

animal protein, 2.12 (95% CI: 1.17–3.83) for polyunsaturated fat, 1.88 (95% CI: 1.03–3.44) for cholesterol, 2.69 (95% CI: 1.51–4.81) for total energy obtained from fat, and 2.16 (95% CI: 1.21–3.88) for triglycerides. It is worth noting that the association between triglycerides and the risk of breast cancer remained significantly positive irrespective of all other variables investigated (*Table 2*).

DISCUSSION

Breast cancer is the most common cancer among women in Saudi Arabia. The number of reported cases of breast cancer in Saudi Arabia in 1999–2000 was 1157 (out of a female population of 7 788 754) [8]. There is no available data showing the number of deaths that can be attributed to breast cancer in Saudi Arabia. The descriptive epidemiology of breast cancer has demonstrated a rapid increase in the incidence rates in developing countries [16,17]. Identification of the contributing factors for the increasing rate would contribute substantially to our understanding of the epidemiology of breast cancer [16]. Environmental factors rather than genetic factors have been considered as the reason for variation in breast cancer rates among countries [17].

Socioeconomic development is normally associated with increasing wealth, changing lifestyle, disease pattern and increasing life expectancy. This association of changes, known as epidemiologic transition, is seen in many parts of the world and is very well demonstrated in Saudi Arabia, which has experienced rapid socioeconomic changes during the last 3 decades. As food habits mimic changes in lifestyle, there has been a dramatic shift from traditional foods which are based on whole wheat flour, milk and dates towards an affluent diet which is rich in total calories, meat, fat and refined carbohydrates. This change in dietary habit may be related to the increase in the number of breast cancer cases in Saudi Arabia [6–8].

Dietary fat has been proposed as one of the etiologic factors for breast cancer [2,4,5]. However, the relationship between fat intake and the risk of breast cancer has been examined in a number of case-control and cohort studies. The findings reported in the literature are not conclusive enough to establish a pattern for the real cause of the disease [4,5].

Our data suggest that, among women living in Saudi Arabia, a diet that is high in fat predisposes to breast cancer development. In terms of nutrients, this high-risk dietary profile translates to a modest, positive association with total fat intake, saturated fat, and cholesterol. This is in contrast to an earlier study, which has cast doubt on a positive association between dietary fat and breast cancer [4]. However, our findings agree with those of Toniolo et al. [18] and Zaridze et al. [19] who showed a positive association between high dietary fat intake and breast cancer. Also high animal protein intake was significantly associated with breast cancer in our study, which supports the findings of De Stefani et al. [20] and Levi et al. [21] who showed a positive relationship between high dietary meat consumption and breast cancer. Boyd et al. in their quantitative summary of all papers published up to July 2003 on dietary fat and the risk of breast cancer found intake of saturated fat and meat consumption is associated with an increased risk of breast cancer [22].

High consumption of sugar-rich foods, meat and other animal products rich in saturated fats has been recorded in Saudi Arabia [Khan MA, unpublished report, 1996]. Despite the inconclusive evidence about diet and disease, it is important to educate the population about the possibility of a link between dietary habits and cancer and to encourage them to adopt a diet that is low in calories, saturated fat and meat intake.

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PATTERN OF CANCER IN SAUDI ARABS REFERRED TO KING FAISAL SPECIALIST HOSPITAL*

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A total of 7251 histologically confirmed new cases of cancer (4117 males and 3134 females) were seen in the 6-year period 1979 to 1984 at the King Faisal Specialist Hospital and Research Centre in Riyadh, Saudi Arabia. The crude relative frequencies of cancer at various primary sites have been determined with reference to sex, age, geographic origin, and year of diagnosis. The most common cancer sites among males were non-Hodgkin's lymphomas, esophagus, lung, liver, stomach, and nasopharynx. Breast cancer was the most common tumor among the females, followed by non-Hodgkin's lymphomas and cancers of the thyroid, esophagus, cervix, and ovary. The most marked deviations were found in the Southern Region for cancers of the oral cavity (2.4 times higher), bladder (1.8 times higher), and lung (4.3 times lower).

Known etiologic factors, such as local chewing, smoking habits, and schistosomiasis are likely to be responsible for these differences. Upward trends in cancers of lung, breast, colon and rectum, and the downward trend in esophageal cancer may reflect the rapid pace of modernization. Cuncer 58:1172-1178,1986. Saudi Arabia has been undergoing unprecedented economic development since the early 1970s. This is having a profound impact on air and water quality, diet and consumption patterns, lifestyle, and occupational conditions. These changes are likely to have altered the patterns of exposure to environmental cancer risk factors.

Simultaneously, the widespread availability of modern medical facilities and increasing public awareness of cancer has made possible the detection and reliable diagnosis of cancer in most regions of the country.

^[1] This provides a unique opportunity to study the trends in frequency of different types of cancer over time that may be expected to accompany rapid economic and social transformation.

* Cancer. 1986 Sep 1, 58(5):1172-8

Being a vast country of some 2,240,000 square kilometers with regions of varying climatic, topographic, and cultural backgrounds, the frequency of different types of cancers may vary significantly from one place to another.^[2]

This study investigates the geographic and temporal patterns of cancer occurrence in Saudi Arabs. Most previous studies^[2-6] have been limited with respect to the geographic area from which the patient population was drawn, time interval covered, or total number of cancer patients seen. The current study draws from 725 1 patients referred from all parts of the country over a 6-year period to King Faisal Specialist Hospital and Research Centre, which is situated in Riyadh, the central region of Saudi Arabia.

MATERIALS AND METHODS

The King Faisal Specialist Hospital and Research Centre, established in Riyadh in 1975, is a national referral hospital and the principal center for cancer therapy in Saudi Arabia. It has been operating a fully computerized cancer registry since April 1982. New patients first seen before this date were entered into the registry retrospectively from medical records. Operating on a PDP 11/70 computer (Digital Equipment Co., Maynard, MA), the cancer registry consists of detailed patient records that include personal background, diagnosis, treatment, and follow-up information.

During the period 1979 to 1984, the years for which complete computerized cancer registration

are currently available, 725 1 new patients with histologically confirmed neoplasms were admitted. There were 41 17 males and 3134 females. The vast majority were Saudi nationals coming from virtually every region of the country, though a somewhat disproportionate number arrived from the Central Region (*Table 1*). The mean age was 44.6 years.

Patients were generally accepted for treatment only after the diagnosis of cancer had been histologically proven. Pathological diagnoses made elsewhere were not considered final until the slides had been reviewed by our pathology staff. Neoplasms were classified by both anatomic site and morphology according to the coding schemes of the International Classification of Diseases (9th Revision).^[7] For the purpose of studying geographic variations in the crude relative frequency (CRF) of cancer, the country was divided into seven major geographic regions (*Table 1*). These divisions often correspond to administrative boundaries, but some, such as the line between Regions 2 and 3 are primarily topographic and are intended to provide more even distribution of population among the regions (*Figure 1*). Less than 0.5% of patients were referred from outside the country. Time trends were estimated by ity, and central nervous system (CNS). The commonest calculating CRF for individual years.

RESULTS

cancers among females were breast cancer, non-Hodghn's lymphomas, cancers of the thy-

Table 1: Different Regions of Saudi Arabia and Their Percentage of Case Referrals

Region	No.	Main cities & areas	% referred cases	Population (100,000)*
Central	1	Riyadh, Qasim, Kharj	36.6	17.13
Western	2	Jeddah	11.8	32.17
Western	3	Makkah, Medina, Taif	19.2	
Eastern	4	Dhahran, Dammam, Al-Khobar, Al-Ahsa, Qatif	11.7	8.59
Northern	5	Tabuk, Hail, Al-Jawf	5.7	6.05
Southern	6	Asir, Jizan, Najran	12.3	8.32
Al-Rub Al-Khali (Empty Quarter)	7		0.2	-
Abroad			0.5	-
Nonsoecified			2.0	-

* Population estimated from 1974 census adjusted for subsequent years by correction for births and deaths per region.

roid, esophagus, cervix, ovary, oral cavity, myeloid leukemia, cancers of the uterus and CNS. Unlike most Western countries, cancers of the The CRF of the most common cancers are given in *Table 2* for males and females. The commonest cancers in males were non-Hodgkin's lymphomas, cancers of the esophagus, lung, liver, stomach, and na-

sopharynx, Hodgkin's disease, lymphoid leukemia, cancers of the oral cavskin as well as of the colon and rectum were comparatively uncommon (*Tables 2 and 4*). The overall male to female ratio was 1.3. The largest male:female ratios in non-sex organs were found in cancers of the larynx (7.2), bladder (4.4), liver (4.4), pancreas (3.4), lung (3.3), Hodg-

Figure 1: Map of Saudi Arabia showing the seven geographic regions for the purpose of cancer registration.

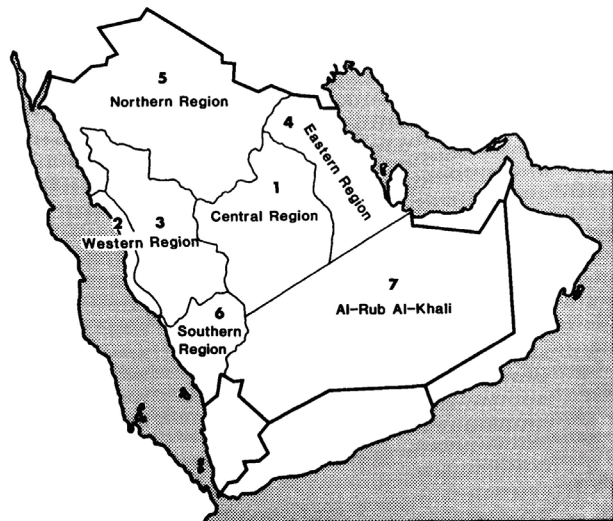


Figure 2: Age and sex distribution of all cancer patients seen at the King Faisal Specialist Hospital between 1979-1984.

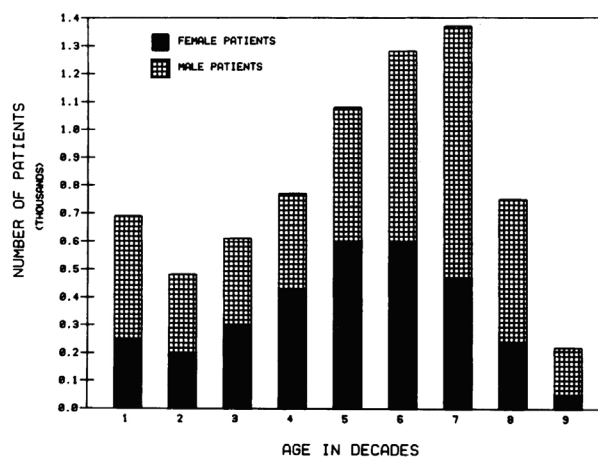


Table 2: Crude Relative Frequency and Rank Order of Most Common Cancers

RO	Both sexes		Males		Females	
	Description	CRF %	Description	CRF %	Description	CRF %
1	NH lymphoma	10.3	NH lymphoma	12	Breast	17.2
2	Breast	7.6	Esophagus	6	NH lymphoma	1.9
3	Esophagus	5.6	Lung	5.8	Thyroid	5.6
4	Lung	4.3	Liver	5	Esophagus	4.9
5	Oral cavity	4.3	Stomach	4.8	Cervix	4.6
6	Lymphoid leukemia	3.8	Nasopharynx	4.7	Ovary	4.5
7	Stomach	3.8	Hodgkin's	4.6	Oral cavity	4.4
8	Thyroid	3.7	Lymphoid leukemia	4.5	Myeloid leukemia	3.1
9	Nasopharynx	3.6	Oral cavity	4.1	Uterus	3
10	Hodgkins	3.6	CNS	3.9	CNS	2.9
11	Liver	3.5	Skin, non-melanoma	3.8	Lymphoid leukemia	2.9
12	Myeloid leukemia	3.5	Bladder	3.7	Stomach	2.7
13	CNS	3.5	Myeloid leukemia	3.3	Skin, non-melanoma	2.5
14	Skin, non-melanoma	3.2	Bone sarcoma	2.6	Nasopharynx	2.3

RO: relative frequency; CRF: crude relative frequency; NH: non-Hodgkin's; CNS: central nervous system.

kin's disease (2.7), cancer of the nasopharynx (2.6), skin melanoma (2.4), and cancer of the stomach (2.3). Only thyroid cancer exhibited a markedly low male:female ratio of 0.54. The largest number of cancers was seen in the 6th and 7th decades in males and in the 5th and 6th decades in females.

A secondary peak in the first decade of life was seen in both sexes (*Figure 2*).

Over one third of all cancer patients came from the

Central Region-1 (Nejd). The rest were well distributed among the other populated areas. The CRF of specific types of cancers are compared among these regions in *Table 3*. The most dramatic deviations from national norms were seen in patients referred from the Southern Region-6. For example, the CRF of oral cavity cancer in females (12.9%) was three times the rate in the country as a whole (4.4%), and in males it was twice as high (8.2% versus 4.1%). The CRF of bladder cancer in this region was roughly double that of the rest of the country (6.0% versus 3.7% in males, and 2.4% versus 1.1% in females).

On the other hand, lung cancer was much less frequent (1.2% versus 5.8% for males, and 0.6% versus 2.3% for females). Jeddah and the developed coastal strip comprising the Western Region-2 had the highest CRF of lung cancer (9.7% in males) and

the lowest CRF of stomach cancer (2.8% in males). This region also had the highest CRF of breast cancer in females (24.3%). The Northern Region-5 had the highest CRF of female thyroid cancer (11.3%), twice the national average (5.6%). CRF of esophageal cancer was the highest in the Central Region-1 (Nejd) 6.5%, in both males (7.5%) and females (5.1%). The lowest CRF of esophageal cancer in males was found in the Eastern Region-4 (4.6%) and the Southern Region-6 (3.8%).

In females, this difference in CRF was not well demonstrated.

Non-Hodgkin's lymphomas and nasopharyngeal carcinomas were common in all regions compared to other countries.^[8,9] The number of new cancer cases seen each year has shown a steady rise from 911 to 1979 to 15 11 in 1984 and the male to female ratio has steadily declined from 1.5 to 1.3. The CRF by primary site and year of diagnosis for males and females is given in *Table 4*. During this period the CRF of esophageal carcinoma has steadily declined (from 8.1% to 4.7% in males, and from 6.7% to 5.6% in females). Colorectal cancers appear to be on the rise (from 2.9% to 4.8% in males and from 1.9% to 2.7% in females.) Following the worldwide trend, lung cancer is steadily increasing from 5.2% to 6.5% in males and from

Table 3: Trends of Crude Relative Frequency and Rank Order of Some Cancers by Geographic Region

	Region											
	1		2		3		4		5		6	
	CRF%	RO	CRF%	RO	CRF%	RO	CRF%	RO	CRF%	RO	CRF%	RO
Males												
Oral cavity	2.9	10	4.0	5	4.4	7	4.9	6	2.6	10	8.2	2
Esophagus	7.5	2	6.6	3	7.4	3	4.6	7	6.2	4	3.8	7
Stomach	5.8	3	2.8	10	3.5	10	3.3	11	7.0	3	5.0	3
Lung	4.2	6	9.7	2	7.9	2	7.9	2	4.0	8	1.2	16
Bladder	3.2	9	3.3	8	3.7	9	3.5	10	3.1	9	6.0	4
Females												
Oral cavity	2.7	11	3.0	8	3.6	5	5.4	5	4.4	5	12.9	2
Esophagus	5.1	3	3.8	6	6.2	4	5.4	5	3.8	6	4.0	6
Bladder	0.7	21	0.3	18	1.9	14	0.6	16	0.6	11	2.4	10
Breast	17.6	1	24.3	1	18.1	1	17.0	1	17.0	1	13.5	1
Thyroid	4.9	4	3.9	6	7.2	3	5.7	4	11.3	2	4.9	4
Lung	1.8	15	4.4	4	2.1	10	3.3	9	1.9	9	0.6	15

CRF: crude relative frequency; RO rank order.

Table 4: Trends of Crude Relative Frequency and Rank Order of Some Cancers by Year

	Year											
	1979		1980		1981		1982		1983		1984	
	CRF%	RO	CRF%	RO	CRF%	RO	CRF%	RO	CRF%	RO	CRF%	RO
Males												
Esophagus	8.1	2	7.8	2	6.7	2	4.9	6	6.0	3	4.7	6
Colon	1.3	16	2.1	14	0.5	19	1.5	16	0.8	19	1.8	18
Rectum	1.6	14	1.4	15	2.8	11	1.5	16	1.4	15	3.0	13
Lung	5.2	4	4.6	6	4.7	6	6.4	2	6.4	2	6.5	2
Thyroid	1.4	15	2.1	14	2.8	11	2.2	14	2.6	12	2.4	14
Females												
Esophagus	6.7	2	6.5	3	2.9	9	4.8	5	3.8	6	5.6	4
Colon	0.8	16	0.3	18	1.9	14	1.0	19	0.8	17	1.2	18
Rectum	1.1	15	3.1	8	2.1	13	1.2	18	2.3	10	1.5	16
Lung	1.9	12	2.3	11	1.3	17	2.0	13	2.9	8	2.8	9
Thyroid	3.3	8	4.9	5	6.5	3	5.8	4	5.7	3	6.5	3
Lung	14.5	1	12.9	1	19.8	1	16.9	1	16.0	1	20.6	1

CRF crude relative frequency; RO: rank order.

1.9 to 2.8% in females. Thyroid malignancies also appear to be rising in both males (from 1.4% to 2.4%) and females (from 3.3% to 6.5%). In women, breast cancer is increasing (from 14.5% to 20.6%). No clear trend is currently discernable in stomach cancer.

DISCUSSION

Since the incidence of specific cancers varies considerably in different age groups, comparison of CRF between countries is likely to be very skewed if these countries have very different population age distributions. Thus, cancers which are more common in childhood will have an exaggerated CRF in young populations. More accurate comparisons can only be made with age standardized data.

With available non age standardized data, comparison with other countries will be limited to cancers whose CRF differs by unmistakably large ratios. Interpretation of data from a single referral hospital has clear limitations. First, the referral procedure itself is a selective process that biases the composition of patients admitted. Second, the number of cancer cases cannot be viewed with reference to a well-defined population base.

Although population incidence (i.e., new cancer cases per year per 100,000 population) is not cur-

rently available, a number of significant comparisons can still be made.

The most striking feature is the unusually high CRF of non-Hodgkin's lymphoma, which is the most common type of cancer seen in males and the second most common in females. Overall, 744 cases were confirmed, accounting for 10.3% of all neoplasms. This is over 4 to 6 times the CRF in most other parts of the world^[8,9] (over view in *Table 5*). In one series of childhood non-Hodgkin's lymphomas, 79% presented with the unique abdominal form.^[10] In adults, gut lymphomas constituted 19.8% of all non-Hodgkin's lymphomas.^[11] There was no increase in incidence of enteric (2%) or parasitic (3%) infections among those patients compared to the general population. In the current survey, non-Hodgkin's lymphomas appear to be very common in all regions of Saudi Arabia. This is consistent with their elevated frequency throughout the Middle East^[12-16] suggesting etiologic factors affecting the Middle Eastern populations in general.

The CRF of lymphoid and myeloid leukemias in Saudis is generally 3 to 4 times higher than in other parts of the world (e.g., 3.2 times higher than Denmark, 4.1 times higher than the USA, and 2.8 times higher than Bombay, India).^[8-9] The most dramatic CRF ratios are seen in nasopharyngeal carcinoma

Table 5: Crude Relative Frequencies of Non-Hodgkin's Lymphomas in Saudi Arabia and Several Other Countries.

Location and period		Crude relative frequency (%)	Ref.
Saudi Arabia (KFSH)	1979-1984	10.3	-
Saudi Arabia (KFSH)	1975-1978	11.5	2
Saudi Arabia (West)	1974-1977	12.8	4
Saudi Arabia (East)	1950-1961	15.2	3
Lebanon	1953-1960	11.7	11
Iraq (Mosul)	1971-1975	13.5	14
Iran (Fars Prov.)	1963-1968	7.6*	15
PDR Yemen (Aden)	1958-1962	3.8	12
India (Bombay)	1973- 1975	2.3	8
Brazil (Sao Paulo)	1973	1.9	8
USA (est.)	1973- 1977	1.9	9
Denmark	1968- 1976	1.6	8

* Malignancies of lymph nodes, spleen, thymus, and tonsils including metastases of unknown primary.
KFSH: King Faisal Specialist Hospital.

(e.g., 33.3 with respect to Denmark, over 20 with respect to the USA, and 8.0 with respect to Bombay, India). Certain lymphoproliferative malignancies and nasopharyngeal carcinomas may have in common a potential link with Epstein-Barr virus,^[17] although its precise etiologic role is neither established nor understood.

The incidence of esophageal carcinoma is markedly more frequent in Saudi Arabia than in Western countries (ie., 6.7 times higher than Denmark and 7.9 times higher than the USA). The average age is 62 years for males and 58 years for females. The M to F ratio is 1.65. This is appreciably lower than in the USA (M:F=2.4), which may suggest an equal exposure of both sexes to an environmental factor. Many patients with cancer of the esophagus reported consumption of very "thermally" hot food, and came from one particular area, Qasim, in the northern part of Region 1.^[18] No difference was found in their age or sex distribution compared to the rest of the country. High CRF ratios are also found for cancer of the oral cavity (5.9 with respect to Denmark, 3.6 for USA).

The observed frequency of oral cavity cancer in the Southern region equals the unusually high rate in Bombay, India. The CRF ratio between the Southern region and the USA is 8.5. The chewing of several tobacco-like substances such as shamma and qat, prevalent mainly in the Southern region particularly the Jizan area and neighbouring Yemen, may contribute to the high frequency of oral cancer.^[19]

In this study, the frequency of lung cancer is much lower than in Western countries (e.g., CRF ratios of 0.37 with respect to Denmark, 0.39 for USA), most likely reflecting the much lower levels of smoking and industrial air pollution. However, the apparent rise in CRF of lung cancer within the short span of 6 years is both alarming and consistent with increasing smoking habits, particularly among the younger population. Colorectal cancer is markedly less common than in the West (e.g., CRF ratios of 0.23 and 0.30 with respect to Denmark and the USA respectively), for which dietary factors, particularly lower animal fat intake, may play a role. The CRF ratios for skin melanoma and non-melanoma are also very low with respect to Western populations (e.g., 0.37 for Denmark, 0.12 for the USA), but large compared to Bombay, India (CRF ratio 2.3). The low rate of skin cancers (despite bright sunlight) may be attributed to cultural habits of avoiding exposure to solar ultraviolet radiation and the wearing of headdresses (ghutra, shma, and veil).^[20] The observed rate of prostatic cancer in men is much lower than in the West (CRF ratio 0.21 with respect to Denmark, 0.16 for the USA), but close to the rate in Bombay, India (CRF ratio 0.81). The frequencies of breast and uterine cancers are very close to other developed countries. The greater CRF ratio of cervical (4.6) compared to uterine cancer (3) may be mainly due to more referrals of cervical cancer for radiation treatment available in our institution.

Western Region-2, including Jeddah, comprises an area that has historically been economically developed and open to outside influences. The pattern of cancer in this region reflects what is known about the impact of modernization: highest CRF of lung cancer in the country, lowest rate of stomach cancer, and highest rate of breast cancer in women. However, the frequency of colorectal cancer is not elevated compared with the rest of the country.

Consistent with the high level of education and urbanization in Western Region-2, its male to female ratio for cancer referrals is closest to unity. By contrast, the Northern and Southern Regions, being the least exposed to outside influences, exhibit the lowest apparent rates of lung cancer and

among the highest rates of stomach cancer. They also have the highest male to female referral ratios in the country.

The differences between the Southern region, and the rest of Saudi Arabia are multifactorial. It is culturally more closely associated with Yemen. As a predominantly mountainous region, it has a generally cooler and less arid climate and has the most intense concentration of traditional agriculture. Within this region, Jizan, in particular, is known to have the highest levels of schistosomiasis infestation in its perennial surface water reservoirs.^[21] Schistosomiasis in man is believed to be an etiologic agent in bladder cancer.^[22,23] Because this region has the highest CRF of bladder cancer in the country, a causal or increased risk relationship must be considered. The association of elevated frequency of cancer of the oral cavity and the local habit of chewing shamma and gat, is supported by in vitro tests which have demonstrated the potential carcinogenicity of shamma.^[24] The apparently low CRF of lung cancer in the Southern region may be associated with the local preference for smoking water pipes rather than unfiltered tobacco. It is conceivable that passing the smoke through water reduces levels of some carcinogenic components.

The trends in pattern of cancer over time are consistent with the consequences of modernization witnessed in virtually every part of the world. The rise in lung cancer is most readily attributable to the increased use of cigarettes in a population that has traditionally shunned smoking. The marked decline in esophageal cancer may be related to both rapidly changing eating habits as well as steadily improving nutrition. The rise in breast cancer follows worldwide trends, although a trend in reproductive habits is not readily discernible. The lack of a clear

trend in stomach cancer may reflect a longer time scale of change or a longer lag period for lifestyle factors to become manifested in an altered cancer frequency. Trend interpretations must be accepted with caution, as referral patterns to a national cancer center are likely to change over time as local hospitals gradually acquire more capabilities to diagnose and treat cancer locally. Nevertheless, the fact that so many trends are apparent within a short 6-year span is remarkable testimony to the rapidity of economic development in Saudi Arabia.

CONCLUSION

As expected, Saudi Arabia, being a vast country with regions of varying climatic, topographic, and lifestyle characteristics, has considerable geographic variation in the frequency of different types of cancer. Rapid economic and social development and increasing availability of modern medical facilities all over the country have influenced the trends in frequency of certain types of cancer over time. Comparison with data from other countries has revealed a significantly different pattern of cancer in Saudi Arabia. A more precise comparison of such patterns within Saudi Arabia and with other countries requires the calculation of age standardized rates and the establishment of a population based cancer registry. This would aid in the development of active studies on cancer epidemiology and shed further light on the specific causes of cancer in the country. Such information will make possible the development of more specific programs for cancer prevention which incorporate studies on environmental, dietary, social, genetic, and other factors that may be responsible for the current and future pattern of cancer in Saudi Arabia.

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PATTERN OF CANCER AT ASIR CENTRAL HOSPITAL, ABHA, SAUDI ARABIA*

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تمت على مدى ثلاث سنوات. ١٩٨٧م-١٩٨٩م معاينة ستمائة وسبع وتسعين حالة سرطان مؤكدة بالفحص النسيجي وذلك في مستشفى عسير المركزي في أبها بالملكة العربية السعودية. وقد حددت بسبب تواتر السرطان (نسبية وتقريبية) في مواضع مختلفة من الجسم. وكانت أكثر المواضع توارداً بين الذكور هي الجلد والكبد والنسيج اللمفاوي (أي الأورام اللمفية غير اللمفاوية) والمثانة. الدم (ابيضاضات الدم) والمعدة والقولون والمريء والجهاز العصبي المركزي والموتة. وكان سرطان الجلد أيضاً أكثر الأنواع توارداً بين الإناث. يليه سرطان الثدي والنسيج اللمفاوي (الأورام الليمفاوية غير اللمفاوية) والدم (ابيضاضات الدم) والدرقية والمعدة والقولون وجوف الفم والمريء وعنق الرحم.

Six hundred ninety-seven histologically confirmed cases of cancer were seen in the three-year period, 1987 to 1989, at Asir Central Hospital in Abha, Saudi Arabia. Percentage (crude relative) frequencies of cancer at various sites were determined. The most common cancer sites among males were skin, liver, lymphoid tissue (i.e., non-Hodgkin's lymphomas), bladder, blood (leukemias), stomach, colon, esophagus, central nervous system, and prostate. Skin cancer was also the most common cancer among females, followed by the breast, lymphoid tissue (non-Hodgkin's lymphomas), blood (leukemias), thyroid, stomach, colon, oral cavity, esophagus, and cervix.

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There is currently no national cancer registry in Saudi Arabia [1]; therefore, the incidence and mortality statistics for cancer cannot be determined accurately. Reports regarding the incidence of cancer originating from the eastern [2], central [3-5], western [6], and Al-Baha [7] region of Saudi Arabia were derived from hospital statistics. No separate figures concerning the pattern of malignancies in the Asir region are currently available. Based on histologically confirmed diagnoses, our study attempts to delineate the pattern of malignancies for the Asir region.

The Asir region (Figure 1) has a high population density. About 75% of the inhabitants live in rural areas and are engaged in agriculture, trade, or government work. There is less involvement in fishing and animal husbandry [8]. Asir Central Hospital (ACH), in Abha, is a 576-bed, regional referral facility for patients of the Asir region. The surgical pathology laboratory of ACH also furnishes routine services to other hospitals located in Khamis Mushait, Bisha, Zahran-al-Janoob, Sarat Abidah, Ahad Ruidah, Rijal Alma, and Muhayl.

MATERIAL AND METHODS

From January 1987 to December 1989 the surgical pathology laboratory at ACH received 18,174 surgical and biopsy specimens. The histopathology reports of the specimens were reviewed and those containing a diagnosis of malignancy were collected. Only one pathology report per patient was included in our data, even though multiple specimens may have been examined. Malignancies were then tabulated according to the organs or affected primary body sites. Uncommon tumors of sites such as lung, bone, nasopharynx, uterus, ovary, testis, salivary glands, adrenals, gallbladder, soft tissue, pancreas, thymus, paraganglia, and maxillary an-

Figure 1: Map of Saudi Arabia, showing the location of the Asir Province.



Table 1: Rank order and percentage frequencies of malignant neoplasms at Asir Central Hospital in 425 males.

Rank order	Site of malignancy	No. (%)
1	Skin	62(14.6)
2	Liver	47(11.0)
3	Non. Hodgkin's lymphoma	41(9.6)
4	Bladder	40(9.4)
5	Leukemia	38(8.9)
6	Stomach	34(8.0)
7	Colon	20(4.7)
8	Esophagus	16(3.8)
9	Central nervous system	11(2.6)
10	Prostate	10(2.3)
11	Others*	106(24.9)

* This category constitutes uncommon tumors of sites such as the lung, bone, nasopharynx, testis, salivary glands, adrenals, gallbladder, soft tissue, pancreas, thymus, paraganglia, and maxillary antrum.

Table 2: Rank order and percentage frequencies of malignant neoplasms at Asir Central Hospital in 272 females.

Rank order	Site of malignancy	No. (%)
1	Skin	62(14.6)
2	Breast	25(9.2)
3	Non. Hodgkin's lymphoma	23(4.8)
4	Leukemia	20(7.3)
5	Thyroid	17(6.3)
6	Stomach	13(4.8)
7	Colon	13(4.8)
8	Oral	11(4.0)
9	Esophagus	10(3.7)
10	Cervix	10(3.7)
11	Others*	96(35.2)

* See Table 1 for explanation of this category.

trum were designated as "others." The sex and nationality of patients in each category were also identified. The nationality for some patients was unknown. To facilitate a comparison of malignancies in each category with previously published data [2-7], percentage (crude relative) frequencies were determined.

During the three-year period, 1987 to 1989, 697

Table 3: malignant neoplasms in Saudi Citizens and other nationals at Asir Central Hospital.

Rank order	Site of malignancy	Saudi	Others	Not specified	Total
1	Skin	78	8	10	96
2	Non. Hodgkin's lymphoma	49			64
3	Leukemia	49		2	58
4	Liver	45		6	54
5	Stomach	35	8	4	47
6	Bladder	25	11	9	45
7	Colon	24	3	6	33
8	Esophagus	21	4		26
9	Breast	15	9		25
10	Thyroid	15	2	4	21
11	Oral	11	4	5	20
12	Central nervous system	16			18
13	Lung	12		0	14
14	Prostate	9		0	10
15	Cervix	9		0	10
16	Others*	17		19	156

* See Table 1 for explanation of this category.

cases of histologically confirmed malignancies were seen (*Tables 1 to 3*). The most common malignancy in males was skin cancer, representing 14.6% of the cases, and then in descending frequency come cancers of the liver, lymphoid tissue (i.e., non-Hodgkin's lymphomas), bladder, blood (leukemias), stomach, colon, esophagus, central nervous system, and prostate. Skin cancer was also the most common malignancy in females, occurring in 12.5%, followed by cancer of the breast, lymphoid tissue (i.e., non-Hodgkin's lymphomas), blood (leukemias), thyroid, stomach, colon, oral cavity, esophagus, and cervix. Other tumors constituted 24.9% of the cases in males and 35.2% of the cases in females.

DISCUSSION

In our study, skin cancer was the most common malignancy in both males and females (14.6% and 12.5%, respectively). Our findings were consistent with the observation of Willen and Patterson^[7] and Stirling et al^[6]. In the Willen and Patterson study of 659 cases of cancers from Al- Saba region of Saudi Arabia, the incidence of skin cancer was 15.2% in males and 14.2% in females.

Stirling et al reported a high proportion of skin cancer (15.5%) among 1000 consecutive cases of malignant neoplasm in Saudi residents of the western region, of Saudi Arabia. Our findings, however, differ from the observations of Elakkad et al^[31] who reported a low rate of skin cancer at King Faisal Specialist Hospital and Research Centre, Riyadh (KFSH&RC), a main referral center for cancer patients from all areas of Saudi Arabia. Many different factors influence the referral to this center. Most skin cancers are not life threatening and are therefore not referred. Moreover, the discrepancy of skin cancer among the various series probably depends on whether the series consists of clinical (KFSH&RC) or pathological (present series) material, the latter usually manifesting a much higher relative frequency of skin cancer. Rabadi^[2] even excluded skin cancers (except melanomas) from his analysis of all cases of malignancy seen at Dhahran Health Center because of the trivial nature of such malignancies.

In the present study, primary hepatocellular carcinoma (PHC) ranked second in frequency in males and accounted for 11% of all malignancies in males. PHC is a commonly observed malignancy in Saudi

Arabia, although its incidence varies according to the time and place of reporting [9]. Our data showed a higher frequency of PHC in the Asir region (11%) as compared with AlBaha (6.5%) [7], Riyadh (5%) [3], and Dhahran (3.3%) [2]. Evidence suggests that hepatitis B virus and schistosomiasis are important factors in the pathogenesis of PHC [10,11] and are common afflictions among the residents of the Asir region [12,13].

In our study, breast cancer was the second most common malignancy in females. A similar high incidence of breast cancer has been reported from Al-Baha [7], Dhahran [2], and Riyadh [3]. The frequencies of gastric carcinomas, lymphomas, and leukemias in the Asir region were similar to those reported from Dhahran [2], Riyadh [3], and Al-Baha [7].

Cancers of the bladder and oral cavity deserve special mention. In our study, bladder cancer was the fourth most common malignancy in males (9.4%). Our results agree with the findings of El-Akkad et al [3], who reported that the crude relative frequency of bladder cancer in the southwestern region of Saudi Arabia was roughly double that of the rest of the country (6.0% versus 3.7% in males and 2.4% versus 1.1% in females). A high incidence of bladder cancer has also been reported from the Al-Baha [7] region (7.1 % in males). The Asir region is a predominantly mountainous area with a generally cool and less arid climate than that found elsewhere in the Kingdom. Because of the widespread practice of traditional agriculture, schistosomiasis is common in the Asir region [9], and this disease is considered a contributing factor in the development of bladder cancer [14].

El-Akkad et al [3], at KFSH&RC, observed that the crude relative frequency of oral cancer for females (12.9%) from the southwestern region of Saudi Ara-

bia was three times that for the country as a whole (4.4%), and in males it was twice as high (8.2% versus 4.1%) [3]. The authors attributed this finding to the chewing of Shamma, which is a mixture of tobacco, slaked lime, black pepper, oils, flavoring, and other ingredients. In contrast, our preliminary findings revealed a low incidence of oral cancer in the Asir region (2.1% in males and 4.11% in females). The difference may be because El-Akkad et al [3] included the Jizan area in their report, while we limited our population to that of the Asir region. In a study conducted by Amer et al [15], 33 of 68 patients with oral cancer referred to KFSH&RC admitted using Shamma. Of these users, 85% were referred from the Southern province, particularly from the Jizan area (73%). A further study that concentrate on the Jizan area would more accurately depict the true incidence of oral cancer in that area. Additionally, because the use of Shamma has been barred since 1983 [9], a decline in the incidence of oral cancer should be expected.

Colorectal cancer occurs at varying frequencies in the populace of different areas of the world. It is the second most common cancer in the United States [16]. Preliminary findings from several investigators [3,4,17-19], as well as our data, have implied that carcinoma of the rectum and large bowel is not as common in the residents of Saudi Arabia as it is for those of Western Europe and North America.

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CANCER IN AL-QASSIM, SAUDI ARABIA: A RETROSPECTIVE STUDY (1987-1995)*

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Regional differences in the pattern of cancer are obvious in Saudi Arabia. From January 1987 to December 1995, 1106 new cases of cancer (642 males, 464 females) were seen at the King Fahd Specialist Hospital in Buraidah, Al-Qassim. Overall, lymphomas, non-Hodgkin's and Hodgkin's disease combined were the most common malignancy seen (15.10%), followed by esophageal carcinoma (7.77%). Thyroid cancer was the most common malignancy among females (12.50%), followed by breast cancer (9.48%). The majority of the patients were in the younger age group (77% were <50 years of age). Among the hematological malignancies, acute lymphoblastic leukemia was the most frequent type (36.23%). Lymphomas were the most common malignancy (66.12%) seen in the pediatric age group (0-14 years), followed by leukemias and brain tumors. The pattern of cancer in Al-Qassim is generally similar to other regions of Saudi Arabia, with few regional variations. Prominent among such variations is the high frequency of non-Hodgkin's lymphomas (NHL), esophageal and thyroid carcinomas. Ann Saudi Med 1997;17(6):595-600.

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The study of the geographical distribution of malignant tumors has greatly influenced our understanding of the cause of cancer. In Saudi Arabia, which is the largest country in the Middle East, regional variations in the prevalence of different cancers have been documented from data taken from the tertiary care centers.^[1] Pending the availability of results from the national cancer registry, information regarding the relative frequency of different tumors can be obtained from sources such as pathology and admissions departments of hospitals in different regions.^[2] The purpose of this study was to evaluate the pattern of cancer in the Al-Qassim region by analyzing data from the departments of Oncology and Pathology at King Fahd Specialist Hospital (KFSH) in Buraidah. Al-Qassim region has a total population of approximately 578,000.^[3] It is situated in the central region of Saudi Arabia, and the majority of the population are involved in either agriculture or trading. KFSH, a 570-bed hospital, is the regional referral center for cancer patients, where the majority of cancer patients are seen.

PATIENTS AND METHODS

All histologically confirmed cases of malignant disease seen at KFSH from January 1987 to December 1995 were included in the study. All cases were indexed by medical record number, name, age, sex, nationality, site of tumor and histopathology. The tumor sites and morphology were coded according to the International Classification of Diseases. We studied the frequency by age and sex of different malignant tumors seen among these patients. The observed figures were compared to available data from other regions of Saudi Arabia and the Middle East.

RESULTS

During the nine-year period (1987-1995), 1106 cases of cancer were seen at KFSH. There were 642 males and 464 females, a male to female ratio of 1.38:1. Of these, 966 were Saudis and 140 were non-Saudis. As shown in *Table 1*, the most common malignancy in the whole group of patients was lymphoma (167/1106 or 15.10%). This included both non-Hodgkin's lymphoma (NHL) and Hodgkin's disease (HD). Carcinoma of the esophagus ranked second (86/1106 or 7.77%), the majority of these (73/86 or 84.88%) being squamous cell, 11 adenocarcinomas and two of the anaplastic type. The median age at presentation was higher in males (61.5 years) than in females (59 years). Similarly, the median age of gastric carcinoma was higher in males (64 years) than in females (58 years). The

Table 1: Rank order of ten common malignant tumors among 1106 patients seen at KFSH in Al-Qassim region, both sexes combined (January 1987-December 1995).

Site or type	Number	Percentage
HD/NHL	167	15.10
Esophagus	86	7.77
Thyroid	76	6.87
Stomach	71	6.42
Blood/bone marrow	69	6.23
Skin (SCC, BCC, melanoma)	63	5.69
Liver	64	5.78
Breast	55	4.97
Lip, oral cavity	43	3.88
Colorectal	43	3.88

HD=Hodgkin's disease; NHL=non-Hodgkin's lymphoma; SCC=squamous cell carcinoma; BCC=basal cell carcinoma.

histological types of thyroid carcinoma consisted of papillary 69 (69/77, or 89.61%), follicular 5 (6.5%), anaplastic type (2), and one lymphoma. The median age at presentation in females was 39 years.

Acute lymphoblastic leukemia was the most frequent hematological malignancy (25/69, or 36.23%) followed by acute myelogenous leukemia (AML) (31.9%), chronic myelogenous leukemia (CML) (8.69%), chronic lymphocytic leukemia (CLL) (8.69%), acute leukemia of unclassified type (8.69%), and multiple myeloma (5.8%). Basal cell carcinoma (46/67, or 68.65%) was the most common type of skin cancer, followed by squamous cell (22.38%), malignant melanoma (2.98%), lymphoma (2.98%), and Kaposi's sarcoma (2.98%). The median ages at presentation were 59 and 61 years for females and males, respectively. Among bladder tumors, transitional cell carcinoma predominated (25/39 or 64%), followed by squamous cell carcinoma (28%), adenocarcinoma (5%) and anaplastic (2.5%). Adenocarcinoma was the most frequent type of bronchial tumor diagnosed (13/36, or 36%), followed by squamous cell (27.7%), anaplastic (13.8%) and others (22.2%).

Common tumors among the pediatric age group (0-14 years) included lymphomas (41/62, or 66.12%), HD (34%), NHL (32%), leukemias (19.35%) and tumors of the brain (6.45%). The age-related distribution of all cancer sites in males and females is shown in *Tables 2 and 3*, respectively. *Tables 4 and 5* show the rank order of the 10 most common malignancies seen in Saudi males and

Table 2: Age-related distribution of malignant tumors in males at KFSH in Al-Qassim region (January 1987-December 1995).

Site or type	0-14	15-20	21-30	31-40	41-50	51-60	61-70	71-80	>80	Unk	Total	%	NS
HD/NHL	22	7	12	12	13	17	19	6	4	0	112	17.45	12
Liver	0	0	2	3	6	15	16	8	2	3	55	8.57	4
Esophagus	0	0	0	3	7	13	16	7	4	0	50	7.79	5
Stomach	0	0	0	2	3	13	11	14	4	0	47	7.32	3
Skin (SCC, BCC, melanoma)	0	0	1	2	7	8	17	6	4	1	46	7.16	5
Leukemia/myeloma	5	3	6	9	6	5	3	1	1	0	39	6.07	10
Prostate	0	0	0	0	1	8	10	8	8	0	35	5.45	4
Bladder	0	0	0	2	8	7	6	4	5	0	32	4.98	4
Lip, oral cavity, pharynx	0	0	3	6	6	4	5	2	1	0	27	4.21	3
Unknown primary	0	0	3	3	2	7	6	2	1	0	24	3.74	7
Bronchus, lung	0	0	0	3	3	9	5	2	0	0	22	3.43	4
Thyroid	0	2	1	8	1	1	3	0	1	1	18	2.80	5
Colon	0	0	0	2	5	5	2	1	1	0	16	2.49	4
Brain	3	1	1	3	0	2	2	2	0	0	14	2.18	1
Testis	0	2	6	3	1	0	0	1	0	0	13	2.02	3
Rectosigmoid, rectum	0	0	0	1	1	5	3	1	0	0	11	1.71	3
Soft tissue sarcoma	0	0	3	3	3	0	1	0	0	0	10	1.56	3
Kidney	0	0	1	2	1	4	1	1	0	0	10	1.56	2
Nasal cavity	0	0	0	1	0	4	2	1	0	1	9	1.40	0
Pancreas	0	0	0	0	2	1	3	3	0	0	9	1.40	1
Gall bladder, biliary tract	0	0	0	2	1	3	2	1	0	0	9	1.40	2
Larynx	0	0	0	1	0	3	3	1	0	0	8	1.25	0
Bones, joints	3	3	2	0	0	0	1	0	0	0	6	0.93	1
Other urinary	0	0	0	0	0	2	1	1	0	0	4	0.62	0
Others	0	1	1	1	3	4	4	1	1	0	16	2.49	1
All sites	33	16	42	72	80	140	142	74	37	6	642	100	87

Unk=unknown age; NS=non-Saudi; BCC=basal cell carcinoma; SCC=squamous cell carcinoma; HD=Hodgkin's disease; NHL=non-Hodgkin's lymphoma.

females of the Al-Qassim region, respectively, as compared to data from other regions of the Kingdom.

DISCUSSION

A male preponderance of 1.38:1, and the increased prevalence of cancer in old age, with more than 65% of patients belonging to the over-40-year age group, are an expected phenomenon. HD and NHL together are the most common malignancies seen in the Middle East and in Saudi Arabia.^[7,10,11] NHL is the most common tumor seen among Saudi

males in the Al-Qassim region, with an overall relative frequency of 11.35%. This is higher than many other regions of the Kingdom (*Tables 4 and 5*).^[4-9] No doubt, data from many of these series included non-Saudi patients as well. In Gizan, lymphoma and leukemia combined ranked second among males and third among females.^[5] However, the breakdown of the exact types of hematological malignancy is not available from that data. NHL also ranked first among males in a study from Riyadh (12.72%), with an overall relative frequency of 9.35%.^[7] Data from Medina also indicate that lymphoma rank first

Table 3: KFSH-age related distribution of malignant tumors in females in Al-Qassim region.

Site	0-14	15-20	21-30	31-40	41-50	51-60	61-70	71-80	>80	Unk	Total	%	NS
Thyroid	0	6	14	8	9	10	4	3	0	4	58	12.5	6
Breast	0	0	6	24	12	6	3	4	1	0	55	11.85	16
HD/NHL	19	6	6	4	1	9	5	4	1	0	55	11.85	4
Esophagus	0	0	1	0	7	11	12	4	1	0	36	7.67	1
Leukemia/myeloma	7	5	1	6	3	2	2	1	1	2	30	6.47	2
Stomach	0	0	0	0	6	8	8	1	1	0	24	5.17	0
Unknown primary	0	1	2	1	4	4	4	5	0	1	22	4.74	3
Skin (SCC, BCC, melanoma)	0	0	1	1	2	3	5	2	2	1	17	3.66	0
Colorectal	0	0	1	3	3	5	3	2	0	0	17	3.66	1
Ovary	0	1	3	4	3	4	2	0	0	0	17	3.66	2
Lip, oral cavity, pharynx	0	0	4	3	4	2	0	1	1	1	16	3.45	2
Bronchus, lung	0	0	1	1	4	2	4	2	0	0	14	3.02	0
Gall bladder, biliary tract	0	0	0	1	3	3	1	3	1	0	12	2.59	0
Cervix	0	0	1	3	5	1	1	1	0	0	12	2.59	4
Brain	1	3	1	2	3	1	0	0	0	0	11	2.37	2
Liver	0	0	0	0	1	2	3	3	0	0	9	1.94	0
Soft tissue sarcoma	1	1	2	3	1	1	0	0	0	0	9	1.94	0
Kidney	1	1	1	2	1	1	1	1	0	0	9	1.94	0
Uterus	0	0	0	0	4	2	0	0	1	0	7	1.51	1
Bladder	0	1	0	0	0	1	3	0	1	1	7	1.51	0
Other genital	0	0	1	1	1	1	0	0	0	0	4	0.86	2
Other urinary	0	0	2	1	0	0	1	0	0	0	4	0.86	2
Pancreas	0	0	0	1	1	1	0	0	0	0	3	0.65	0
Others	0	2	0	1	1	5	5	1	1	0	16	3.45	5
All sites	29	27	48	70	79	84	67	38	12	10	464	100	53

Unk=unknown age; NS=non-Saudi; BCC=basal cell carcinoma; SCC=squamous cell carcinoma; HD=Hodgking's disease; NHL=non-Hodgkin's lymphoma.

among males and third in females, but again the figures combine HD and NHL.^[6] The peculiarities of the pattern of lymphoma in this region have been reported elsewhere.^[10] NHL was more common than HD, which corroborates other studies from Saudi Arabia and the Middle East.^[10-13]

Thyroid cancer was the most common malignancy observed in Saudi females of this region (12.65%), with a male to female ratio of 1:4. The median age at diagnosis of 39 years in females and the peak incidence in the 21-30- year age group is similar to the data from Riyadh.^[12,14] Papillary carcinoma (PC) was more frequent than the follicular type. The marked predominance of PC that we saw has

been noted in many other series.^[12,14-16] Iodine deficiency is believed to play a role in causing follicular carcinoma of thyroid in countries where goiter is endemic. Iodine replacement may have decreased the incidence of follicular carcinomas, but at the same time it may be a factor in papillary carcinogenesis.^[15] This may explain the high incidence of PC recently reported, especially in females.^[14,15] The high relative frequency of thyroid carcinoma in the Al-Qassim region is in contrast to other parts of the Kingdom.^[5,6,8,9] Other little understood contributing factors responsible for the high relative frequency of thyroid carcinoma in this region need to be explained.

Table 4: Relative frequency of ten common malignancies seen among 555 Saudi males in Al-Qassim region compared to other regions.

Site (#)	Al-Qassim*	Riyadh ⁴	Gizan ⁵	Madina ^{6**}	Riyadh ^{7**}	Abha ^{8**}	Al Baha ^{9**}
NHL (64)	11.53	8.5	NA	NA	12.72	9.6	10.4
Liver (51)	9.17	14.48	18.72	9.4	5.5	11	6.5
Esophagus (45)	8.09	2.98	1.83	6.6	5.72	3	2.7
Stomach (44)	7.91	7.35	3.28	7.5	4.54	8	11.3
Skin (41)	7.38	2.75	12.51	8.8	3.97	14.6	15.2
Hodgkin's disease (36)	6.47	3.9	NA	NA	4.96	NA	NA
Prostate (31)	5.57	3.9	4.2	3.2	1.87	2.3	4.2
Bladder (28)	5.03	4.82	8.58	5.1	3.52	9.4	7.5
Lip, oral cavity (24)	4.31	NA	13.24	1.8	5.45	NA	4.5
Colorectal (20)	3.59	3.9†	2.46	6.7	3.26	4.7	4.8

#=The number of Saudi patients with malignancy at that site in the present series; *present series; **includes non-Saudis of that region;† rectum only.

Table 5: Relative frequency of ten common malignancies seen among 555 Saudi males in Al-Qassim region compared to other regions.

Site (#)	Al-Qassim*	Riyadh ⁴	Gizan ⁵	Madina ^{6**}	Riyadh ^{7**}	Abha ^{8**}	Al Baha ^{9**}
Thyroid (52)	12.65	10.44	2.24	4.6	5.72	6.3	5.7
Breast (39)	9.48	13.29	9.09	20.1	16.76	9.2	9.8
NHL (30)	7.29	8.22	NA	NA	7.96	8.4	6.1
Esophagus (35)	8.51	4.74	2.83	6.3	4.64	3.7	1.2
Stomach (24)	5.84	5.37	2.36	4.2	2.62	4.8	11.4
Hodgkin's disease (21)	5.11	2.53	NA	NA	2.36	NA	NA
Skin (17)	4.14	NA	11.6	4.4	2.87	12.5	14.2
Colorectal (20)	3.89	NA	2.95	5.9	2.74	4.8	5.3
Ovary (15)	3.64	3.799	2.95	3	4.33	NA	4.9
Lip, oral, cavity (14)	3.41	NA	19.95	1.9	5.91	4	3.2

#=The number of Saudi patients with malignancy at that site in the present series; *present series; **includes non-Saudis of that region.

Carcinoma of the esophagus ranked 3rd and 4th among Saudi males and females, respectively. The male to female ratio of 1.28:1 is similar to the data from Riyadh, but lower than that of the USA.^[12,17] The high incidence of esophageal carcinoma in males in the West is probably due to the effect of substances like alcohol and tobacco.^[18] Perhaps by virtue of strict adherence to Islamic principles, these factors play little role in the causation of esophageal carcinoma in this population. However, other factors, including food preparation and storage, and differences in soil composition, are accepted etiologic factors which may be of significance in this area.^[19] Recently, human papilloma virus infection of the esophageal epithelium has been suggested

to be an important etiologic factor.^[20]

Gastric carcinoma closely followed esophageal cancer in rank order in both sexes, being more frequent in males, at a ratio of 1.8:1. Contamination of drinking water has been considered an important etiologic factor for the causation of upper gastrointestinal tract cancers in Al-Qassim region.^[21] However, this has yet to be confirmed.

Breast cancer, the most common cancer among females in the Riyadh and Medina regions, ranked second among the Saudi females in our series.^[4,6,12,22] The majority of patients we saw were below 50 years of age (42/55 or 76.36%). This age distribution is unlike the data from the West, but in conformity with other series from Saudi Arabia and

the Middle East.^[7,12,13,22] This might be an indication of the younger constitution of the Saudi population, where 93.38% are below the age of 50 years.^[3] Hepatocellular carcinoma (HCC) occurs more frequently in men than in women.^[23] The high male to female ratio of 5.6:1 noted in our study has already been reported from other regions of the Kingdom.^[1,5-8] The risk factors for HCC include viral infection, hemochromatosis, alcoholic liver disease and metabolic disorders. HCC has been reported subsequent to exposure to substances like aflatoxin, nitrosamines and thorotrast.^[23] However, the most important risk factor for HCC is infection by hepatitis B (HBV) and hepatitis C (HCV) viruses. While the integration of HBV virus DNA in the cellular genome of tumors has been documented in many studies, it is only recently that HCV infection, with its cirrhosis, has been recognized as an important risk factor for HCC.^[24,25] Data on the prevalence of HBV and HCV in the Al-Qassim region is not yet available. Skin cancer, reported to be the highest in rank order in the southern regions of the Kingdom, ranked 5th for males and 7th for females, with a male to female ratio of 2.4:1 in our series.^[5,8,9] Both the relative frequency and the male to female ratio are similar to the data from the Medina region.^[6] The rarity of melanoma in the Kingdom has been reported in other studies as well.^[4,5,22] The two malignant melanomas we saw were of the acral type. The importance of exposure to sunlight as an etiologic factor for melanoma is well established.^[26] Although the Kingdom has abundant sunshine, the low incidence of malignant melanoma may be due to multiple reasons, including racial factors, strict observance of hejab (a mode of dressing whereby all parts of the body are covered) by females, as well as the cultural habits of the population related to the method of dressing. It is interesting to note that tumors of the lip, oral cavity and pharynx were less frequent than in the Gizan region.^[5] Smoking is considered a social taboo in this region. This may account for the low frequency of these tumors, as well as those of the lung. The latter are more frequently seen in the eastern and northern regions.^[22] The male to female ratio of 1.28:1 of carcinoma of the lung among Saudi patients in Al-Qassim is one of the lowest. This is contrary to the male preponderance reported from other regions of the Kingdom and the Middle East, where one of the highest male to female ratios has been noted.^[4,5,7,13] Colorectal carcinoma had a male to female ratio of 1.58:1. The overall low frequency of colorectal carcinoma, as compared to Western countries, may be due to the dietary habits of the local popula-

tion, as has been reported from other regions.^[12,22] Prostatic carcinoma had a relative frequency of 5.57%, which is similar to the data from Riyadh and Al Baha.^[4,9] The overall median age at presentation of prostatic carcinoma (69.5 years) is similar to other studies.^[12,27] Prostatic carcinoma constituted 97% of all male genital cancers seen in men older than 60 years. Interestingly, not a single case of penile carcinoma was recorded by us. Carcinoma of the bladder was less common than in the southern regions of the Kingdom.^[5,8,9] Compared to Gizan, where squamous cell carcinoma occurs with equal frequency as transitional cell carcinoma, the latter predominated in our series.^[5] Unlike Gizan, Al-Qassim is not an endemic area for schistosomiasis.

Carcinoma of the ovary was more frequent than cervical cancer among Saudi females, having relative frequencies of 3.4% and 1.94% respectively. The lower relative frequency of cervical carcinoma has been reported from some regions of the Kingdom,^[4,5,9] whereas studies from other regions have reported a higher relative frequency of cervical cancer.^[6-8] Unfortunately, some of the larger studies have not provided us with detailed data regarding female genital tract cancer.^[12,22] Adherence to Islamic moral codes and circumcision of males may be the main reasons for the low incidence of cervical neoplasia in this country. However, remarriages, multiparity and early age of marriage are all risk factors, including laxity in observing Islamic moral codes. All these factors may be responsible for the regional variations in the relative frequency of cervical cancer. A recent study from Jeddah region has reported the high prevalence of this disease, based on cytological studies.^[28]

Among childhood tumors, lymphomas were more common than leukemias (62.12% vs. 19.35 %). This is in contrast to the data from the USA, where leukemias predominate, comprising approximately 31% of all malignant tumors of childhood, followed by the central nervous system neoplasia (17.6%).^[29]

The pattern of cancer in the Al-Qassim region is different from the published data from other regions of the Kingdom. The predominance of lymphomas, thyroid, breast and esophageal cancers is obvious. On the other hand, lung and colorectal carcinomas are less frequent. It will be interesting to compare this data with the results of the national cancer registry.

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THE SPECTRUM OF BREAST DISEASES IN SAUDI ARAB FEMALES: A 26 YEAR PATHOLOGICAL SURVEY AT DHAHRAN HEALTH CENTER*

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In an attempt to delineate the spectrum of breast diseases in Saudi Arab females, we carried out a retrospective study of all cases of breast biopsies and mastectomies accessioned in the files of surgical pathology in our laboratory for 26 years (1967-1992). A total of 915 cases were collected. Fibroadenoma was the most common lesion encountered (30.7%), followed by fibrocystic condition (21.1%), carcinoma (14.9%), acute mastitis (7.2%), duct ectasia (4.9%), lactational adenoma (4.8%), intraductal papilloma (2.6%), galactocoele (2.4%) and several less frequent lesions. Pathological conditions associated with lactation such as acute mastitis, abscess, granulomatous mastitis, galactocoele and lactational adenomas constituted 16.2% of the cases in this series. This high frequency is related to the high fertility rate among Saudi Arab females.

The mean age of Saudi Arab females with ductal carcinoma was 47.1 years as compared to 54 years in Western countries. Many patients presented with a large size tumor, skin and/or nipple involvement, as well as a high frequency (61.7%) of axillary nodal metastases in those who underwent axillary nodal dissection.

The high frequency of fibroadenoma could be related to the large number of young females in our population. A great increase in the number of cases in the last five years has been observed. This could be related to more awareness among Saudi Arab females of their health problems and the expansion of our medical services. *Ann Saudi Med* 1995;15(2):125-132.

The high frequency and the diverse variety of breast lesions has prompted many workers in various medical fields to embark on numerous and exhaustive studies of many aspects of these disease conditions. In addition, carcinoma of the breast ranks first among malignant tumors affecting females in many parts of the world, including Saudi Arabia.^[1] Wide variations in the spectrum of breast diseases and the epidemiology

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of mammary carcinoma in various countries^[2-9] or ethnic groups^[10-12] have been reported.

In the Arab world, most of the studies on pathological conditions of the breast are related to its malignancies.^[13-19] Few studies address themselves to the whole spectrum of breast diseases in Arab females in general.^[20-22] Surprisingly, the subject of breast diseases in Saudi Arab females, except for a few studies, mostly on carcinoma of the breast,^[22-27] has not been given its fair share of attention in the Saudi medical literature.

We present here our findings in a retrospective survey of pathological material examined in our laboratory, spanning more than 26 years and giving insight into the changing pattern of breast diseases among Saudi Arab females during a period that has witnessed dramatic improvements in social and economic conditions in Saudi Arabia.

MATERIAL AND METHODS

The Medical Services Organization of the Saudi Arabian Oil Company (Saudi ARAMCO) covers the medical needs of Saudi ARAMCO employees and their families, totaling at last count about 220,000 people. Eighty-eight percent of this population are Saudi Arabs,^[28] the vast majority of whom reside in the Eastern Province. All major surgical procedures performed on this population, with very few exceptions, are done at Dhahran Health Center, a 400-bed secondary care hospital. All surgical specimens are examined at our surgical pathology laboratory, one of the earliest laboratories of its kind in the Kingdom, starting its services in 1956. All surgical pathology records are available starting in 1965 and the histopathological slides are available from 1967 onward. In addition, Dhahran Health Center has maintained a hospital-based tumor registry since 1987. Diagnostic mammography started in 1982 and the number of cases examined has risen sharply in the last few years. An outpatient breast clinic was initiated in 1988. Its staff included surgeons with interest in breast diseases, a medical oncologist with an interest in breast cancer and a radiologist specializing in mammography. The clinic receives referrals from general practice clinics and specialty clinics in all Saudi ARAMCO facilities as well as self-referrals.

The surgical pathology records for the years 1967 to 1992 inclusive were reviewed and details of all female patients with breast lesions were obtained. Information retrieved included the name of the patient, her age and nationality, laterality, multiplicity, size, diagnosis and associated conditions. Additional information in cases of malignancy

included the status of the lymph nodes if axillary lymphadenectomy was done, the hormonal receptor status, if determined, the presence of more than one focus of tumor (multicentricity), skin and nipple involvement, and any recurrences.

Patients with more than one specimen for the same lesion were counted once. Patients with multiple or bilateral similar lesions, even if excised at different times, were counted once. Cutaneous tumors or inflammatory conditions affecting the skin overlying the breasts were not included. Cases of accessory breast tissue, encountered particularly in the axillae, were excluded. Patients who were found clinically to have "masses" which proved to be normal breast tissue, either with normal lactational changes or involuting unremarkable breast tissue, were not included. Only Saudi Arab patients were targeted for this study. There were a large number of American patients and many patients from Britain, other Arab countries, and Asian countries who were not part of the present work.

A total of 972 reports out of a grand total of 143,100 surgical pathology reports seen during this period (0.64%) were found to belong to 915 Saudi patients. All the data obtained on these patients were tabulated and analyzed.

Slides of histological sections of selected cases were reviewed by one pathologist (SSA) and most of the cases of breast pathology encountered in the last seven years were reviewed by all three pathologists as part of the ongoing peer review program in our department.

RESULTS

The histopathological findings in the population of this study with the corresponding number of affected patients and the mean age are listed in *Table 1*. Fibroadenoma has the lead and includes about one-third of the cases, followed by fibrocystic change (mammary dysplasia), carcinoma and mastitis in that order. The age distribution of these four leading pathological conditions is shown in *Table 2*. The trends of the frequency of various pathological entities over the span of 26 years are demonstrated in *Table 3*, with each period of five successive years grouped together. The last year of the study, 1992, is placed on its own and represents the situation at the time of preparation of the study. This table clearly demonstrates a progressive decrease in the ratio of cases of mastitis, an increase in the ratio of cases of fibrocystic change, a peak for the ratio of fibroadenoma in the late 1970s and early 1980s, and a progressive increase in the number of cases of breast carcinoma, although their ratio is

Table 1: Pathological findings and mean age in 915 Saudi Arab females with breast masses.

Type of Lesion	No. of Patients	% of Total	Mean Age (Years)
Inflammatory conditions			
Acute mastitis and abscess	66	7.2%	32.4
Chronic mastitis	11	1.2%	27.8
Granulomatous mastitis	16	1.8%	40.9
Duct ectasia	45	4.9%	51.1
Galactocele	22	2.4%	27.2
Hydatid cyst	1	0.1%	40.0
Subtotal	161	17.6%	
Proliferative nonneoplastic conditions			
Fibrocystic change	193	21.1%	38.1
Fibrous mastopathy	12	1.3%	26.3
Sclerosing adenosis	10	1.1%	33.6
Virginal hypertrophy	3	0.3%	17.0
Juvenile papillomatosis	3	0.3%	23.0
Subtotal	221	24.1%	
Benign tumors			
Fibroadenoma	281	30.7%	24.2
Juvenile fibroadenoma	8	0.9%	17.3
Benign phylloides tumor	3	0.3%	30.6
Intraductal papilloma	24	2.6%	40.9
Lactational adenoma	44	4.8%	24.2
Lipoma	13	1.4%	44.3
Hemangioma	3	0.3%	46.3
Granular cell tumor	1	0.1%	24.0
Chondrolipoma (Choristoma)	1	0.1%	29.0
Subtotal	378	41.2%	
Malignant tumors			
Ductal carcinoma	125	13.7%	47.1
Medullary carcinoma	7	0.8%	50.5
Lobular carcinoma	3	0.3%	47.5
Intraductal carcinoma	2	0.2%	46.5
Liposarcoma	1	0.1%	32.0
Lymphoma	1	0.1%	30.0
Subtotal	139	15.2%	
Others			
Intramammary lymph nodes	16	1.8%	40.1
Subtotal	16	1.8%	
Total	915	100%	

decreasing due to the numerical increase in other pathological conditions of the breast.

Fibroadenoma was the most common lesion encountered, with 36.6% of the patients (103 cases) below the age of 20 and 82.5% (232 cases) below the age of 30; 128 cases (45.5%) were detected in the left breast and 113 cases (40.2%) in the right breast. Both breasts were involved in 20 patients (7.1%). The side was not recorded in 20 patients (7.1%). Multiple fibroadenomas were encountered in 35 patients (12.4%); 18 patients had two, 12 had three, two had four, and three had more than four. In 32 tumors (12.3%), lactational changes within the fibroadenoma or the surrounding breast tissue were detected. Three fibroadenomas were infarcted. Eight cases of juvenile fibroadenoma were found. All were detected in adolescent girls between the ages of 14 and 19 years. Most were of relatively large size, ranging between 5.5 and 11 cm, average 7 cm in diameter, as compared to the average size of the more conventional fibroadenoma, which is about 2 cm. There were three cases of phylloides tumor, formerly known as cystosarcoma phylloides, all benign histologically.

Other benign tumors include lactational or lactating adenoma (44 cases), considered by some authors to be a hyperplastic process involving mammary tissue during lactation and not a true neoplasm. The patients' ages ranged from 16 to 44 years (mean 24.2 years). Thirty patients were less than 26 years of age and 41 patients were less than 31 years of age. Twenty-four patients had intraductal papillomas, with an age range between 25 and 63 years (mean 40.9 years). Seven had associated fibrocystic changes. Other less common benign tumors encountered were mesenchymal in origin and included 13 lipomas, three hemangiomas and a single case each of granular cell tumor and chondrolipoma which was also labeled as mammary choristoma.

Fibrocystic change or mammary dysplasia is the second breast lesion in frequency, accounting for 21.1% of all cases. The age distribution of this lesion is distributed almost evenly between the ages of 21 and 55 years, with a slight peak at the age range of 31 to 35 years. A broad spectrum of histopathological findings were encountered in this group, ranging from minimal cystic dilatation of ducts with foci of adenosis to florid proliferative processes. However, in the vast majority of the cases, the lesions did not carry an increased risk of development of carcinoma in the future according to the criteria set forth by the consensus committee on malignant potential of fibrocystic change.^[29] There

Table 2: Age distribution of major breast lesions in Saudi Arab females.

Age Group (Yrs)	Abscess & Mastitis		Fibrocystic Change		Fibroadenoma		Ductal Carcinoma	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
11-15	0	(0.0)	0	(0.0)	17	(6.1)	0	(0.0)
16-20	8	(12.1)	11	(5.7)	86	(30.6)	0	(0.0)
21-25	12	(18.2)	24	(12.4)	84	(29.9)	1	(0.8)
26-30	16	(24.2)	22	(11.4)	45	(16.0)	11	(8.8)
31-35	8	(12.1)	29	(15.0)	20	(7.1)	11	(8.8)
36-40	8	(12.1)	20	(10.4)	10	(3.6)	17	(13.6)
41-45	6	(9.1)	27	(14.0)	8	(2.9)	14	(11.2)
46-50	4	(6.1)	27	(14.0)	5	(1.8)	21	(16.8)
51-55	2	(3.0)	23	(11.9)	1	(0.3)	14	(11.2)
56-60	1	(1.5)	5	(2.6)	0	(0.0)	20	(16.0)
61-65	1	(1.5)	5	(2.6)	1	(0.3)	10	(8.0)
66-70	0	(0.0)	0	(0.0)	0	(0.0)	5	(4.0)
71-75	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
76-80	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Unknown	0	(0.0)	0	(0.0)	4	(1.4)	0	(0.0)
Total	66	(100)	193	(100)	281	(100)	125	(100)

Table 3: Distribution of breast lesions in Saudi Arab females by years of study.

Category of Lesions	1967-1971		1972-1976		1977-1981		1982-1986		1987-1991		1992	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Inflammatory conditions	18	(29.5%)	10	(18.9%)	20	(12.6%)	33	(15.3%)	60	(18.9%)	20	(18.5%)
Proliferative nonneoplastic conditions	8	(13.1%)	12	(22.6%)	29	(18.2%)	53	(24.5%)	83	(26.1%)	36	(33.3%)
Benign tumors	20	(32.8%)	21	(39.6%)	85	(53.5%)	103	(47.7%)	115	(36.2%)	34	(31.5%)
Malignant tumors	15	(24.6%)	10	(18.9%)	25	(15.7%)	27	(12.5%)	45	(14.1%)	17	(15.7%)
Others	0	(0.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	15	(4.7%)	1	(0.9%)
Total	61	(100%)	53	(100%)	159	(100%)	216	(100%)	318	(100%)	108	(100%)

were 12 cases of fibrous mastopathy, their ages ranging from 17 to 47 years. Sclerosing adenosis, a lesion related to fibrocystic change, was the sole pathologic finding in ten patients, their ages ranging from 21 to 64 years, with a mean of 33.6 years. Other proliferative breast lesions occurred in young females and included three cases of vaginal hypertrophy with marked enlargement of one breast requiring surgical intervention and three cases of ju-

venile papillomatosis, known also as Swiss cheese disease of the breast due to the presence of many dilated cysts associated with florid papillomatosis.

Carcinoma of the breast ranked third in this series. The vast majority of the cases (125 out of 137) were infiltrating ductal carcinoma. There were only two cases of intraductal carcinoma (ductal carcinoma in situ) and three cases of lobular carcinoma. In addition to seven cases of medullary carcinoma,

there were other histological patterns and varieties of ductal carcinoma including scirrhous, tubular, papillary, cribriform, comedo, mucinous and cystic hypersecretory patterns. However, in most of the cases more than one pattern would be found and it was decided to consider all these cases as infiltrating ductal carcinoma. The mean age of our patients is 47.1 years. If the mean age at menopause in Saudi Arab females is arbitrarily considered as 50 years, then 60% of our cases are premenopausal and 40% are postmenopausal; 9.6% of the patients are less than 31 years of age.

Both breasts were about equally affected by carcinoma. Involvement of the right breast was seen in 64 cases (46.7%), the left breast in 67 (48.9%), and both breasts in one case only, which was lobular carcinoma histologically. In five cases, the side was not recorded. Of 97 cases with recorded measurements of the size of the tumor, 36 cases (37.1%) were less than 2.5 cm in maximum diameter and 61 cases (62.9%) were more than 2.5 cm. Seventeen patients (12.4%) had more than one focus or nodule of tumor in the same breast.

In 15 cases (11%), the tumor attained quite a large size and was associated with ulceration of the skin with formation of a fungating mass. Three cases exhibited massive nipple involvement by direct extension from underlying tumor. Four more patients showed clinical and histological features of involvement of the nipple by Paget disease, one associated with intraductal carcinoma and the rest involved with infiltrating ductal carcinoma.

Eighty-one patients underwent mastectomy with axillary lymphadenectomy. Thirty-one cases (38.3%) had negative lymph nodes for metastatic deposits and 50 cases (61.7%) had positive lymph nodes. Of the latter group, 17 cases (21%) had metastases in one to three lymph nodes and 33 cases (40.7%) in more than three lymph nodes.

It should be stated that most of the patients with advanced involvement of the breast, including the ones with ulceration or fungation, were among the 56 patients who had biopsy or simple mastectomy

only.

We started sending tumor tissue for assay of estrogen and progesterone receptors (ER and PR) to referral laboratories in 1984. A total of 42 cases were tested. Of these, 14 cases (33.3%) were positive for both and 22 cases (52.4%) were negative for both. Four cases were ER positive, PR negative while two cases were ER negative, PR positive.

It is clear from these findings that our patients with infiltrating carcinoma of the breast presented with a more advanced disease and that their tumor was biologically more aggressive as evidenced by the high frequency of poorly differentiated tumors. *Table 4* summarizes all the features of advanced disease and aggressive behavior of cancer of the breast in our patients.

Intraductal carcinoma was encountered in only two patients, one of whom was associated with Paget disease of the nipple. Three cases of lobular carcinoma were seen, one of them affecting both breasts. In a few cases of infiltrating ductal carcinoma, foci of lobular carcinoma in situ were noted. Mixed type ductal and lobular carcinoma is known to occur; however, since the lobular component in our cases was minimal, we decided to consider these lesions as ductal carcinomas.

Two rare malignant neoplasms are included. One is a case of primary lymphoma of the breast in a 30-year-old woman. The tumor was first noticed when she was pregnant but was diagnosed after delivery by needle aspiration cytology. Histologically it was a diffuse large cell lymphoma of B-cell origin as demonstrated by immunocytochemistry. The other case is a myxoid liposarcoma in a 32-year-old woman.

Inflammatory conditions of the breast, particularly acute mastitis and breast abscess, constitute the fourth major category in this series. *Table 2* shows that 66.6% of the patients were less than 36 years of age, reflecting the association of this lesion with lactation and pregnancy. Other inflammatory conditions include duct ectasia, known also as plasma cell mastitis, which affects a different type of popu-

Table 4: Features of advanced disease and aggressive behavior of cancer of breast in Saudi Arab females.

61.7% of cases with axillary lymphadenectomy had positive lymph node
66% of cases with positive lymph nodes had more than three nodes involved
62.9% of cases with data on their size were more than 2.5 cm in diameter
11% of all cases showed skin ulceration and/or fungation
52.4% of cases tested for estrogen and progesterone receptors were negative for both

lation. The mean age of this group is 51 years and 64.4% of the patients are over 50 years of age. Granulomatous mastitis was the dominant lesion in 16 cases, with a mean age of 41 years, ten years more than the patients with acute mastitis. Numerous granulomas were found histologically in a background of mixed inflammatory infiltrate. One case of tuberculous mastitis is included in this group. There was a past history of pulmonary tuberculosis with involvement of the pleura and extension to the chest wall with spread to the breast. Some of the other cases were lactating females with previous history of acute mastitis and one patient with a draining sinus. Granuloma formation was encountered in seven cases of acute mastitis with abscess formation due to extravasation of milk secretions from disrupted ducts, but these cases were not included under the granulomatous mastitis group because of the dominance of the neutrophilic infiltrate and because the granulomas were few. There were 11 cases of chronic mastitis, four having lactational changes within the mammary lobules.

Galactocele was seen in 22 cases. Their ages ranged from 19 to 39 years (mean 27.2 years). Most of these cases had some degree of chronic mastitis. There was a single case of hydatid disease (*Echinococcus granulosus*) involving the breast, an uncommon site for this parasitic infection.

With the introduction of mammography, many intramammary nodules were detected, some of them soft and nonpalpable. Some of these nodules proved on histological examination to be intramammary lymph nodes. Sixteen patients had such nodes, their ages ranging between 20 and 57 years (mean 40.1 years), half of them over 40 years of age. Most of the lymph nodes showed reactive hyperplastic change and about two-thirds showed melanin pigment deposits within macrophages, similar to what is seen in cases of dermatopathic lymphadenopathy, a condition seen in lymph nodes draining areas affected by certain skin disease.

DISCUSSION

This retrospective study of breast diseases in Saudi Arab females covers a relatively stable well-defined population in the Eastern Province over an extended period of time. Certain social factors and demographic findings contribute to the pattern of diseases of the breast encountered in this study. Saudi Arab females tend to marry at a young age, according to the traditional conservative values of the society, with childbearing extending practically over the entire reproductive period of life. These facts are reflected by the occurrence of many lacta-

tion-related conditions, including acute and chronic mastitis, granulomatous mastitis, galactocele and lactational adenomas which amount to 17.3% of all cases in this study. Due to the conservative nature of the society, many females will refrain from seeking medical advice out of shyness until their disease becomes far-advanced, particularly in cases of carcinoma of the breast. Fifteen percent of the patients presented with advanced tumor associated with skin ulceration or extension to the nipple or both. Many of these cases were encountered in the earlier periods of the study but some such cases have been seen recently, especially in older females, in spite of efforts by the Division of Health Education and the nursing staff in various clinics to encourage females to seek medical help if they feel a breast lump. However, such efforts are more successful among younger females who are utilizing the available facilities such as the breast clinic and the mammography service more frequently.

Retrospective studies such as the present one carry an inherent bias in the selection of patients for surgery and biopsy by the treating surgeon. Many patients with breast disease are treated by medication without resorting to surgical procedures. Other patients have their cysts aspirated without a need for biopsy. As stated earlier, some patients will refuse or postpone visiting a physician for a mass in the breast. Until recently, many patients in our clinics were reluctant to allow examination of the breasts, thus adding another bias to the selection of the material.

Benign tumors are the largest group (41.2%) in this series. Fibroadenomas are the most frequent lesions encountered, constituting 30.7% of all cases and 75% of all benign tumors. This is higher than the reported frequency in England (7.7%),^[2] the USA (18.5%),^[3] and Jordan (21%),^[21] but is slightly lower than American blacks (34.7%),^[30] Africans,^[31,32] and the Caribbean islands of Trinidad (39.3%)^[7] and Jamaica (32.4%).^[8] The high frequency of fibroadenomas in black females with breast masses has been reported by several authors.^[30-34] In India, fibroadenoma is the most frequent benign lesion of the breast.^[35] It is apparent that the high frequency of fibroadenoma in Saudi Arab females is similar to what has been observed in black American, African and Indian females and contrasts with the lower frequency in Western white females. The causes of this increased frequency are not clear. Racial predisposition could be a factor. Demographic factors might play a role, considering the relatively large number of young females within the population of these groups. The rate

of growth of fibroadenomas may increase during pregnancy^[36] and this could alarm those patients who will seek medical help with subsequent excision of the mass, thus adding a bias of selection. In the present study, 32 patients (12.3%) with fibroadenomas showed lactational changes histologically.

Intraductal papillomas in this series (2.6%) are less common than has been reported in a series from New York (3.5%)^[3] and another on breast lesions in blacks (5.7%).^[30] This could be partially due to the exclusion of cases of papillomatosis associated with other lesions such as fibrocystic change and juvenile papillomatosis. Another factor could be the absence of histological evidence of papillomas in some cases labeled as such by the surgeon. The problem of localizing intraductal papillomas by the surgeon and the pathologist has been alluded to by Azzopardi,^[36] who pointed to the need for demarcation of the suspected lesion area by a stitch, so that the pathologist can expose the usually small friable tumor.

Lactational adenomas constituted 4.8% of the cases. This is quite an elevated frequency when compared with studies from neighboring Jordan (1.2%).^[16,21] In general, the lactating nodule is a lesion unique to the physiologic state of pregnancy and the lactational state in the postpartum period.^[38] The nature of these nodules is still controversial. They are considered by some authors as distinct neoplasms, labeled as lactating adenomas or breast tumors of pregnancy,^[39] but others suggest that they are variants of fibroadenoma or lobular hyperplasia with changes caused by altered physiological condition.^[40]

There are 18 benign mesenchymal tumors in this series. Thirteen of these are lipomas. The average age is 44.3 years, with nine patients over 40 years of age. There are three benign vascular neoplasms, two of which are cavernous hemangiomas and the third is a venous hemangioma. Special attention was paid to differentiating these lesions from angiosarcoma of the breast, a lesion known for its deceptively benign microscopic appearance and its notoriously aggressive behavior and lethal outcome. Rosen and his associates delineated these vascular neoplasms in a series of articles emphasizing their histological differences from angiosarcoma.^[41,42] One case of granular tumor (granular cell myoblastoma) in a 24-year-old female was observed. Preoperatively, the lesion was suspected to be malignant because it was firm and poorly circumscribed. On frozen section, the nature of the lesion was recognized and mastectomy was avoided. In a report of four cases of granular cell

tumor of the breast, two underwent mastectomy because the lesions were not identified histologically on frozen section - one was labeled as carcinoma, the other as an unusual tumor infiltrating fat and thought to be malignant.^[43] A rare case of chondrolipoma of the breast was encountered in a 29-year-old female.

This lesion is usually a well-circumscribed mass composed of fibrous and fatty tissue with islands of hyaline cartilage. Some authors label such lesions as choristomas of the breast.^[44]

Proliferative nonneoplastic conditions of the breast are the second largest group in the present study, accounting for 24.1% of cases. Fibrocystic change or condition is the most frequent entity in this group. This lesion is the most common breast mass in studies from the UK (37%)^[2] and the USA (33.9%).^[3] In the past, several terms such as mammary dysplasia, cystic mastitis and fibrocystic disease were used to describe the pathologic spectrum of apparently related clinical abnormalities of the breast. Now there is a consensus to use the term fibrocystic condition or change as the preferred diagnostic term, the degree of risk of development of malignancy stated according to the presence or absence of various microscopic elements.^[29]

Although some authors recognize fibrosis of the breast or fibrous mastopathy as a distinct clinicopathological entity,^[45,46] others have their doubts and consider it a variation of the normal involution of the breast.^[47] We encountered 12 cases of this lesion affecting females, mainly in the third decade of life with only two in the second decade. Typically, this lesion affects young females with voluminous breasts and is discovered accidentally by the patient. On palpation, it is perceived as a hard disk of variable size. At the time of surgery, it is better palpated than seen, not encapsulated and rather submerged in the midst of the normal breast tissue surrounding it.^[46]

In 1980, Rosen described peculiar breast masses in 36 young females. These masses were characterized by a combination of changes within the breast, none of which was specific in itself. They include papillomatosis, cyst formation, apocrine metaplasia, sclerosing adenosis and duct ectasia.^[48] He labeled it "juvenile papillomatosis", which is now widely recognized as a specific clinicopathologic entity. The presence of florid epithelial changes and extensive cyst formation impart to the lesion a Swiss cheese appearance. This should differentiate it from the usual case of fibrocystic change, which shares many of the above described histological features, and is a clue to the correct diagno-

sis. Pathologists should keep it in mind, especially when it occurs in young females. We encountered three cases of juvenile papillomatosis in our study; their ages were 19, 20 and 28 years. One of them was subjected three times to surgery for total excision of the lesion. The only other cases of juvenile papillomatosis in Arab females were reported in a study on breast disease in Jordan.^[21] A relatively high frequency of breast carcinoma was discovered among female relatives of patients affected with this condition,^[49,50] a fact which calls for careful clinical surveillance of both the patients and their female relatives.^[50]

Acute mastitis and breast abscesses in the present study are more frequent than reported in other series,^[3,7,33] however, we believe the figures for breast abscesses are underestimated because most are drained and only a minority are biopsied. The figures for mastitis in the present study are close to those reported from Jordan.^[22] In both Saudi Arabia and Jordan, females tend to have more children than Western females and childbearing extends over almost the entire reproductive life with a broad peak occurring in the 20 to 35 year age group. This is manifested in an increase in the number of problems associated with lactation such as acute mastitis and abscesses.

Granulomatous inflammatory changes in the breast can be related to specific infectious agents such as mycobacterium tuberculosis, noninfectious disease such as sarcoidosis, foreign material such as silicon, paraffin or suture material, or trauma with fat necrosis and granuloma formation. In addition, granulomatous mastitis had been described in young parous females presenting with an extra-areolar tender breast lump following pregnancy by a period ranging from one to 78 months,^[51] and suspected clinically in some cases to be malignant.^[52] The lesion shows a predominantly lobular involvement of the breast parenchyma and has a tendency for recurrence. Surgery does not always offer the best treatment.^[53] We had 16 cases of granulomatous mastitis, one tuberculous, while the remaining 15 cases fit into the category of granulomatous lobular mastitis.

In our hospital, cancer of the breast ranks first among malignant neoplasms affecting females.^[54] There are few studies on cancer of the breast in Saudi Arab females.^[23-27] In one study from a university teaching hospital in the Eastern Province,^[25] 130 females with breast cancer were studied, 80 of whom were Saudi Arabs. Their mean age was 43.4 years, which is close to our figure of 47.1 years. Seventy-eight percent of the patients who had axil-

lary lymphadenectomy (107 patients) were positive for metastatic deposits compared with our figure of 61.7%.

In another study from a university teaching hospital in Jeddah, details of 34 cases of breast carcinoma were reported.^[23] Forty-seven percent of the patients were less than 45 years of age, 60% had axillary lymph node metastasis and 78% had a tumor which was more than 3 cm in diameter.

Data from our study and from other studies in Saudi Arabia are comparable to the data available on other Arab females from Egypt,^[13,14] Kuwait,^[13] Sudan,^[18] Lebanon,^[19] Jordan^[15,16,21] and Palestine.^[55] The similarities shared in these studies on Arab females with breast cancer include their young age, which is on the average 10 years less than Western females,^[3] and the presence of several poor prognostic factors including large size of tumor and higher frequency of axillary lymph node metastasis. This probably reflects delays in the presentation of the patient to the physician due to social or cultural factors, or it could point to a more aggressive tumor occurring in Arab females, especially in the light of an increased frequency of high grade carcinomas as judged by histopathological findings such as nuclear pleomorphism and atypia and increased mitotic figures. Further work is needed to shed more light on the natural history of breast carcinoma in Saudi Arab females and probably a collaborative multicenter study which includes oncological centers in various parts of the Kingdom can fulfill this goal.

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DO NOT FORGET TO EXAMINE THE BREASTS

A PLEA TO MY COLLEAGUES



Dr. Samia Al-Amoudi

Breast Cancer Survivor and Global Advocate



كرسي الشيخ محمد حسين العمودي لأبحاث سرطان الثدي
Sheikh Mohammed Hussein Al-Amoudi Scientific Chair for Breast Cancer Researches



INVITATION

TO ALL RESEARCHERS, HEALTH CARE PROVIDERS & STUDENTS
TO APPLY FOR PROJECT FUNDING BY

SHEIKH MOHAMMED HUSSEIN AL-AMOUDI SCIENTIFIC CHAIR FOR BREAST CANCER RESEARCHES

PROJECT INFORMATION

Project Title				
Proposal Summary				
Project Type				
Proposed Total Budget	Saudi Riyals			
Estimated Duration	() Months			
Research Team		Name	Research Status	Role
	1			PI
	2			CO-I
	3			CO-II
Key Words (max. 4)	1.		2.	
	3.		4.	

Name		Faculty	
e-mail		Mobile	

