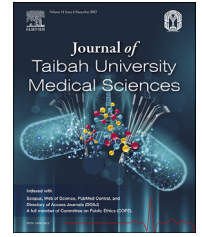




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Original Article

Visualizing breast cancer research trends in KSA: A bibliometric analysis

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المخلص

أهداف البحث: ظهر التحليل البيبليومتري كأسلوب مطلوب للتعامل مع المجالات الناشئة في مجال البحث. لقد حافظ سرطان الثدي على مرتبته الثابتة كأكثر أنواع السرطان شيوعاً بين الإناث على مستوى العالم. تم تصميم هذه الدراسة لإلقاء الضوء على التحليل البيبليومتري لأبحاث سرطان الثدي التي أجريت في المملكة العربية السعودية خلال العقدين الماضيين ولتقديم نتائج البحث في مجال الرنا الدقيق في سرطان الثدي.

طرق البحث: تم اختيار قاعدة بيانات "ويب أوف ساينس" و "بوميد" لاسترجاع البيانات نظراً لتغطيتهما الواسعة، وتضمينهما للمجلات ذات التأثير العالي والوصول السهل إلى المنشورات ذات الجودة العالية. تم تحليل البيانات باستخدام "إنسايتس" من "ويب أوف ساينس"، و "بوميد" وبرنامج "في أو إس فيوير".

النتائج: تم تحديد أكثر المؤسسات ديناميكية، والمؤلفين والهيئات التمويلية النشطة وتم فحص النتائج عن البحث في مجال الرنا الدقيق. تم تحليل المعايير البيبليومتري بما في ذلك عدد المنشورات ومؤشر الاقتباس. كان هناك 3,831 منشور في مجال البحث. لوحظ ميلان حاد في بحوث سرطان الثدي. تم الإبلاغ عن أقصى عدد من المنشورات في عام 2021. قامت جامعة الملك سعود ومستشفى الملك فيصل التخصصي ومركز البحوث بتمويل معظم المشاريع وساهمت في أقصى عدد من المنشورات. لوحظ تقدم واضح في استكشاف الدور التشخيصي والتنبؤي للرنا الدقيق وإمكاناته العلاجية في سرطان الثدي.

الاستنتاجات: لقد جذب بحث سرطان الثدي الكثير من الاهتمام كما يتضح من الزيادة الملحوظة في المنشورات العلمية خلال العقدين الماضيين في المملكة العربية السعودية. توفر هذه المعايير البيبليومترية معلومات حاسمة حول مساهمة البحث من مختلف المؤسسات والمؤلفين. في مجال الرنا الدقيق، يلاحظ وجود استثمار بحثي معقول ولكن توجد فجوة كبيرة. لذا، توفر هذه الدراسة مرجعاً مفيداً لأطباء الأورام، والباحثين وصناع السياسات في التخطيط للبحث المستقبلي.

الكلمات المفتاحية: دراسة بيبليومترية؛ الرنا الدقيق؛ سرطان الثدي؛ الإنتاج العلمي

Abstract

Objectives: Bibliometric analysis has emerged as a valuable method for identifying emerging areas in a given research field. Breast carcinoma has maintained a stable rank as the most common cancer affecting women worldwide. This study performed bibliometric profiling to shed light on breast cancer research conducted in KSA over the past two decades and to present the research output in the field of microRNAs (miRNA) in breast cancer in KSA.

Methods: The Web of Science (WoS) and PubMed databases were selected for data retrieval, because of their high coverage, inclusion of high impact journals and easy access to high quality publications. Data retrieval was performed on January 31, 2022. Data were analyzed with Incites from WoS, PubMed and VOSviewer software version 16.1.8.

Results: The most dynamic institutions, authors and active funding bodies were identified, and output on research in the field of miRNA was assessed. Bibliometric parameters including the number of publications and

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citation index were analyzed. A total of 3831 publications in the field were identified. A steep increase was observed in breast cancer research. The maximum number of publications was observed in 2021. King Saud University and King Faisal Specialist Hospital & Research Centre funded most of the projects and contributed the most publications. Visible progress was seen in research exploring the diagnostic and prognostic roles of mRNAs and their therapeutic potential in breast cancer.

Conclusion: Breast cancer research has attracted substantial attention, as reflected by a notable increase in scientific publications over the past two decades in KSA. The bibliometric parameters revealed crucial information regarding research contributions from various institutions and authors. In the field of miRNAs, notable research investment was observed, but a significant lacuna exists. This study provides a reference that may aid oncologists, researchers and policymakers in planning future research.

Keywords: Bibliometric study; Breast cancer; MicroRNA; Scientific output

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Introduction

Breast cancer continues to be an unrelenting cancer among women worldwide, including in KSA. A recent report from the World Health Organization (WHO) has confirmed that breast cancer has surpassed all malignancies and become the most common cancer worldwide. Approximately 2.3 million new cases of breast cancer and 685,000 breast cancer deaths worldwide were reported in 2020.¹ This disquieting situation is evidenced by not only rising incidence and mortality, but also a major shift in research focus in terms of the number of publications.

Breast cancer has surpassed lung cancer as the most frequently diagnosed malignancy, and an estimated 2,261,419 new cases have been registered worldwide.²

According to IARC Globocan 2020 reports, the incidence of breast cancer in KSA has reached 3954 (14.2%). Breast cancer remains the most frequently diagnosed malignancy in KSA³ and has an age standardized risk of 27.3 per 100,000 in incidence and 7.5 per 100,000 in mortality.⁴ A worrying rising trend has been observed over the past decade.^{5,6} A similar trend has been reported by Beshan et al., who have observed an increase in age standardized risk from 15.4/100,000 in 2004 to 27.2/100,000 in 2016 in KSA, according to data extracted from the Saudi Cancer Registry between 2004 and 2016. An increase in the aging population, prevalence of obesity, consumption of unhealthful and highly caloric diets, lack of exercise, smoking and genetic predisposition are major contributors to the observed increase in breast cancer incidence. The authors also conducted a regional analysis of breast cancer prevalence and found that 75% of the breast cancer burden in KSA was found in Riyadh, Makkah and the central region.⁷

Outcomes of available treatment protocols remain unsatisfactory, because breast cancer has the highest mortality rate, at 8.5% (cumulative risk 0.81%), among all cancers in KSA.³ The American Cancer Society has indicated that the 5-year survival rate for non-metastatic invasive cancer is 90%; the survival rate decreases to 86% for cancers with nodal involvement and steeply decreases to 28% with distant metastasis.⁸ Otaibi et al. have explored prognostic factors for breast cancer in KSA, and have associated advanced grade with fivefold greater mortality. Moreover, men with breast cancer are at a much higher risk than women of dying of breast cancer. Moreover, divorced women are at higher risk than married women.⁹ According to the WHO, a major geographical difference is observed in survival rate, wherein survival rates are above 90% in high income countries, 66% in India and 40% in South Africa. Such geographical discrepancies have been attributed to early detection and advanced treatment options in developed countries.¹⁰ Moreover, between 1980 and 2020, a 40% decline in mortality occurred in high income countries, thus decreasing the yearly mortality by 2–4%. This decline in mortality has been predicted to prevent 2.5 million deaths between 2020 and 2040,¹ representing a substantial achievement in high income countries. To bring about similar global change, every country must play its part, starting with focused and directed research.

Detailed, complex involvement of multiple genes, transcription factors, the proteome, the metabolome and microRNAs (miRNAs) has been uncovered in many recent studies. Accumulating evidence indicates that molecular alterations are important contributor to carcinogenesis.¹¹ High throughput metabolomic, proteomic¹² and miRNA¹³ analyses, and their roles in predicting survival and developing treatment guidelines, prompted our quest to explore bibliometric data in this specific field.

The discovery of miRNAs has revolutionized understanding of gene regulatory networks. miRNAs are important players in carcinogenesis, because of the proximity of their genes to chromosomal break points. These RNAs have been shown to regulate important biological pathways in cell proliferation and apoptosis. MicroRNA research has become a major research focus in the past two decades, and the therapeutic potential of miRNAs is a key reason for this research expansion.^{14,15}

Bibliometric analysis is an excellent tool to reveal the visual landscape of research trends in a given field. This method organizes existing data and depicts changing trends. Research output is an important parameter for measuring institutional extraordinariness. Bibliometric analysis provides quantitative research output and identifies leading researchers. It further enables documentation of actively contributing countries. By mapping the structure and dynamics according to existing data, this method identifies current research gaps and directions future research.^{16–18} Major research investments in KSA have been reflected by increases in publications and citations.

This study was aimed at profiling breast cancer research in KSA, to identify hotspot areas, explore research creativity in the field of miRNA, identify gaps in research and guide researchers to focus on novel research ideas in this era of precision medicine.

Materials and Methods

The search was performed on January 31, 2022, after Institutional Review Board approval was obtained from King Abdullah International Medical Research Center (KAIMRC) NRC22R/158/03. The most comprehensive and databases, Web of Science and PubMed, were searched with the keywords of “breast cancer,” breast carcinoma,” “breast tumor” and “KSA.” After analysis of the results for breast cancer, we limited our search to “breast cancer,” “microRNA” and “KSA.” Keywords were combined with Boolean search operators (AND, OR) to maximize the relevant results.

Strict inclusion and exclusion criteria were decided upon. We limited the search to original articles, review articles, meeting abstracts, clinical trials, case reports and books published between January 1, 2001, and December 31, 2021. Only peer reviewed content was selected. Editorial content

and letters were not considered. Articles published in languages other than English were also excluded. Data files were transferred to MS Excel format for further analysis. Information on contributions from different universities was also retrieved, and statistical analysis of the top authors and most dynamic institutions was performed. Data were also collected on funding bodies. Articles published on breast cancer and miRNA in KSA were retrieved to identify authors, author affiliations, research focus and research impact.

VOSviewer version 16.1.8 software was used to generate clusters of the most productive authors and dynamic institutions.¹⁹

Results

After a search for content on breast cancer, a total of 723,408 articles were retrieved. After application of the

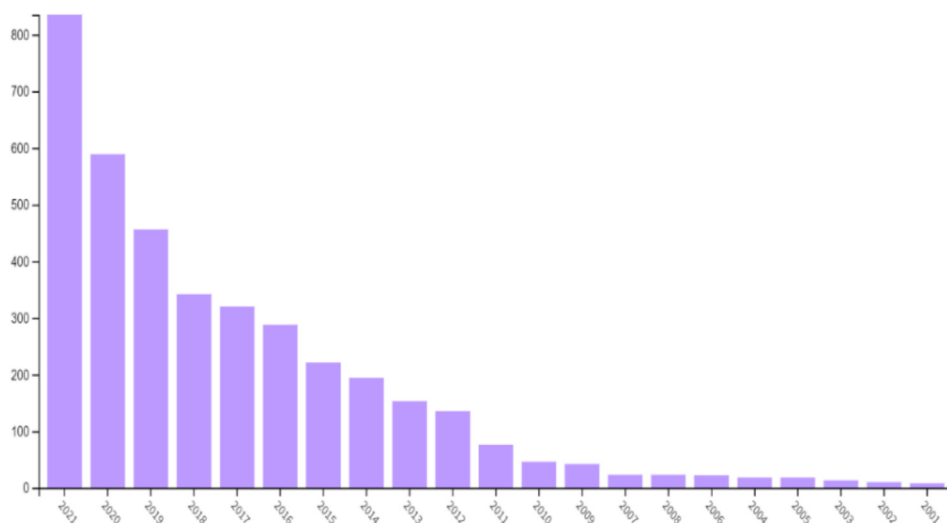


Figure 1: Yearly publication output of breast cancer research from KSA between 2001 and 2021.

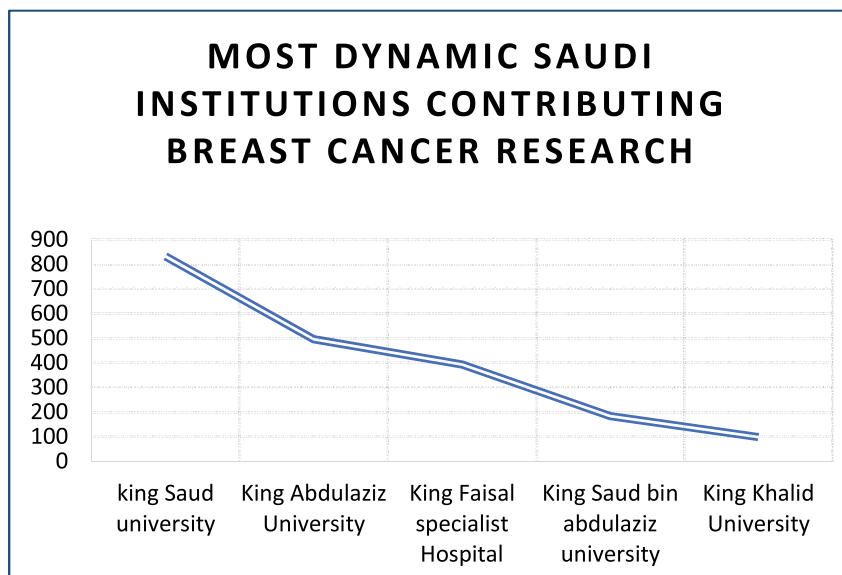


Figure 2: Breast cancer research productivity of Saudi universities.

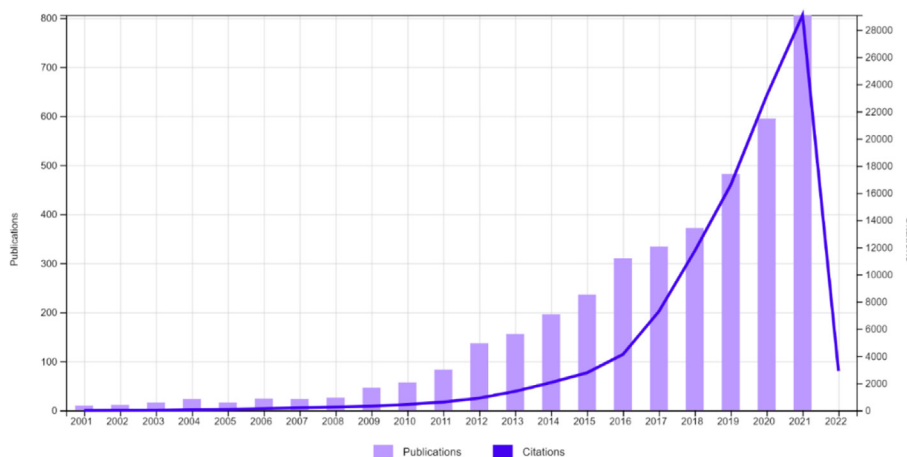


Figure 3: Citation distribution of articles on breast cancer contributed by KSA.

inclusion criteria, the number of retrieved documents decreased to 349,812. Y. Wang was the leading researcher, with a total of 3410 publications, and Y. Zhang was the second leading researcher, with 3218 publications. Most articles were published in PLoS One (7607), which was followed by the journal Breast Cancer Research and Treatment. The United States Department of Health funded 74,398 projects, the National Institutes of Health in the USA funded 73,647, and the People’s Republic of China funded 50,811 projects. Other major research funding was contributed by England (22,013), Germany (20,346) and Italy (19,069).

After analysis of the global status of breast cancer research, we focused on our main objective of visualizing the status of KSA. A total of 3831 publications were retrieved in our search on breast cancer and KSA. A steep increase in the number of publications occurred over the past two decades (Figure 1). In

2001, only eight research articles were published, whereas this number increased to 835 in 2021. Publications appeared in different journals. The most articles (111) were published in Molecules, followed by Molecular Based Switzerland (108), and the Saudi Medical Journal (76). The most dynamic Saudi institutes performing breast cancer research are shown in Figure 2. The top funding sources from KSA were King Saud University (KSU), which approved 462 research grants; King Abdulaziz City for Science and Technology and Princess Norah Binte Abdulrahman University, which funded 47 projects each; Taif University, which funded 33 projects; and King Abdullah University of Science and Technology, which funded 24 projects. Figure 3 shows the citation report of articles from KSA. A sharp increase in citation index occurred after 2016 and peaked in 2021. The hotspot research areas were oncology, pharmacology,

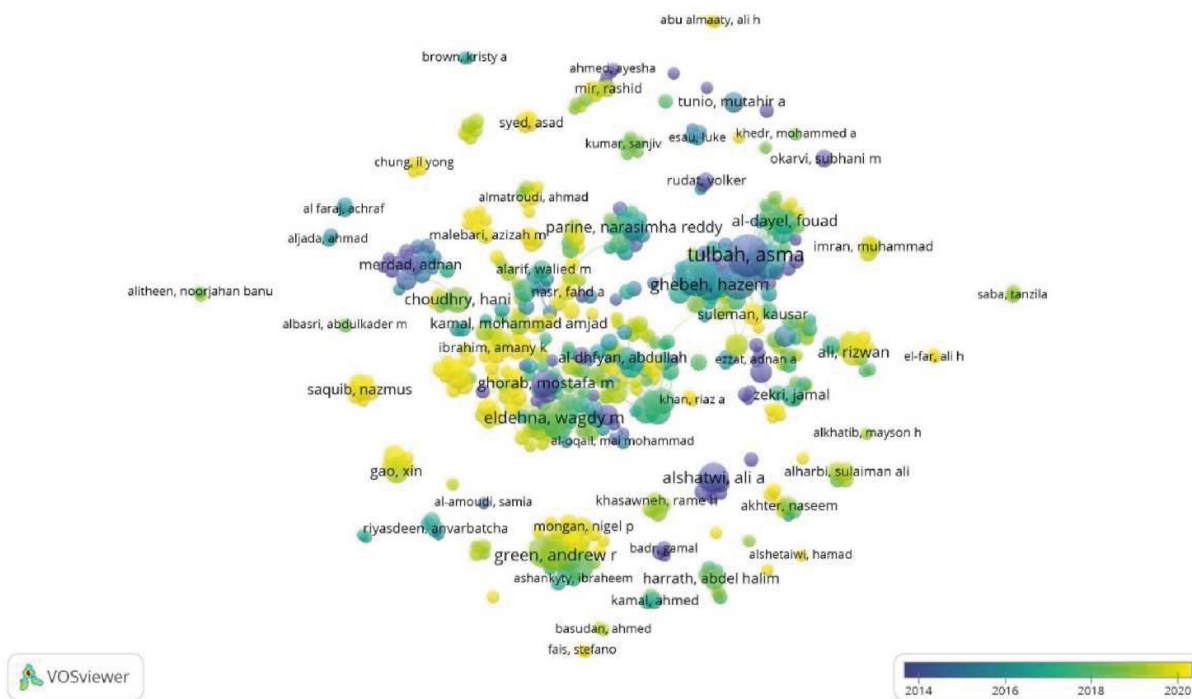


Figure 4: Leading researchers in the field of breast cancer in KSA.

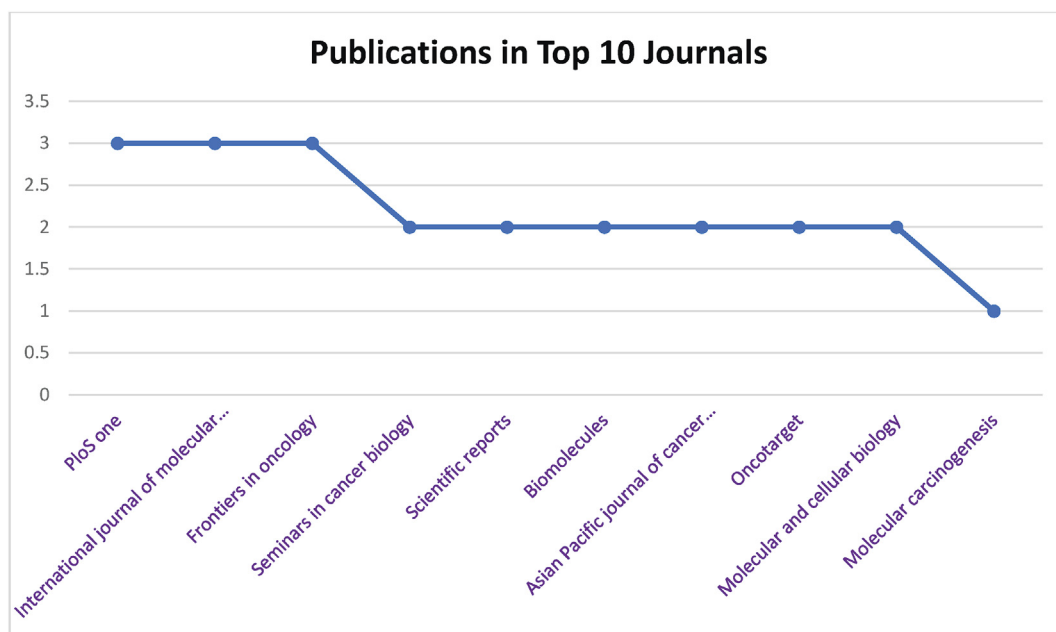


Figure 5: Top ten journals publishing miRNA research conducted in KSA.

biochemistry, cell biology and chemistry. Asma Tulbah, Abdelilah Aboussekhra, Andrew Green, Tahir al Tuwejari and Emad Rakha were the leading researchers, who contributed the most publications. Interestingly, among these distinguished authors and researchers, Asma Tulbah, Abdelilah Aboussekhra and Tahir al Tuwejari were affiliated with King Faisal Specialist Hospital & Research Centre (KFSH&RC), Riyadh (Figure 4). A positive and encouraging feature of research in KSA is collaboration with both local institutions as well as international research collaboration. Our data search indicated local collaboration on various projects among KSU, KFSH&RC and KAIMRC, associated with King Saud Bin Abdulaziz University for Health Sciences, National Guards Health Affairs, Riyadh. In addition, many projects were

international collaborations among institutions in the USA, United Kingdom, Egypt, Korea and Qatar.

KSA has shown substantial research progress in the field of molecular biology. The trends in miRNA research were analyzed. The first article on miRNA was published in 2012, by Shatawi et al.²⁰ A total of 36 publications were retrieved for miRNA research in breast cancer in KSA. The major focus was on diagnostic and prognostic roles of miRNAs. Only ten publications targeted therapeutic implications of miRNAs. PLoS One, International Journal of Molecular Sciences and Frontiers in Oncology had highest number of publications (Figure 5).

Shatawi et al. performed miRNA expression profiling and demonstrated the applicability of circulating miRNAs as diagnostic and prognostic biomarkers. This publication

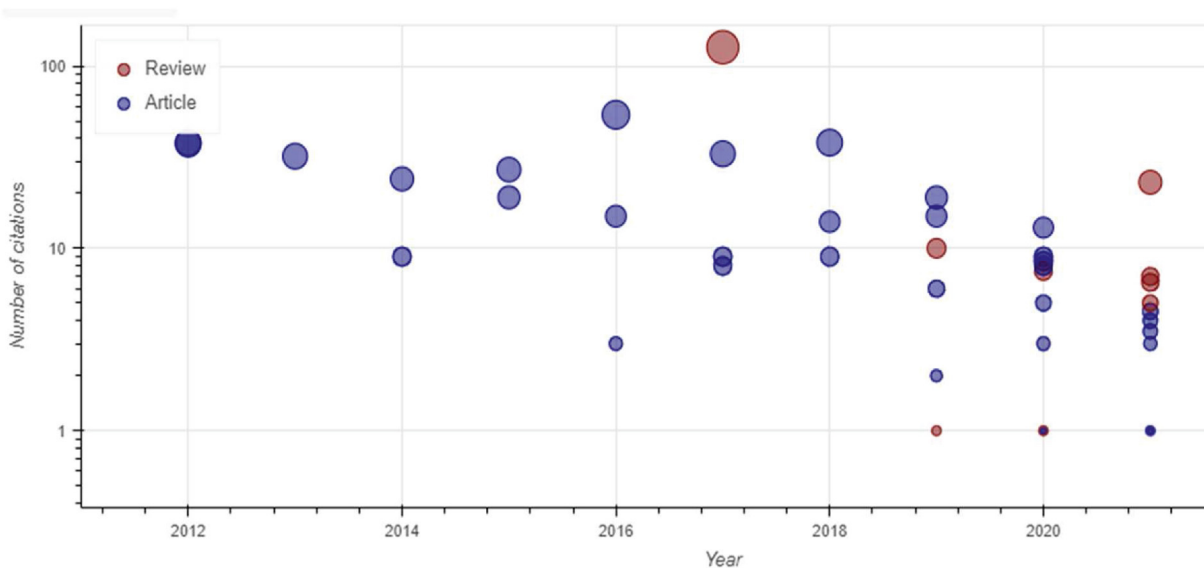


Figure 6: Citation of research articles on microRNA in breast cancer contributed from KSA (2012–2021; extracted from PubMed).

appeared in PLoS One and received the highest number of citations. Figure 6 displays the citation numbers for articles on miRNA and breast cancer from KSA between 2012 and 2021. Mir et al. identified a link between miRNA 423 alleles and metastatic disease in 2012.²¹ Hamam et al. performed global miRNA expression analysis in 2016 and identified panels of miRNAs enabling early detection.²² Elango et al., in 2020, reported a comprehensive analysis of lymph node associated miRNAs, and revealed the roles of miR-205 and miR-214 in suppressing nodal metastasis.²³

“Circulating microRNAs in breast cancer: novel diagnostic and prognostic biomarkers,” by Hamam et al., received attention among readers and achieved a high number of citations.²² Another article receiving attention was published by Elango et al. in 2018, in *Frontiers in Oncology*.²³ The comprehensive miRNA analysis was performed on breast tissue specimens from King Khalid University Hospital and provided new insights into the potential roles of miRNAs in lymph node metastasis, and their potential to serve as novel therapeutic agents. KFSH&RC and KSU were leaders in miRNA research. Abdelilah Aboussekra and Amal Qattan from KFSH&RC were actively involved in miRNA research.

Discussion

An increase in published scientific data directly indicates research coming to fruition. This article highlighted a steep rise in research conducted in the field of breast cancer in KSA. Whereas published data were scarce until the mid-1990s, the scientific output began to increase thereafter, thus clearly indicating growing research interest. KSA is the second leading Arab country after Egypt contributing to breast cancer research.²⁴ Egypt and KSA accounted for 58.2% of the cancer literature published by researchers in Arab countries but only 1.52% of the global publications in the field of oncology.

Steady research growth in this field has occurred since 2005, and a sharp increase occurred after 2015, when 75.69% of the total Arab cancer-associated content was published.²⁵ Governmental support and university research funding are key factors underlying the research growth in these countries. In comparison, other Arab countries have lagged in research, possibly because of a lack of infrastructure, coordination among institutes and inadequate funding. Research and development are critical in KSA Vision 2030, which aims to greatly increase research to improve ratings on the Global Competitiveness Index. To this end, the Ministry of Education is coordinating with universities, stakeholders and partners in research and development to plan several promising initiatives. It also aims to coordinate communication channels between universities and their affiliated institutions to achieve the intended goals.²⁶

In this study, we analyzed productivity in breast cancer research over the period of 2001–2021. Few articles were identified before 2005. Thereafter, slow but gradual progress in research productivity was observed, and a steep rise occurred after 2016. The maximum publications were observed in 2021, followed by 2020, thus suggesting increased research interest and output from the Kingdom. The observed increase in research is likely to be associated with the increasing burden of breast cancer, which in turn is

associated with adoption of a Western lifestyle. Owing to the consumption of highly caloric diets and lack of exercise, a substantial percentage of Saudi women are overweight (28%) or obese (35%).²⁷

Although a national screening program for breast cancer was established in KSA in 2007, studies have revealed markedly lower screening rates than those in Western countries. This finding emphasizes the need for community awareness campaigns to educate people about the roles of screening in early detection and improved survival.^{27–29}

KSU and KFSH&RC played a major role in breast cancer research and funded most of the projects. Affiliations with tertiary care teaching hospitals; well-resourced, technologically advanced oncology units; and innovative research culture and allocation of funds were likely contributors to the increased research productivity. We observed that most of the research came from universities in Riyadh, the capital of KSA. This finding was expected, given that most Saudi universities are in Riyadh; however, it also indicates the need to improve research output from other cities and universities to achieve more generalizable results. A lack of funding might have impeded the establishment of robust research infrastructures outside Riyadh. Another possible reason might have been that most institutions are patient centered and prioritize clinical management over research. Therefore, research policies in institutions throughout KSA should be revisited. Greater research output from other cities and universities would provide more precise and credible data revealing local pathological dynamics.

A citation burst reflects a sharp increase in the frequency of citation and hence indicates research productivity and quality.³⁰ As shown in Figure 2, the citation number increased after 2016, and a burst was observed from 2019 to 2021, thus again indicating higher research quality and magnitude.

Publications appeared in both international and national journals. The highest number of publications was in the journal *Molecules*. Among local journals, the *Saudi Medical Journal* had the highest number of publications. This reputable indexed journal receives 49% international manuscripts and maintains strict standards, as evidenced by a rejection rate of 35%. A devoted editorial team, enthusiastic reviewers and submission of quality research were associated with the improvement in the citation index and impact factor of the *Saudi Medical Journal* from 0.172 in 1999 to 1.055 in 2017. Acceptance of research by the *Saudi Medical Journal* is indicative of research quality.^{31,32}

The diversity of research was apparent in subject dispersion analysis. Studies are increasingly investigating the molecular aspects of breast cancer and exploring their roles in cancer screening, and the potential ability to forecast survival and introduce personalized treatment. Research is increasingly highlighting the roles of genetic mutations and epigenetic alterations in breast cancer.

Identification of miRNAs has led research along inventive pathways. The roles of miRNAs in carcinogenesis have been studied since their discovery. Accumulating evidence confirms the roles of miRNAs in facilitating tumor progression and their potential as therapeutic targets.^{33–35}

The first study on miRNA was performed in 2012 by Shatawi et al., thus suggesting that molecular research has not been static in KSA. A total of 36 articles examining the roles

of miRNAs in breast cancer in KSA were identified. After the first publication in 2012, the maximum number of publications was observed in 2019 and 2021.²⁰ Likewise, bibliometric analysis of the miRNA research by Shaw et al. showed a six-fold increase in miRNA research between 2012 and 2019.³⁶ The trends in miRNA research in KSA are somewhat in line with those reported globally, and research productivity has increased in recent years. However, the quantity of research in the field of miRNA is very deficient with respect to that in leading countries, such as China and the USA. These findings should provide valuable information for health policy decision-makers, funding bodies, research directors and oncologists in identifying research targets.

The USA and China are the two main contributors of miRNA research, and are followed by Germany, Italy, Japan and England.³⁷ Thus, although miRNA research has expanded, substantial room exists for more promising research projects. Some research might have been published in non-indexed journals; hence, we emphasize that our findings may underestimate the actual research activity. Moreover, contributions from Saudi researchers practicing outside KSA who do not hold Saudi institutional affiliations were likely to have been overlooked.

Innovative research focusing on the roles of miRNAs in personalized treatment are likely to increase the citation index as well as introduce researchers to a plethora of molecular alterations involved in breast carcinogenesis.

Strength and limitations

The study provides an overview of the published literature in the field of breast cancer in KSA, including information on authors, institutions, publication years, citation index values and the research status for miRNA in breast cancer. The findings indicated a lack of data on the therapeutic potential of miRNAs and emphasizes future research direction. Because the data were retrieved from only Web of Science and PubMed, the richest repositories, there is a slight chance of alteration in the metrics shared if other repositories were included in the data gathering.

Conclusion

This study describes an expansion in breast cancer research in KSA over the past two decades. We highlighted the dynamic institutions, authors and areas of study. Moreover, we revealed the current status of miRNA research. Our findings may prompt researchers, oncologists and policymakers to use these metrics to plan research to enrich screening, personalized treatment and preventive strategies for breast cancer in KSA.

Source of funding

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Conflict of interest

The authors have no conflict of interest to declare.

Ethical approval

This study was approved by the Institutional Review Board of King Abdullah International Medical Research Center, approval No. NRC22R/158/03.

Authors' contributions

RA and NM conceived and designed the study; analyzed the data; and were involved in manuscript writing, reviewing and editing of the draft. ZA and SA collected the data, and conducted the biostatistical analysis and interpretation of the results. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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