Original Article

The epidemiological and clinicopathological features of breast cancer in Riyadh, Saudi Arabia

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ABSTRACT

الأهداف: سرطان الثدي هو أكثر أنواع السرطان شيوعا بين النساء في جميع أنحاء العالم. تهدف هذه الدراسة إلى دراسة السمات الوبائية والسريرية والمرضية الأساسية للمرض في المملكة العربية السعودية وذلك بهدف تعزيز القرارات المتعلقة بتخصيص الموارد ومكافحة المرض ومعالجته

المنهجية: قمنا بدراسة سجلات جميع المرضى الذين تم تشخيصهم بسرطان الثدي المثبت تشريحيا في مدينة الملك فهد الطبية بين عامي 2019، 2020. تم تحليل البيانات كميا والتعبير عن النتائج باستخدام المتوسط، التكرار، والنسب المئوية.

النتائج: تضمنت الدراسة 419 مريضاً. كان متوسط العمر للمرضى 50.13 (± 10.96) سنة. كان غالبية المرضى يعانون من السمنة (56.6٪)، وكان لربعهم تقريبًا تاريخ في استخدام حبوب منع الحمل، أو خزعة الثدي، أو إصابة أحد أفراد الأسرة بالمرض. جاءت معظم الحالات من المنطقة الوسطى (80.1٪)، تليها المحافظات الجنوبية (12.7٪). كان الشعور بكتلة في الثدي هي الشكوى الأكثر شيوعًا (89٪) في حين أن ارتفاع ضغط الدم والسكري كانت أكثر الأمراض المصاحبة شيوعًا (28.5٪ و24.2٪ على التوالي). من الناحية النسيجية، كان سرطان الأقنية الغازية هو النوع الأكثر شيوعًا (89.7٪). كان تصنيف غالبية المرضى في المرحلة الثانية والثالثة للمرض (30.9٪ و24.3٪ على التوالي) بينما كان 27.7٪ مصابين بانتشار بعيد للمرض. شملت الطرائق العلاجية استئصال الثدي الجذري المعدل (63.8٪)، والعلاج الكيميائي المساعد الجديد (60.4٪)، والعلاج الإشعاع المساعد (82.9٪).

الخلاصة: في المملكة العربية السعودية، قد يكون هناك نمط لانتقال حالات الإصابة بمرض سرطان الثدي نحو المرضى الأكبر سناً. ومع ذلك، فإن التنبؤ بالمرض المتقدم والعدواني يتطلب تعزيز برامج الفحص المبكر وبروتوكولات موحدة لمكافحة المرض ومعالجته. الكلمات المفتاحية: سرطان الثدي، المرضية الإكلينيكية، علم الأوبئة، الرياض، المملكة العربية السعودية

Objectives: To investigate the epidemiological and clinicopathological features of breast cancer (BC) in Saudi Arabia to improve decisions regarding resource allocation, disease control, and management.

Methods: We retrieved the records of all patients who presented with histologically proven BC at King Fahad Medical City between 2019 and 2020. The data were analyzed quantitatively, and the results were expressed as percentages and frequencies.

Results: This study comprised 419 patients. The mean age was 50.13 (± 10.96) years. The majority of the patients were obese (56.6%), and approximately a quarter had a history of oral contraceptive pill use, breast biopsy, or an affected family member. Most cases were from the central region (80.1%), followed by the southern provinces (12.7%). Breast lumps were the most common complaint (89%), whereas hypertension and diabetes mellitus were the most common comorbidities. Invasive ductal carcinoma was the most common pathologic type (89.7%). Most patients presented with TNM stages II and III (55.2%), and 27.7% had metastasis. The main therapeutic modalities included radical mastectomy (63.8%), neoadjuvant chemotherapy (60.4%), and adjuvant radiotherapy (82.9%).

Conclusion: In Saudi Arabia, a trend of BC incidence migration towards older patients may be ensuing. However, prediction of an advanced and aggressive presentation requires the enhancement of screening programs and standardized protocols for disease management.

Keywords: Breast cancer, epidemiology, clinico-pathologic, Riyadh, Saudi Arabia

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Breast cancer (BC) is the most prevalent cancer in women, ranking second among the most commonly diagnosed cancers worldwide.[1] The World Health Organization (WHO) has rated this disease as one of the most serious global health problems.[2] The escalating burden of the disease has essential implications for preventive and therapeutic policies and healthcare expenditure, particularly in developing countries and under-resourced settings.[3] In Saudi Arabia, the incidence of BC is alarmingly increasing, and the disease is currently the most diagnosed cancer in Saudi Arabia.[4] According to the National Cancer Registry (SCR) data, the age-standardized incidence (ASR) of BC has almost tripled over the last few decades in the country.[5] Moreover, such statistical indicators are expected to rise further in the foreseeable future in proportion to observable social and environmental changes within Saudi society.[6,7] Therefore, BC should be a frontline concern on the agenda of health authorities in Saudi Arabia so that legitimate disease control strategies that resonate with demographic and clinical ramifications can be established.[8]

Breast cancer in Saudi Arabia is characterized with certain risk patterns and epidemiological features. An example is the presumed different biological behavior of tumors in their aggressiveness and tendency to affect younger women compared to elderly ones in Western communities.[9] The evolution and magnitude of the risk factors, types of inheritance, and BC gene mutations in the pathogenesis of the disease provide additional perspectives.[2,10] Despite the breadth of BC research in Saudi Arabia, a paucity of data regarding the epidemiological, etiological, and pathological profiles of the disease were reported.[1,5,10] Besides, continuous epidemiological surveys are recommended to elucidate BC distinctive features, and buttress efforts to monitor the disease and ameliorate its social and economic consequences.[11,12] The aim of this study is to investigate the patterns of age at diagnosis, interplay of risk factors in the etiology of the disease, and its primary clinical and pathological characteristics. A comparison of such data with existing information in Saudi Arabia and reports from regional and international countries would provide insightful information on the current disease status and its evolution.

Methods. This retrospective, descriptive study involved patients who were diagnosed with BC at King Fahad Medical City (KFMC), a tertiary care center at Riyadh, a hub city in the central region, and the largest in Saudi Arabia. Data were retrieved from the records of all patients diagnosed with BC at KFMC in the period between September 2019 and December 2020. The main inclusion criteria were BC patients confirmed by histopathology, who visited the center during the study interval. Cases in which BC is not confirmed by histopathology were excluded. We adopted the WHO classification of overweight and obesity using body mass index (BMI) to define and categorize patients with BC in relation to obesity.[13] Ethical approval to conduct this research was issued by the Institutional Review Board (IRB) of KFMC (21-291E). A questionnaire containing variables designed to fulfill the study objectives was developed following a review of the literature. The questionnaire subsumed items, including the demographic criteria of the patients, risk factors, clinical and pathological features, treatment applied, and mortality due to BC at the time of this report (**Appendix**).

Statistical analysis. Data were analyzed using the STATA software (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC). Descriptive statistics were applied, and the results were presented as means, frequencies, and percentages.

Results. The records of 419 patients were analyzed. Regarding demography, 417 (99.5%) patients were females and 2 were men. The study population comprised of 336 (80.4%) Saudi nationals, and 82 (19.6%) foreigners. The mean age at diagnosis was 50.13 ± 10.96, the age range was (25-87) years, and the patients at or below the age of 50 years were 226, representing 53.9%. Regarding marital status, 370 (88.5%) of participants were married, 23 (5.5%) were single, 13 (3.1%) were divorced, and 12 (2.9%) were widows. Regarding menopausal status, 230 women were premenopausal (57.1%), and 171 (42.4%) were postmenopausal. The majority of patients (335, 80.1%) were from the central region, followed by the southern (53, 12.7%), northern (12, 2.9%), eastern (10, 2.4%), and western regions (8, 1.91%). Table 1 shows the risk factors for BC in the study population. The majority of the patients were obese (56.6%), and approximately a quarter had a history of oral contraceptive pill use, breast biopsy, or an affected family member.

Breast lumps were the primary presenting complaint of BC among the study population of 373 (89%)

Table 1 - Risk factors of breast cancer in the study population (N=419).

Variable	n (%)
Parity (n=210) (missing=209)	
Parous/multiparous	182 (86.7)
Nulliparous	28 (13.3)
Breastfeeding (n=147) (missing=272)	
Breastfed	111 (75.5)
No breastfeeding	36 (24.5)
Menarche (n=63) (missing=356)	
Age in years	12.95 (9-16)
Family history (n=256) (missing=163)	
First degree consanguinity	58 (22.7)
Second degree consanguinity	9 (3.5)
None	189 (73.8)
Body mass index (n=389) (missing=30)	
Underweight	9 (2.3)
Normal	49 (12.6)
Pre-obesity	111 (28.5)
Class-I obesity	119 (30.6)
Class-II obesity	67 (17.2)
Class-III obesity	34 (8.7)
Oral contraceptive pills (OCP)(n=120) (missing=299)	
Used OCP	31 (25.8)
No use of OCP	89 (74.2)
History of breast biopsy (n=392) (missing=27)	
Yes	103 (26.3)
No	289 (73.7)

Table 2 - Comorbidities, complications and the site of metastasis (N=419).

Variable	n (%)
Comorbidities (n=414) (missing=5)	
Hypertension	118 (28.5)
Diabetes mellitus	100 (24.2)
Thyroid disease	77 (18.6)
Musculoskeletal disease	41 (9.9)
Dyslipidemia	30 (7.3)
Bronchial asthma	26 (6.3)
Gynecological disease	24 (5.8)
Cardiovascular disease	22 (5.3)
Renal disease	9 (2.2)
Hepatitis	5 (1.2)
Complications (n=417) (missing=2)	
Progression to advanced stage	33 (7.9)
DVT/PE	8 (1.9)
Arm lymphedema	5 (1.2)
Recurrence (local)	4 (1.0)
Pathological fracture	3 (0.7)
Progression to invasive cancer	3 (0.7)
Obstructive jaundice	1 (0.2)
Spinal cord compression	1 (0.2)
Sepsis	1 (0.2)
None	358 (85.6)
Site of metastases (n=403) (missing-16)	
Lungs/pleurae (n=398)	57 (14.3)
Bone (n=397)	67 (16.9)
Liver (n=397)	50 (12.6)
Brain (n=397)	27 (6.8)
Mediastinal lymph nodes (n=396)	3 (0.8)
Supraclavicular lymph nodes (n=397)	1 (0.3)

patients, followed by skin changes in 74 (17.7%) patients, inflammatory changes in 15 (3.6%) patients, nipple discharge in nine patients (2.2%), Paget's disease in one (0.2%) patient, and mammographic lesions in 15 (3.6%) patients. Two hundred twelve (50.6%) patients had tumors in the right breast and 198 (47.3%) in the left breast, while the tumor was bilateral in 9 (2.2%) patients. Within the affected breast, the tumor was located in the upper-outer quadrant in 199 patients (54.1%), followed by the upper-inner quadrant in 41 (11.1%), central portion in 79 (21.5%) patients, lower-outer quadrant in 24 (6.5%), lower-inner quadrant in 22 (6%), axillary tail in 1 (0.3%), and occult in 2 (0.5%). Axillary lymph nodes were palpable in 249 (62.1%) patients, and BC diagnosis was established during pregnancy or the postpartum period in 11 (2.6%) patients. Synchronous (concomitant) cancers and tumors were encountered in 21 (5%) patients, whereas metachronous tumors were identified in 12 (2.9%) patients. Table 2 shows the remaining clinical manifestations including, comorbidities, complications, and the sites of metastasis. Table 3 shows the main pathological features of breast cancer. Invasive ductal carcinoma is the most common pathological type, with poor differentiation and a hormone-positive status. Table 4 details the therapeutic modalities administered

to patients with BC, which mainly involved modified radical mastectomy, neoadjuvant chemotherapy, and adjuvant radiation. Moreover, treatment for cure has been attempted in most patients. Table 5 shows the sites and types of metachronous and synchronous tumors encountered in association with BC, with thyroid cancer being the most common. Given the retrospective nature of this study, some of the patients' files were deficient in one or more of the questionnaire variables. However, we retained all available data for statistical analysis and highlighted missing information where relevant. Although this approach could jeopardize the statistical power of some variables, it augmented others when data were available.

Discussion. The aim of this study was to highlight the age patterns, risk factors, clinical and pathological features, and main therapeutic modalities used in patients with BC in a specialized healthcare center in Riyadh, Saudi Arabia. Our objective was to compare the results of this study to relevant published literature in Saudi Arabia, neighboring regions, and worldwide,

Table 3 - Pathological features of breast cancer (N=419).

Variable	n (%)
Type	
Ductal	376 (89.7)
Lobular	33 (7.9)
Adenocarcinoma	5 (1.2)
Angiosarcoma	3 (0.7)
Cystosarcoma Phyllodes	1 (0.2)
Mixed (ductal & lobular)	1 (0.2)
Subtype (n=13)	
Mucinous	4 (30.8)
Tubular	3 (23.1)
Medullary	3 (23.1)
Papillary	2 (15.4)
Cribriform	1 (7.7)
TNM stage (n=401) (missing=18)	
Stage I	66 (16.3)
Stage II	125 (30.9)
Stage III	98 (24.3)
Stage IV	112 (27.7)
Differentiation (n= 412) (missing=7)	
Poorly differentiated	190 (46)
Moderately differentiated	198 (47.9)
Well-differentiated	20 (4.8)
Undifferentiated	4 (1.0)
Receptor status (n=397) (missing=22)	
Hormone positive/her negative	226 (56.9)
Triple positive	66 (16.5)
Hormone negative/her positive	39 (9.7)
Triple negative	66 (16.5)
In-situ carcinoma (n=414) (missing=5)	
DCIS*	14 (3.4)
LCIS**	2 (0.5)
None/not known	398 (96.1)
*BRCA****	
BRCA positive	5 (1.2)
BRCA negative/not known	414 (98.8)
Heterogenous breast cancer (n=419)	
Yes	5 (1.2)
No	414 (98.8)

*Ductal carcinoma in-situ, **Lobular carcinoma in-situ, ***Breast cancer gene (BRCA)

Table 4 - Therapeutic intention and modalities for breast cancer (N=419).

Variable	n (%)
Intention (n=410) (missing=9)	
Curative	303 (73.9)
Palliative	107 (26.1)
Type of Surgery (n=398) (missing=21)	
Modified radical mastectomy	254 (63.8)
Breast-conserving surgery	79 (19.9)
None	65 (16.3)
Lymph node dissection (n=242) (missing=177)	
Axillary lymph node dissection	106 (43.8)
Sentinel lymph node biopsy	67 (27.7)
None	69 (28.5)
Neo-adjuvant chemotherapy (n=343) (missing=76)	
Yes	207 (60.4)
No	136 (39.7)
Chemotherapy (n=368) (missing=51)	
Adjuvant	299 (81.3)
Palliative	65 (17.7)
None	4 (1.1)
Radiotherapy (n=357) (missing=62)	
Adjuvant	296 (82.9)
Palliative	57 (16.0)
None	4 (1.1)
Hormonal therapy (n=274) (missing=145)	
Yes	192 (70.1)
No	82 (29.9)
Fate (n=415) (missing=4)	
Alive	388 (93.5)
Died	27 (6.5)

Table 5 - Site/type of synchronous/metachronous tumors (n=33).

Site/Type	n (%)
Thyroid	8 (1.9)
Breast	4 (1.0)
Hematological	3 (0.7)
Endometrial	3 (0.7)
Stomach	2 (0.5)
Hepatocellular carcinoma	1 (0.2)
Pituitary adenoma	1 (0.2)
Meningioma	1 (0.2)
Appendicular adenocarcinoma	1 (0.2)
Colorectal	1 (0.2)
Renal cell carcinoma	1 (0.2)
Duodenal/bowel	1 (0.2)
Lung	1 (0.2)
Pleomorphic adenoma	1 (0.2)
Parathyroid adenoma	1 (0.2)
Osteosarcoma	1 (0.2)
Ewing sarcoma	1 (0.2)
Ovarian cancer	1 (0.2)

to emphasize any epidemiological differences, and to set the stage for sound policies to control the disease in the study area. The primary findings of this study include a tendency of BC incidence migration towards older patients, and an ongoing style of advanced and aggressive presentation, which are discussed further in the below sections.

Age pattern and geographical distribution. The mean age in the study sample was 50.13 years, which is similar to that reported in other studies in Saudi Arabia and Middle Eastern countries.[6,14-19] By contrast, the mean age in this study was greater than that reported in other parts of Saudi Arabia.[9,20-22] Interestingly, an almost 10-year increase existed between the median age recorded in this study and that reported a few decades earlier in the country.[23,24] Previous studies in Saudi

Arabia have indicated the tendency of BC to affect young females, with a median age of approximately 40 years at diagnosis.[4,12,25] The increased incidence of BC among young Saudi females has been attributed to the predominance of the young population in Saudi society, although this notion has not been fully explained by other researchers.[10,14,23] Recently, several epidemiological studies reported that BC tends to affect older women.[5,7,11,18,26] For instance, a bimodal incidence pattern similar to that in Western countries was predicted in Saudi Arabia in the near future, with a second peak in late life.[24] However, the observed migration of incidence towards older women may simply reflect the aging of the population and the westernization of life.[3,7,11,14] As younger age and aggressive features are the hallmarks of disease attributes in Saudi Arabia, it remains unclear whether the migration of incidence towards older patients is accompanied by any corresponding changes in the clinical presentation of the disease or its pathological profile.[5] Nevertheless, the verification of such epidemiological observations requires correlation analysis in large-scale studies, which could be the basis for future research projects.

Geographically, the number of cases reported in the Southern and Northern regions exceeds those reported in the Eastern and Western parts of the country. These regional variations are contrary to findings reported in the literature, given the higher populations in the latter locations.[5,6,7,11] However, evidence indicates that some areas in the Southern and Northern regions are among the locations with the highest annual percent changes in disease incidence.[11,12] However, the reported regional differences in disease incidence in this study may simply reflect variations in accessibility to screening and specialized breast care services.[3,11]

Risk factors' evaluation. The predisposition to BC is related to the interplay between several mediators, including genetic, hormonal, social, and environmental factors. The Body Mass Index (BMI) in this study indicated that most patients (85.1%) were either obese or pre-obese. Obesity is a common health problem in Saudi Arabia, and may play an essential role in its pathogenesis.[11,27] The high BMI reported in this study is congruent with the findings of other studies and aligns with the outcomes of obesity surveys conducted in Saudi Arabia.[6,10,11,16,20] These results may reflect the remarkable changes in the dietary and lifestyle habits of the Saudi population. A family history of first- or second-degree consanguinity with breast or ovarian cancer was reported in 26.2% of the study population, similar to the rates reported in other studies in Saudi Arabia.[14,25,26] Close consanguinity marriage, and cultural and public awareness issues may be responsible factors.[2]

A history of previous breast biopsy or surgery was identified in 26.3% of the patients, which is much lower than the corresponding rate reported in another study (89%).[25] Benign breast disease is generally considered a contributing factor to the development of BC.[6,25]

Most patients in this study did not use oral contraceptive pills (OCP), and the reported results on the incidence of breast cancer associated with OCP are controversial.[25,26] However, the risk of BC corresponds to the duration of contraceptive use and increases with longer periods of drug ingestion.[15] Most patients in this study gave birth to children, but the data on breastfeeding were inconclusive, and the duration of breastfeeding was unknown. Although breastfeeding and parity have been postulated to play a protective role against BC, other studies in Saudi Arabia have not found significant correlations.[10,14,16,20,25-27] The average age at menarche in this study was 12.95 years, which corresponds to the findings of some studies in Saudi Arabia although it was much higher than that reported by others.[10,14,16,25,26] A delayed pattern of menstruation in young Saudi females has been hypothesized and may require further elaboration in future studies.[6] Nevertheless, the above-mentioned BC risk factors related to childbirth and gynecological history can be interpreted in view of the changing social roles of women currently observed in the Saudi community.[5,6,26]

Clinical and pathological features. Breast lumps were the most common presenting complaint of BC in this study, which aligns with the results of other studies in Saudi Arabia.[9,21] These findings critique the feasibility of breast screening programs and necessitate the enhancement of public awareness and accessibility to specialized breast care services.[10,22] Most patients in this study presented with advanced-stage disease, and more than one-quarter had distant metastases. Considering the significant proportion of high-grade tumors, triple-negative receptor status, human epidermal growth factor receptor overexpression, and axillary lymph node metastasis, the findings of this study reflect the trend in BC aggressiveness reported elsewhere in Saudi Arabia.[10,14,18,21-24,28-32] Arguably, the aggressive presentation of BC in Saudi Arabia may be related to the different biological behaviors of tumors.[9] However, this requires further analysis, and could be a target for future prospective studies. In terms of cancer therapy, the aggressive behavior of tumors was reflected in this study in a higher percentage of patients undergoing mastectomy, neoadjuvant chemotherapy, and radiation regimens, which is consistent with the findings of previous reports in Saudi Arabia.[9,10,14,23,33] Such findings may also warrant insightful and practical solutions for

timely diagnosis and standardized treatment.[3,34] The pattern of comorbidities in this study was consistent with those reported in other studies, with hypertension and diabetes mellitus being the most frequently reported comorbidities.[26,35] However, a noticeable association between benign and malignant thyroid diseases was observed, and requires further analysis, as these data could have significant implications for BC diagnosis and management.

Study limitations. Given its retrospective design, this study was limited by missing data in the patient records, which could have improved the study outcomes' credibility. We are also aware that the findings of this study reflect the BC situation in the study location and may not be generalizable to other settings. However, the availability of such results may set the stage for better decisions to ameliorate the consequences of BC and open the door for further research in this field.

In conclusion, BC is a major health problem in Saudi Arabia and is a leading cause of morbidity and mortality among women. The disease continues to affect young females; however, a pattern of preponderance towards older patients is probably emerging. The ongoing, advanced, and aggressive presentation of the disease may critique the feasibility of current breast screening programs and undermine the magnitude of public awareness, necessitating a comprehensive revision of the guidelines and strategies for disease control and optimal treatment. These findings highlight the health, social, and economic burdens of the disease and the ultimate need for standardized protocols for BC diagnosis and management.

In addition, the findings of this study revealed unexpected patterns in the geographical distribution of BC in Saudi Arabia that require further demographic research, in addition to reassessing the populations' accessibility to specialized breast care services.

References

1. Saggu S, Rehman H, Abbas ZK, Ansari AA. Recent incidence and descriptive epidemiological survey of breast cancer in Saudi Arabia. *Saudi Med J* 2015; 36: 1176-1180.

2. Mohammed EM. High number of familial breast cancer cases in the Arabian Gulf countries: investigating the reasons. *Breast Cancer (Auckl)* 2022; 2816:11782234221107121.

3. AlSaleh KA. Efficacy of breast cancer screening program in Kingdom of Saudi Arabia. *Saudi Med J* 2022; 43: 428-430.

4. Al-Khamis NK. Low awareness of breast cancer and considerable barriers to early presentation among Saudi women at a primary care setting. *J Cancer Educ* 2018; 33: 391-397.

5. Basudan AM. Breast Cancer Incidence Patterns in the Saudi female population: A 17-year retrospective analysis. *Medicina (Kaunas)* 2022; 58: 1617.

6. Almutlaq BA, Almuazzi RF, Almuhayfir AA, Alfouzan AM, Alshammari BT, AlAnzi HS, Ahmed HG. Breast cancer in Saudi Arabia and its possible risk factors. *J Cancer Policy* 2017; 12: 83-89.

7. Bazarbashi S, Al Eid H, Minguet J. Cancer incidence in Saudi Arabia: 2012 data from the Saudi Cancer Registry. *Asian Pac J Cancer Prev* 2017; 18: 2437-2444.

8. Althubiti MA, Nour Eldein MM. Trends in the incidence and mortality of cancer in Saudi Arabia. *Saudi Med J* 2018; 39: 1259-1262.

9. Akhtar SS, Nadrah HM. Assessment of the quality of breast cancer care: a single institutional study from Saudi Arabia. *Int J Qual Health Care* 2005; 17: 301-305.

10. Rudat V, Brune-Erbe I, Noureldin A, Bushnag Z, Almuraikhi N, Altuwaijri S. Epidemiology of breast cancer patients at a tertiary care center in the Eastern Province of Saudi Arabia. *Gulf J Oncolog* 2012: 45-49.

11. Albeshan SM, Alashban YI. Incidence trends of breast cancer in Saudi Arabia: A joinpoint regression analysis (2004–2016). *J.King Saud Univ Sci* 2021; 33; 101578.

12. Alghamdi IG, Hussain II, Alghamdi MS, El-Sheemy MA. The incidence rate of female breast cancer in Saudi Arabia: an observational descriptive epidemiological analysis of data from Saudi Cancer Registry 2001-2008. *Breast Cancer (Dove Med Press).* 2013; 17: 103-109.

13. Purnell JQ. Definitions, Classification, and Epidemiology of Obesity. [Updated 2023 May 4]. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. Endotext. South Dartmouth (MA): MDText.com, Inc.; 2000.

14. Alabdulkarim B, Hassanain M, Bokhari A, AlSaif A, Alkarji H. Age distribution and outcomes in patients undergoing breast cancer resection in Saudi Arabia. A single-institute study. *Saudi Med J* 2018; 39: 464-469.

15. Elkablawy MA, Albasri AM, Mohammed RA, Hussainy AS, Nouh MM, Alhujaily AS. Ki67 expression in breast cancer. Correlation with prognostic markers and clinicopathological parameters in Saudi patients. *Saudi Med J* 2016; 37: 137-141.

16. Karim SM, Baeshen W, Neamatullah SN, Bin B. Oral contraceptives, abortion and breast cancer risk: a case control study in Saudi Arabia. *Asian Pac J Cancer Prev* 2015; 16: 3957-3960.

17. Najjar H, Easson A. Age at diagnosis of breast cancer in Arab nations. *Int J Surg* 2010; 8: 448-452.

18. Ibrahim EM, Zeeneldin AA, Sadiq BB, Ezzat AA. The present and the future of breast cancer burden in the Kingdom of Saudi Arabia. *Med Oncol* 2008; 25: 387-393.

19. Nafissi N, Khayamzadeh M, Zeinali Z, Pazooki D, Hosseini M, & Akbari ME. Epidemiology and histopathology of breast cancer in Iran versus other Middle Eastern countries. *Middle East J Cancer* 2018; 9: 243-251.

20. Babiker S, Nasir O, Alotaibi SH, Marzogi A, Bogari M, Alghamdi T. Prospective breast cancer risk factors prediction in Saudi women. *Saudi J Biol Sci* 2020; 27: 1624-1631.

21. Al Nemer A. The pathological profile of Saudi females with palpable breast lumps: Knowledge that guides practice. *Saudi J Health Sci* 2017; 6: 92-95.

22. El Saghir NS, Khalil MK, Eid T, El Kinge AR, Charafeddine M, Geara F, Seoud M, Shamseddine AI. Trends in epidemiology and management of breast cancer in developing Arab countries: a literature and registry analysis. *Int J Surg* 2007;5: 225-233.

23. Ibrahim EM, al-Mulhim FA, al-Amri A, al-Muhanna FA, Ezzat AA, Stuart RK, Ajarim D. Breast cancer in the eastern province of Saudi Arabia. *Med Oncol 1998*; 15: 241-247.

24. al-Idrissi HY, Ibrahim EM, Kurashi NY, Sowayan SA. Breast cancer in a low-risk population. The influence of age and menstrual status on disease pattern and survival in Saudi Arabia. *Int J Cancer* 1992; 19; 52: 48-51.

25. Al-Qutub ST, Al-Raddadi RM, Bin Sadiq BM, Sait W, Al-Gahmi A, Al-Amoudi S. Potential breast cancer risk factors among Saudi women aged 19-50 years in Jeddah: a case-control study. *J Egypt Public Health Assoc* 2013; 88: 165-1670.

26. Alsolami FJ, Azzeh FS, Ghafouri KJ, Ghaith MM, Almaimani RA, Almasmoum HA, Abdulal RH, Abdulaal WH, Jazar AS, Tashtoush SH. Determinants of breast cancer in Saudi women from Makkah region: a case-control study (breast cancer risk factors among Saudi women). *BMC Public Health* 2019; 21; 19: 1554.

27. Al Diab A, Shoeb Q, Al Saleh KA, Al Qahtani FH, Aleem A, Alghamdi MA, Alsaif A, Bokhari AA, Qureshi VF, Qureshi MR. Review on Breast Cancer in the Kingdom of Saudi Arabia. *Middle East J Sci Res* 2013; 14: 532-543.

28. Zekri J, Saadeddin A, Alharbi H. Frequency and clinical characteristics of HER2 over-expressed breast cancer in Saudi Arabia: a retrospective study. *BMC Womens Health* 2021; 21: 10.

29. Abulkhair O, Moghraby JS, Badri M, Alkushi A. Clinicopathologic features and prognosis of triple-negative breast cancer in patients 40 years of age and younger in Saudi Arabia. *Hematol Oncol Stem Cell Ther* 2012; 5:101-106.

30. Satti MB. Oestrogen receptor/progesterone receptor and human epidermal growth factor receptor 2 status in breast cancer: a 9-year study at Princess Noorah Oncology Center, Saudi Arabia. *Histopathology* 2011; 59: 537-542.

31. Ezzat AA, Ibrahim EM, Raja MA, Al-Sobhi S, Rostom A, Stuart RK. Locally advanced breast cancer in Saudi Arabia: high frequency of stage III in a young population. *Med Oncol* 1999; 16: 95-103.

32. Albasri A, Hussainy AS, Sundkji I, Alhujaily A. Histopathological features of breast cancer in Al-Madinah region of Saudi Arabia. *Saudi Med J* 2014; 35: 1489-1493.

33. Al-Gaithy ZK, Yaghmoor BE, Koumu MI, Alshehri KA, Saqah AA, Alshehri HZ. Trends of mastectomy and breast-conserving surgery and related factors in female breast cancer patients treated at King Abdulaziz University Hospital, Jeddah, Saudi Arabia, 2009-2017: A retrospective cohort study. *Ann Med Surg (Lond)* 2019; 41: 47-52.

34. Abdelhadi MS. Breast cancer management delay - time for improvement: a reflection from the eastern province of Saudi Arabia. *J Family Community Med* 2008; 15: 117-122.

35. Arif JM, Al-Saif AM, Al-Karrawi MA, Al-Sagair OA. Causative relationship between diabetes mellitus and breast cancer in various regions of Saudi Arabia: an overview. *Asian Pac J Cancer Prev* 2011; 12: 589-592.