2,811
Proceedings paper	2	1.2	20	10	2,745	1,373

APP – number of authors per publication; AU – number of authors; CPP_{2019} – number of citations (TC_{2019}) per publication (TP); TC_{2019} – the total number of citations from Web of Science Core Collection since publication to the end of 2019; TP – number of publications.

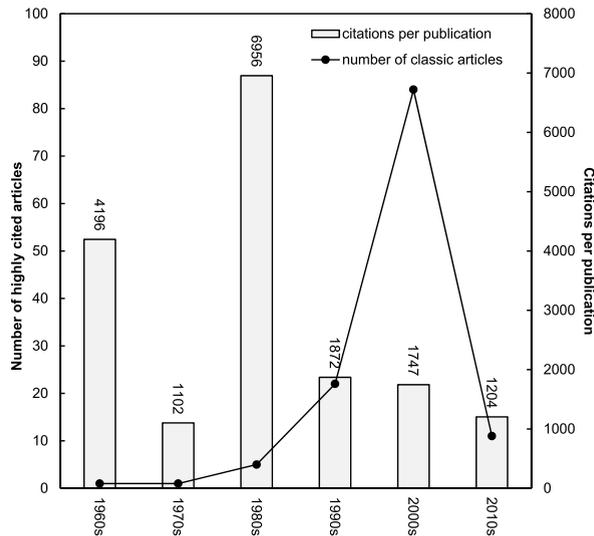


Fig. 1. Number of highly cited articles and citations per publication by decade.

between low microbial-diversity and several disease states, including metabolic diseases such as obesity and diabetes (Everard et al., 2013; Le Chatelier et al., 2013). The decade of the 1980s had the highest CPP_{2019} of 6,956 which can be attributed to the only to one highly cited article with $TC_{2019} > 10,000$, entitled “Homeostasis model assessment: Insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man” (Matthews et al., 1985) with a TC_{2019} of 20,459 (rank 1st) and C_{2019} of 1,403 (rank 1st). This highly cited article is not only the most frequently cited but also the one with the most impact in 2019 in insulin resistance research. However, the 2000s was the most prolific period in terms of highly cited articles in insulin resistance (Fig. 1).

3.3. Web of Science category and journal

The 124 highly cited insulin resistance articles were published in 39 journals classified in 22 Web of Science categories. The Web of Science category of “multidisciplinary sciences” published the most highly cited articles (31 articles; 25% of 124 articles) followed by “endocrinology and metabolism” (23 articles; 19%), “general and internal medicine” (21 articles; 17%), “research and experimental medicine” (19 articles; 15%), “biochemistry and molecular biology” (15 articles; 12%), and “cell biology” (14 articles; 11%). Fig. 2 shows a scatter plot between the number of highly cited articles and journal impact factor (IF_{2019}), which appears to show a positive relationship between the two variables. The top five productive journals published 60 articles (48.4% of 124 articles). Nature ($IF_{2019} = 36.104$), published 15 highly cited articles, Science ($IF_{2019} = 31.364$) published 12 articles, while Diabetes ($IF_{2019} = 8.889$), Journal of Clinical Investigation ($IF_{2019} = 14.152$), and New England Journal of Medicine ($IF_{2019} = 53.484$) published 11 articles each (Fig. 2,

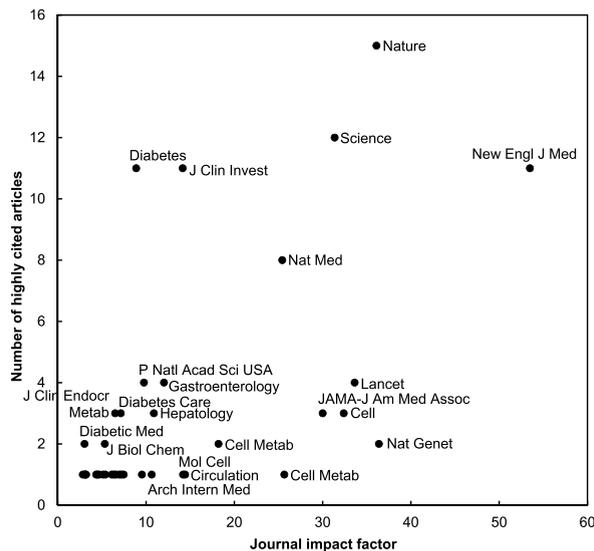


Fig. 2. Scatter plot of the number of highly cited articles against journal impact factors of their publishing journals.

Supplementary Table 1). Highly cited articles published in *Lancet* had the highest *APP* with 244 followed by *Nature Genetics* (*APP* = 156), while highly cited articles published in *British Medical Bulletin*, *British Journal of Nutrition*, and *Journal of Psychosomatic Research* had *APP* of 2.0, respectively. The article entitled “Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: A randomised controlled trial” (Gerstein et al., 2006) in *Lancet* was published by 936 authors from Population Health Research Institute in Canada with a *TC*₂₀₁₉ of 1,206. highly cited articles published in *Diabetologia* had the highest of *CPP*₂₀₁₉ with 20,459, while *Journal of Biological Chemistry* had only 1,012. As expected, the highly cited publications were published in journals with high impact factors (Aksnes, 2003) with the *New England Journal of Medicine* also having the highest *IF*₂₀₁₉ of 53.484. The *Journal of Psychosomatic Research* had the lowest journal impact factor (*IF*₂₀₁₉ = 2.842).

3.4. Countries, institutions, and authors

Among the 124 highly cited insulin resistance articles, 42 articles (34% of 124 articles) were international collaborations by 22 countries and 82 (66%) were not international collaborations and were published by 10 developed countries. The *CPP*₂₀₁₉ for the 82 non-international collaborative articles (*CPP*₂₀₁₉ = 2,089) was higher than that for the 42 international collaborative articles (*CPP*₂₀₁₉ = 1,663). However, both group of articles had the same average number of authors (*APP* = 20 authors). The maximum amount of authors in an article were 303 and 936 for international collaborative articles and non-international collaborative articles, respectively. Table 2 lists the top 10 productive countries and describes five publication indicators; total number of highly cited articles (*TP*), country independent (single country) highly cited articles (*IP*), internationally collaborative highly cited articles (*CP*), first-author highly cited articles (*FP*), and corresponding-author highly cited articles (*RP*) (Y.-S. Ho and Kahn, 2014). USA dominated in all five publication indicators with *TP* of 82 articles (66% of 124 articles), *IP* of 54 articles (66% of 82 country independent articles), *CP* of 28 articles (67% of 42 internationally collaborative articles), *FP* of 74 articles (60% of 124 first-author articles), and *RP* of 76 articles (61% of 124 corresponding-author articles). Furthermore, USA was the only country that has published single-author highly cited articles.

In total, 94 articles (76% of 124 articles) were inter-institutional collaborations and 30 (24%) were institutionally independent articles. Table 3 lists the top 11 productive institutes with the above mentioned five publication indicators. Six of the 11 institutes were located in USA, with two in Italy, and one in each of the UK, Finland, and Japan. Harvard University in USA dominated all the five publication indicators with *TP* of 24 articles (19.3% of 124 articles), *IP* of 5 articles (16.6% of 30 institute independent articles), *CP* of 19 articles (20.2% of 94 inter-institutionally collaborative articles), *FP* of 11 articles (8.9% of 124 first-author articles), and *RP* of 12 articles (9.7% of 124 corresponding-author articles). Yale University in USA was also ranked top in institute independent articles. One single-author highly cited article has been published by Dana-Farber Cancer Institute in USA, Yale University in USA, Veterans Affairs Medical Center in USA, and Temple University in USA, respectively.

Among the 2,181 authors contributing to 124 highly cited insulin resistance articles, eight authors have published five highly cited articles or more (Supplementary Table 2). Both G.S. Hotamisligil from Harvard University in USA and G.I. Shulman from Yale University in USA published the most articles (*n* = 7 article each). T. Yamauchi from University of Tokyo in Japan, G. Marchesini from University of Bologna in Italy, and S.E. Kahn from VA Puget Sound Health Care System in USA published the most first-author articles

Table 2
Twenty-four countries published highly cited insulin resistance articles.

Country	<i>TP</i>	<i>TPR</i> (%)	<i>IPR</i> (%)	<i>CPR</i> (%)	<i>FPR</i> (%)	<i>RPR</i> (%)
USA	82	1 (66)	1 (66)	1 (67)	1 (60)	1 (61)
Italy	16	2 (13)	2 (7.3)	3 (24)	3 (7.3)	3 (6.5)
France	14	3 (11)	N/A	2 (33)	7 (2.4)	9 (1.6)
UK	14	3 (11)	2 (7.3)	4 (19)	4 (6.5)	3 (6.5)
Japan	12	5 (10)	2 (7.3)	7 (14)	2 (8.1)	2 (8.1)
Canada	10	6 (8.1)	5 (4.9)	7 (14)	5 (3.2)	5 (3.2)
Finland	8	7 (6.5)	N/A	4 (19)	10 (0.81)	11 (0.81)
Netherlands	8	7 (6.5)	7 (1.2)	6 (17)	7 (2.4)	7 (2.4)
Australia	6	9 (4.8)	7 (1.2)	9 (12)	10 (0.81)	11 (0.81)
Belgium	6	9 (4.8)	6 (2.4)	13 (10)	5 (3.2)	5 (3.2)
Sweden	6	9 (4.8)	7 (1.2)	9 (12)	10 (0.81)	11 (0.81)
Germany	5	12 (4.0)	N/A	9 (12)	10 (0.81)	9 (1.6)
Switzerland	5	12 (4.0)	N/A	9 (12)	9 (1.6)	7 (2.4)
South Korea	4	14 (3.2)	N/A	13 (10)	10 (0.81)	N/A
Denmark	3	15 (2.4)	N/A	15 (7.1)	10 (0.81)	N/A
Greece	2	16 (1.6)	N/A	16 (4.8)	N/A	N/A
Spain	2	16 (1.6)	N/A	16 (4.8)	N/A	N/A
Austria	1	18 (0.81)	7 (1.2)	N/A	10 (0.81)	11 (0.81)
China	1	18 (0.81)	N/A	18 (2.4)	N/A	N/A
Croatia	1	18 (0.81)	N/A	18 (2.4)	N/A	N/A
Iceland	1	18 (0.81)	N/A	18 (2.4)	N/A	N/A
Saudi Arabia	1	18 (0.81)	N/A	18 (2.4)	N/A	N/A
South Africa	1	18 (0.81)	N/A	18 (2.4)	N/A	N/A

CPR (%) – rank of internationally collaborative highly cited articles and percentage in all internationally collaborative highly cited articles; *FPR* (%) – rank of first-author highly cited articles and percentage in all first-author highly cited articles; *IPR* (%) – rank of single country highly cited articles and percentage in all single country highly cited articles; N/A – not available; *RPR* (%) – rank of corresponding-author highly cited articles and percentage in all corresponding-author highly cited articles; *TP* – total number of highly cited articles; *TPR* (%) – rank of total number of highly cited articles and percentage.

Table 3
The top 11 most productive institutes with $TP \geq 4$.

Institute	TP	TPR (%)	IPR (%)	CPR (%)	FPR (%)	RPR (%)
Harvard University, USA	24	1 (19)	1 (17)	1 (20)	1 (8.9)	1 (9.7)
Yale University, USA	9	2 (7.3)	1 (17)	8 (4.3)	2 (5.6)	2 (5.6)
Beth Israel Deaconess Medical Center, USA	7	3 (5.6)	N/A	2 (7.4)	4 (3.2)	4 (3.2)
University of Texas, USA	6	4 (4.8)	3 (3.3)	5 (5.3)	4 (3.2)	4 (3.2)
University of Tokyo, Japan	6	4 (4.8)	N/A	3 (6.4)	3 (4.8)	3 (4.8)
University of Washington, USA	6	4 (4.8)	N/A	3 (6.4)	17 (0.81)	17 (0.81)
University of California San Diego, USA	5	7 (4.0)	N/A	5 (5.3)	7 (1.6)	7 (1.6)
University of Helsinki, Finland	5	7 (4.0)	N/A	5 (5.3)	N/A	N/A
University of Bologna, Italy	4	9 (3.2)	N/A	8 (4.3)	6 (2.4)	6 (2.4)
University of Cambridge, UK	4	9 (3.2)	3 (3.3)	11 (3.2)	7 (1.6)	7 (1.6)
University of Turin, Italy	4	9 (3.2)	N/A	8 (4.3)	17 (0.81)	17 (0.81)

CPR (%) – rank of inter-institutionally collaborative highly cited articles and percentage in all inter-institutionally collaborative highly cited articles; FPR (%) – rank of first-author highly cited articles and percentage in all first-author highly cited articles; IPR (%) – rank of single institute highly cited articles and percentage in all single institute highly cited articles; N/A – not available; RPR (%) – rank of corresponding-author highly cited articles and percentage in all corresponding-author highly cited articles; TP – total number of highly cited articles; TPR (%): rank of total number of highly cited articles and percentage.

($n = 3$ articles each). T. Kadowaki from University of Tokyo in Japan and G.I. Shulman from Yale University in USA published the most corresponding author highly cited articles ($n = 5$ articles each). Only G.I. Shulman from Yale University in USA, B.M. Spiegelman from Dana-Farber Cancer Institute in USA, G. Boden from Temple University in USA, and G.M. Reaven from Veterans Affairs Medical Center in USA had single-author highly cited article.

Gerald “Jerry” M Reaven was a pioneer in insulin research, is credited with developing the first quantitative method to measure insulin mediated glucose uptake in humans, which he used to establish the importance of insulin resistance in type 2 diabetes (Roehr, 2018). The hypothesis by Reaven that insulin resistance and the resultant hyperinsulinaemia causes a syndrome which he termed as ‘Syndrome X’, is now more widely known as the metabolic syndrome (Soran et al., 2019). G.I. Shulman’s research work examining intracellular glucose and fat metabolism in humans and transgenic rodent models has led to several paradigm shifts in our understanding of type 2 diabetes, including the molecular mechanisms of insulin resistance (Shulman, 2000). Hence, it is evident that these highly cited authors of highly cited articles have contributed immensely to the development of the Insulin Resistance research landscape.

3.5. Citation history of highly cited articles

Supplementary Table 3 shows the top 13 highly cited insulin resistance articles (with $TC_{2019} > 3,000$) with both citation numbers and rankings of TC_{2019} , C_{2019} and $TCPY$. Citation indicator, C_{2019} , demonstrate high impact articles in the most recent year (2019), while $TCPY$, shows average impact of an article from publication year to 2019. Citation indicator, TC_{2019} , indicates overall high impact or visibility of an article in the given research field. However even highly cited articles would not always have continuous high impact or visibility in research society (Y.-S. Ho, 2014). The history of a publication’s citations with time has long been studied (Avramescu, 2007). Citation history shows characteristics of an article impact over time after publication. Supplementary Fig. 1 shows the citation history of the top ten highly cited articles with $TC_{2019} > 3,200$. The highly cited article by Matthews et al. (1985) not only ranked as the top on annual citations continuously from 2003 to 2019 but it is also the only one article with annual citations more than 1,000 from 2007 to 2019 (Supplementary Fig. 3). Article “Glucose fatty-acid cycle: Its role in insulin sensitivity and metabolic disturbances of diabetes mellitus” (Randle et al., 1963) by Randle et al. ranked 6th with a TC_{2019} of 4,196, had two sharp increases of citations from 12 in 1963 to 77 in 1966 and 39 in 1987 to 150 in 1999 as the maxima annual citations of the article. This article still had impact in insulin resistance research with C_{2019} of 96 (rank 90th).

Although some recently published articles within the past few years show promising potential although they did not have a high TC_{2019} . Thus indicator C_{2019} would be a better indicator to show high impact in 2019, i.e in recent years. For example, articles entitled “Cross-talk between *Akkermansia muciniphila* and intestinal epithelium controls diet-induced obesity” (Everard et al., 2013) and “Richness of human gut microbiome correlates with metabolic markers” (Le Chatelier et al., 2013) has recent high impact with a C_{2019} of 347 (rank 4th) and 345 (rank 5th), respectively. A sharp increasing trend of citations can be found in these two articles after publish year of 2013. Five of the top 13 most cited articles with $TC_{2019} > 3,000$ (Supplementary Table 3) still have a C_{2019} ranked in the top 10 as the impact articles with a $C_{2019} > 297$. The five highly cited articles having high impact in the most recent year are highlighted below;

- 1) “Homeostasis model assessment: Insulin resistance and Beta-cell function from fasting plasma glucose and insulin concentrations in man” (1985) (Matthews et al., 1985) this article was published by Matthews and other five authors from Radcliffe Infirmary in the UK with a C_{2019} of 1,403 (rank 1st) and a TC_{2019} of 20,459 (rank 1st). Matthews and co-workers pioneer the homeostatic model assessment (HOMA) of β -cell function and insulin resistance which was first described in 1985 (Matthews et al., 1985). This technique is a method for assessing β -cell function and insulin resistance from basal glucose and insulin or C-peptide concentrations, and has been widely used by numerous researcher from all over the world since it was first published in 1985 (Wallace et al., 2004).
2. “Definition, diagnosis and classification of diabetes mellitus and its complications part 1: Diagnosis and classification of diabetes mellitus - Provisional report of a WHO consultation” (1998) (Alberti and Zimmet, 1998). This article was published by Alberti and

Zimmet from University of Newcastle Upon Tyne in the UK with a C_{2019} of 407 (rank 2nd) and TC_{2019} of 7,867 (rank 3rd). This article proposed changes to the diagnostic criteria of diabetes and introduced a new category of Impaired Fasting Glycaemia (IFG) to encompass values which are above normal but below the diagnostic cut-off for diabetes.

3. "Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome" (2004) ("Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome," 2004). This article was published by Chang and 28 other authors from Erasmus Medical Center in Netherlands and University of Adelaide in Australia with C_{2019} of 285 (rank 8th) and TC_{2019} of 3,200 (rank 10th). The paper discussed the role and importance of insulin resistance in the reproductive abnormalities in women with polycystic ovary syndrome.
4. "Metabolic syndrome: A new world-wide definition. A consensus statement from the international diabetes federation" (2006) (Alberti et al., 2006). This article was published by Alberti, Zimmet, and Shaw from St Mary's Hospital in the UK and International Diabetes Institute and has a C_{2019} of 279 (rank 9th) and TC_{2019} of 3,067 (rank 12th). The paper aimed to establish a unified working diagnostic tool for the metabolic syndrome (where insulin resistance plays a key role in pathogenesis) that is convenient to use in clinical practice and that can be used world-wide so that data from different countries can be compared (Alberti et al., 2006).
5. "Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance" (2003) (Xu et al., 2003). This article was published by Xu and 10 other authors from Millennium Pharmaceut Inc. in USA and Novartis Institutes for BioMedical Research Inc. in USA had a C_{2019} of 272 (rank 10th) and a TC_{2019} of 4,110 (rank 7th). The authors discussed and proposed that obesity-related insulin resistance is, at least in part, a chronic inflammatory disease initiated in adipose tissue, explaining the molecular mechanisms that are likely to be responsible in the pathogenesis (Xu et al., 2003).

4. Conclusion

Collaborative multidisciplinary research were common in the field of IR. Majority of the publications were arising from developed countries and highly-ranked institutions. More research should be encouraged in developing countries where IR remains a significant issue. At present, the common research fields of insulin resistance publications focused on its identification, studying the molecular mechanisms responsible and evaluating its role in the pathogenesis of a plethora of metabolic diseases. Therefore, it can be concluded that research on these topics will remain a crucial direction for future research on insulin resistance. However, it is important that new research is also conducted on areas of public health in relation to early diagnosis and in the management of insulin resistance.

Data availability

Provided as a Supplementary File 1.

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Authors' contributions

PR and YSH made substantial contribution to conception and study design. YSH was involved in data collection. YSH and PR were involved in refining the study design, statistical analysis and drafting the manuscript. YSH and PR critically revised the manuscript. All authors read and approved the final manuscript.

Declaration of competing interest

Authors declare that they have no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.obmed.2022.100399>.

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