

Ocular malignant tumors

Review of the Tumor Registry at a tertiary eye hospital in central Saudi Arabia

Rajiv B. Khandekar, PG Dip, MS (Ophth), Abdulelah A. Al-Towerki, MD, Hind Al-Katan, MD, Saleh S. Al-Mesfer, MD, Emad B. Abboud, MD, Hailah M. Al-Hussain, MD, Osama H. Sbeikh, MD, Imtiaz A. Chaudhry, MD, Wafa A. Ahmed, BA, Babar M. Zaman, MA, Nasira Asghar, MSc (Stat), Deepak P. Edward, MD.

ABSTRACT

الأهداف: نستعرض ملف الحالات الباثية وحالات إصابة العيون بالأورام الخبيثة بين السعوديين والمسجلة في سجل الأورام الخاص بمستشفى الملك خالد التخصصي للعيون، الرياض، المملكة العربية السعودية.

الطريقة: تم جمع المعلومات الديموغرافية، والسمات الإكلينيكية بما فيها تجانب الورم، والنسيج البصري، وتشخيص المرضى، تم جمعها من سجل الأورام بين العامين 1983م و 2012م. وتم تقدير حالات الإصابة بالأورام الخبيثة عند البالغين السعوديين من سن 15 عام فما فوق والأطفال ممن دون 15 من العمر.

النتائج: اشتمل سجل الأورام على 4,146 حالة إصابة بالأورام [2,509 (60.5%) حميدة و 1,637 (39.5%) خبيثة]، وبلغت حالات الأمراض الخبيثة بين الأطفال (دون 15 من العمر) والبالغين 3.6 و 2.4 من بين مليون طفل ومليون بالغ سنوياً على التوالي، ووجد أن ورم جذبيات الشبكية (763) (91% أكثر أمراض العيون الخبيثة انتشاراً بين الأطفال. أما بين البالغين فوجد أن أكثر الأمراض الخبيثة انتشاراً هي سرطان الخلايا الحرشفية (363: 45.8%) وسرطان الخلايا القاعدية، (186، 23%) وسرطان الغنبيه (میلانوما) (94: 11.9%) وسرطان الغدة الدهنية (n=54: 6.8%) والأورام اللمفاوية (الحجاج، والملحقات الجلدية) (46: 5.8%) وغيرها من الأورام (53: 6.8%) وبالنسبة لورم جذبيات الشبكية (الذي بلغت نسبة الإصابة السنوية به 7.7 بين كل مليون طفل ممن هم دون 5 أعوام) فيعتبر أقل انتشاراً في السعودية من الحالات التي سجلت في دول الخليج لكن نسبة الإصابة في السعودية أعلى منها في الدول الغربية. وسجلت حالات سرطان الخلايا الحرشفية في السعودية نسبة أقل من حالات الإصابة في الدول التي يكون معدل التعرض فيها للشمس مماثلاً في القارات الأخرى ولكن نسبة الإصابة بقيت على ما هي عليه دون تغيير على مر ثلاثة عقود، بل إن نسبة الإصابة بسرطان الخلايا القاعدية شهدت ارتفاعاً كبيراً بين الأعوام 1983-1992م إلى 2012-2003م.

الخاتمة: تقدم هذه الدراسة استعراضاً شاملاً لحالات الإصابة بالأورام الخبيثة في العيون والأجزاء المحيط بها بين السعوديين. ولم تتغير معدلات الإصابة بالأورام الخبيثة على مدى ثلاثة عقود عدا ورم الخلايا القاعدية فقد سجل ارتفاعاً كبيراً.

Objectives: To present the epidemiologic profile and magnitude of ocular malignant tumors (MT) representative of the Saudi population from the Tumor Registry (TR) at King Khaled Eye Specialist Hospital (KKESH).

Methods: This study evaluated the demographic information, clinical features including tumor laterality,

ocular tissue of origin, and diagnosis of patients from the TR registry between 1983 and 2012 at KKESH, Riyadh, Kingdom of Saudi Arabia. The incidence of MT among Saudi adults (≥ 15 years old), and children (< 15 years old) was estimated.

Results: The TR recorded 4,146 neoplasms (2,509 [60.5%] benign tumors, and 1,637 [39.5%] MT). The incidence of MT in children was 3.6 per million/year (M/Y), and 2.4/M/Y for adults. Retinoblastoma (Rb) (n=763, 91%) was the most common ocular malignancy in children. In adults, the most common MT was squamous cell carcinoma (SCC) (n=363, 45.8%), basal cell carcinoma (BCC) (n=186, 23%), uveal melanoma (n=94, 11.9%), sebaceous gland carcinoma (n=54, 6.8%), lymphomas (orbital, adnexal) (n=46, 5.8%), and others (n=53, 6.8%). The Rb (7.7/M/Y in < 5 years old Saudi children) was less frequent than that reported in some Gulf countries, but higher than that reported from the West. The SCC was less frequent in countries with comparable sun exposure than in other continents, but the incidence remained unchanged over 3 decades. There was a significant increase in BCC between 1983-1992 and 2003-2012.

Conclusion: The rates of all cancers remained stable over 3 decades except BCC, which showed a significant rise.

Saudi Med J 2014; Vol. 35 (4): 377-384

From the Department of Research (Khandekar, Al-Towerki, Al-Katan, Al-Mesfer, Abboud, Al-Hussain, Sbeikh, Chaudhry, Ahmed, Zaman, Asghar, Edward), King Khaled Eye Specialist Hospital, Riyadh, Kingdom of Saudi Arabia, and the Wilmer Eye Institute (Edward), Johns Hopkins University School of Medicine, Baltimore, Maryland, United States of America.

Received 27th November 2013. Accepted 20th February 2014.

Address correspondence and reprint request to: Dr. Rajiv B. Khandekar, Department of Research, Ophthalmic Epidemiology and Low Vision Services, King Khaled Eye Specialist Hospital, PO Box 7191, Riyadh 11462, Kingdom of Saudi Arabia. Tel. +966 (11) 4821234 Ext. 1362. Fax. +966 (11) 4829311. E-mail: rkhandekar@KKESH.med.sa

Ocular neoplasms can be life threatening, and detailed information from databases maintained at tertiary level institutions can be important for institutional and public health planning. Registry data can also help in formulating policies and tumor specific management protocols. In the ophthalmic literature, large datasets are available on specific malignant ocular, and periocular neoplasms from many countries.¹⁻³ In the Middle East and Asia, case series of selective ocular malignancies are published.^{4,5} However, there is a relative paucity of literature on the spectrum of malignant ocular and adnexal tumors in the Middle East and Asia.

The King Khaled Eye Specialist Hospital (KKESH) is a tertiary level ophthalmic hospital in Riyadh, Kingdom of Saudi Arabia (KSA) that offers expert care for adult and pediatric patients with ocular tumors (OTs).⁶ The Research Department in the institution in collaboration with the Ophthalmic Oncology team has maintained a TR since 1983.⁷ This dataset provides baseline information on the profile of malignant ocular and adnexal neoplasms evaluated at KKESH. Since it has been the main tertiary ophthalmic referral center for ocular oncology in the entire Kingdom until recent years, the data provides a reasonable estimate of the type and incidence of malignant neoplasms among the Saudi population. In this study, a review of data in the TR was performed to determine the demographic profile of patients, and calculate the incidence of malignant ocular and adnexal tumors.

Methods. The TR was accessed in January 2013 following the approval of the institutional review board of KKESH. The study was carried out at the Department of Research, Ophthalmic Epidemiology and Low Vision Services, King Khaled Eye Specialist Hospital, Riyadh, KSA from January to June 2013 in accordance with the principles of the Helsinki declaration. As the study involved review of health records (registry), we did not obtain consent of patients. A team that included an epidemiologist, ophthalmologists, biostatistician, and clinical coordinators reviewed the data. All cases with tumor, reported and confirmed by histopathological report at KKESH during the study period were included in the TR and in the present study.

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

The TR has been maintained since 1983, and a description of patient recruitment and the data entry process is described below. Patients with ocular and adnexal neoplasms are referred to the Ophthalmic Oncology team from regions throughout the Kingdom for diagnosis and treatment. Once the clinical diagnosis of a neoplasm has been established by a hospital service, the patients are treated by a single or multiple specialty service. The Cornea and/Anterior Segment, Oculoplastics, Pediatric Ophthalmology, and Retina services contributed to the registry. Ancillary testing was performed to establish the clinical diagnosis. Tumor biopsies, lesion excision, enucleation or exenteration, performed for the diagnosis, or treatment were sent to the Ophthalmic Pathology department to establish the final diagnosis. Treatment following the diagnosis was performed in the hospital, or at a specialized Oncology Unit in a hospital within Riyadh. In rare instances, where the systemic condition of the patient was unstable for a variety of reasons, patients were transferred to a general hospital for further care and management. These cases were not recorded in the registry. The TR data on retinoblastoma also included cases that were offered eye sparing conservative therapy, including chemotherapy. The registry recorded patient demographics, clinical details, and tumor classification. The patient demographic information included age, gender, and nationality. Clinical features included the eye involved, ocular tissue of origin, and clinical diagnosis. The final diagnosis was recorded based on the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10 AM) coding data.⁸ In 2008, this codebook was used to convert all the previous disease codes in the TR from previous ICD classifications.

The TR has been maintained using Microsoft Access® software (Microsoft Corp., Redmond, WA, USA) database. For this study, the data were de-identified to maintain patient confidentiality. The TR data from 1983-2012 were extracted to a spreadsheet for analysis using the Statistical Package for Social Sciences version 16 (SPSS Inc, Chicago, IL, USA). For qualitative variables, we calculated frequencies with percentages. For quantitative variables, we plotted the distribution on a histogram with a normal curve. If the data were normally distributed, we calculated the mean and standard deviation. If the distribution was skewed, we calculated the log value of the variable, and then evaluated the distribution. To compare the demographic variables of patients with tumors, we used Open EPI software, and calculated the odds ratio (OR), and 95% confidence interval (CI).⁹ If more than 2 subgroups were

present, we calculated the Chi-square value, degrees of freedom (df), and statistical significance. A $p < 0.05$ was considered statistically significant. Additionally, we estimated the incidence of the most common MT in the adult population (defined as individuals 15 years of age or older), and in children less than 15 years of age. Population estimates of adult and children were acquired from the National Cancer Registry from 2001 onwards to calculate tumor incidence.¹⁰ The population parameters in the National Cancer Registry of the Saudi Oncology Society were based on the census reports published by the Central Department for Statistics (CDS) data, Ministry of Planning of Saudi Arabia. The incidence per million per year (/M/Y) in the Saudi population was reported in the current study. To study the trends of different malignancies over time, the registered cases were divided into 3 groups: the first decade encompassing 1983-1992; second decade encompassing 1993-2002; and third decade encompassing 2003-2012. The TR included data on benign tumors (BTs) affecting the eye and the adnexa. However, we chose not to perform a detailed analysis of benign tumors, as only lesions that were examined by histopathology were included in the TR. It is likely that many of the benign lesions were managed elsewhere, and not referred to KKESH, or patients may not have opted for treatment. We believe that the data on benign lesions is likely to be skewed and may not provide accurate estimates of the incidence, or the distribution of these neoplasms within the hospital, or the Kingdom.

Results. From 1983-2012, 4,146 patients with OTs were registered. Malignant tumors were present in 1,637 patients and BTs were noted in 2,509 patients. The age, gender, laterality, and nationality of patients with MT in children less than 15 years old and adults were compared, as shown in Table 1. Figure 1 plots the incidence of adult MT in the TR based on gender and year of registration. Since reliable population estimates in KSA were available after 2001, we compared the data by gender over the last 12 years. The data from the TR shows a trend towards decreasing incidence of malignant OTs in the adult Saudi population ($p < 0.001$). This decrease was in males and females ($p = 0.405$). Figure 2 plots the incidence of ocular and adnexal MT among Saudi males and females less than 15 years of age at the time of registration. There was a gradual but statistically significant decline in the incidence of OTs among children ($p < 0.001$). The incidence of MT among males and females less than 15 years of age was not different ($p = 0.116$). The number and percentage proportions of MTs by anatomical sites were reviewed. Intra-ocular

Table 1 - Demographics and ocular features of patients with benign, and malignant ocular and adnexal tumors from the Tumor Registry from 1983-2012.

Variables	Malignant	Benign	P-value
Age, years Mean \pm SD	31.4 \pm 27.5	32.7 \pm 27.6	
Age group	n (%)		<0.001*
<5	721 (44.0)	318 (6.1)	
5-9	92 (5.6)	219 (4.2)	
10-14	30 (1.8)	189 (3.6)	
15+	794 (48.5)	1,783 (34.2)	
	$\chi^2=794$, df=3		
Gender			
Male	895 (54.7)	1,316 (52.5)	
Female	742 (45.3)	1,193 (47.5)	
	OR=1.09, 95% CI=0.97-1.24		
Nationality			
Saudi	1,410 (86.1)	2,319 (92.4)	
Non Saudi	227 (13.9)	190 (7.6)	
	OR=1.97, 95% CI=1.6-2.4		
Laterality			
Unilateral	1,389 (84.9)	2,443 (97.4)	
Bilateral	248 (15.1)	66 (2.6)	
	OR=6.6, 95% CI=5.0-8.8		
Tissue of origin			<0.001*
Globe	1200 (73.3)	825 (15.8)	
Orbit	106 (6.5)	374 (7.2)	
Lid and adnexa	305 (18.6)	1185 (22.7)	
Nearby tissues	22 (1.3)	101 (1.9)	
Other	4 (0.2)	24 (0.5)	
	$\chi^2=566$, df=4		
Year of registration			0.48
1983-1992	485 (29.6)	767 (30.6)	
1993-2002	547 (33.4)	839 (33.4)	
2003-2012	605 (37.0)	903 (36.0)	
	$\chi^2=0.52$, df=2		

*significant, χ^2 - Chi-square test, SD - standard deviation, CI - confidence interval, df - degrees of freedom,

tumor was found in 863 (52.8%), orbital MT was noted in 137 (8.4%), ocular surface MT in 342 (20.8%), and peri-ocular skin MT was registered in 294 (18%) of all 1,636 MT cases. Intra-ocular MT comprised half of the registered MT. The cases of retinoblastoma (Rb) registered in the TR were based on histopathology, or clinical diagnosis followed by oncology treatment. The Rb accounted for 90% (597/666) of ocular MT among Saudi children <15 years of age. The incidence of Rb in the last 12 years was 7.7/M/Y among Saudi children <5 years of age, and 3.5/M/Y in children <15 years old. The incidence of Rb was not significantly different between males and females (OR=1; 95% CI: 0.8-1.3). The Rb was bilateral in 179 (30%) children, and unilateral in 480 (70%) children <15 years of age. The ratio of bilateral to unilateral Rb in children less than one year

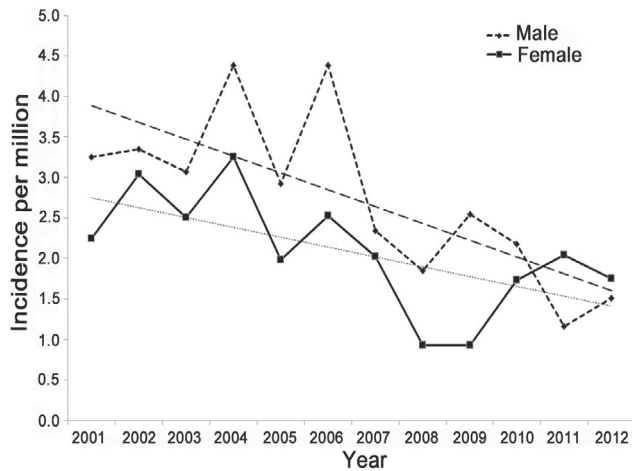


Figure 1 - Incidence of ocular malignancy by year in the adult Saudi population based on Tumor Registry 1983-2012.

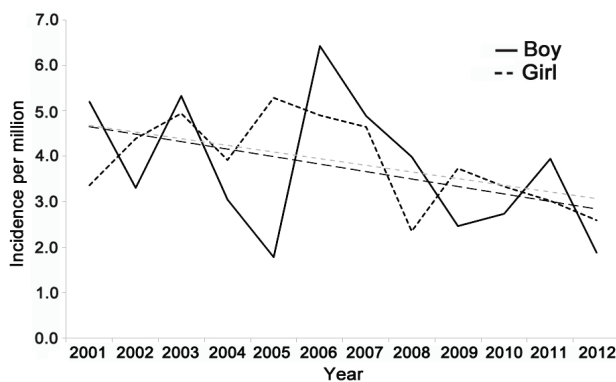


Figure 2 - Incidence of ocular malignancy in Saudi children of 15 years and below based on Tumor Registry 1983-2012.

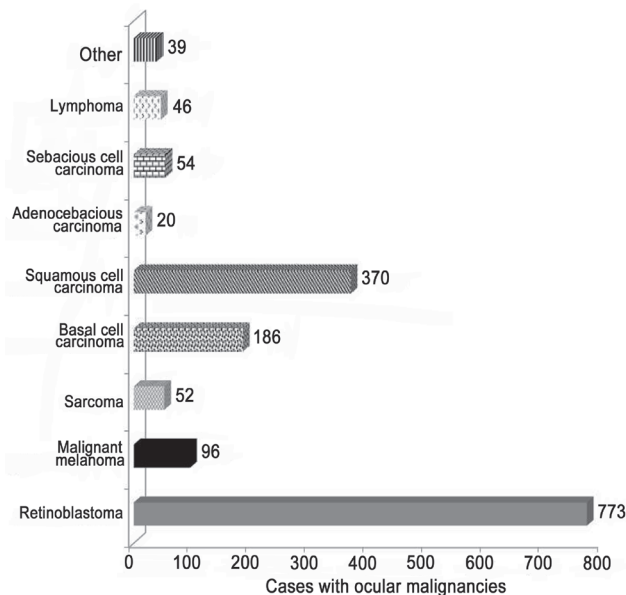


Figure 3 - Distribution of ocular malignancies among Saudi population based on Tumor Registry 1983-2012.

of age was 1:1.4. The ratio of bilateral to unilateral Rb in children \geq one year of age was 1:5.1. This ratio showed some variability over the 3 decades studied, however, showed a trend towards less bilateral tumors over time. Of the total 773 Rb cases in the TR, 186 (22.3%) were non-Saudi nationals. The risk of bilateral Rb between Saudi and non-Saudi was not different (odds ratio [OR]=1.3; 95% confidence interval [CI]: 0.9-1.9). Among non-Saudi patients with Rb, 118 had unilateral Rb, and 67 (36.3%) had bilateral Rb. Of the unilateral cases, 27 (25.2%) were children \leq one year of age, whereas in the bilateral cases, 32 (53.3%) were \leq one year of age. Among the Rb cases in the non-Saudi group, Yemen (n=42) and Egypt (n=20) were the major contributing nationalities. Eight cases of Rb were present in the population older than 15 years of age (7 Saudis [6 girls and one boy]), and one non-Saudi girl with Rb.) Four were 16 years old, while 3 were 20-30 years old. Only one case was 54 years old. Two were bilateral Rb, and 6 had unilateral Rb. Overall, there was no statistical significant change in the rates of Rb cases seen in the 3 decades studied ($p=0.266$). The proportion of different types of MT among Saudi adults was also determined from the TR (Figure 3). Squamous-cell carcinoma (SCC) and basal cell carcinoma (BCC) accounted for 75% of all MT in adults. The other MT included madulo-epithelioma (n=4), metastatic carcinoma (n=3), hemengio-pericytoma (n=3), atypical melonosis (n=4), and one each of different rare conditions).

In this registry, there were 355 Saudi and 15 non-Saudi patients with SCC. Among the Saudi patients with SCC, 298 (83.9%) lesions originated from the conjunctiva, 43 (12.1%) originated from the eyelid, and the remaining from periocular adnexal structures. The incidence of SCC was 1.2/M/Y in adult Saudi males, and 0.8/M/Y in adult Saudi females (OR=1.5; 95% CI: 1.1-2.0). The mean age of Saudis with SCC was 64 ± 12.3 years. Only one case had bilateral involvement, and the distribution of SCC over 3 decades was 122 (35.1%), 104 (29.3%), and 124 (35.6%) cases. The BCC was noted in 169 Saudis, and 17 non-Saudi patients. The incidence of BCC in the adult Saudi male was 0.5/M/Y, and 0.56/M/Y in the adult Saudi female populations. The mean age of Saudi patients with BCC was 69.3 ± 17 years. There was a significant trend towards increasing incidence of BCC over time: 47 (25.4%) in the first decade, 66 (35.5%) in the second decade, and 73 (39.1%) in the third decade ($\chi^2=66.6$, $df=2$, $p<0.0001$). In 98 (58%) patients, BCC involved the lower lid. The TR included eyes with uveal melanoma that were enucleated and sent for

histopathology. The registry recorded 87 cases (57 males and 30 females) with malignant melanoma (MM) of the uvea. The choroid was the most common site of involvement, and was observed in 68 cases (78%). The mean age of patients with MM was 53.1 ± 17.3 years. The incidence of MM was 1.94/M/Y. All cases of MM were unilateral, and were equally distributed over the 3 decades of the study ($\chi^2=2.3$, $df=2$, $p=0.130$). The TR documented 54 cases (23 males and 31 females) of sebaceous gland carcinoma (SGC) among the adult Saudi population. The incidence of SGC in the adult Saudi population was 0.4/M/Y. None of the SGC cases were reported in the non-Saudi population. The mean age of the patients with SGC was 69.2 ± 14.5 years. The upper lid was involved in 26 (48%) cases with SGC. They were equally distributed over the 3 decades of the study ($\chi^2=3.3$, $df=2$, $p=0.072$). Of the 42 cases of orbital and adnexal lymphomas, 27 (64.3%) were male, 40 (95.2%) were unilateral, 23 (54.8%) were in the orbit. The mean age of Saudi patients with orbital and adnexal lymphomas was 38.9 ± 24.5 years. They were equally distributed over the 3 decades of the study ($\chi^2=0.52$, $df=2$, $p=0.518$).

Discussion. This study presents an analysis of a large cohort of patients with ocular and adnexal neoplasms among the Saudi population. The information in the registry spans 30 years, and provides trends for the ophthalmic malignancies over time. The range of experts and subspecialists with expertise in ophthalmic oncology at this tertiary eye care hospital providing care and pathologic confirmation of most tumors indicates that the diagnoses recorded in the TR are reliable. The use of ICD10-AM,⁸ a tool that is widely accepted for grouping neoplasms minimized the risk of misclassification. We believe that the capture rate for malignant ophthalmic tumors from this hospital-based registry provide reasonable national estimates, and the incidence might be only slightly under represented for a variety of reasons. The ophthalmic oncology services remain the main provider of ophthalmic oncology related care in the Kingdom until the last 5 years, where subspecialists trained in ophthalmic plastics are managing periocular cancers; the only group that might be slightly under represented in this registry. General oncology units of other government institutions work in collaboration with KKESH, but do not entertain patients with ophthalmic malignancies directly without consulting the ophthalmic oncologists of KKESH. Hence, all cases with suspected ophthalmic malignancies that need management are referred to KKESH. Even

for treatment abroad under the sponsorship of the government, a letter has to be obtained from experts and administrators of KKESH. Therefore, the incidence of ocular and adnexal malignancies noted in our study is likely to be a reasonable estimate of the entire Saudi population.

A previous study of ocular and adnexal MT was undertaken in 1991 at KKESH with data that spanned 8 years. The authors of this study had suggested that the incidence of ocular malignancies in the Saudi population was different and unique compared with those in the Western countries.^{8,11} The present study confirms earlier observations, provides reasonable population estimates, highlights some unique features of malignant tumors in the Saudi population, and provides information on a 30-year trend. Typically, a national cancer registry monitors malignancies at a national level. The national cancer registry was initiated in 1999 in KSA, whereas the data in the current registry that focused on ophthalmic malignancies is in existence since 1983.

The incidence of Rb in our study was 7.7/M/Y in Saudi children less than 5 years of age. This was lower than that reported in Jordan (9.2/million), and in Oman (8.3/million), but higher than that reported in Western countries where the incidence of Rb was reported to be as low as 3.7/million.¹²⁻¹⁴ As more effective treatment is available within the last decade, more eyes are treated conservatively, and fewer enucleations are performed globally. The KKESH TR includes both Rb cases that were confirmed by histopathology, and eyes treated with chemotherapy, or other modalities. Hence, the lower incidence in our study compared to the rate reported in other countries in the region requires further explanation. It is unlikely that the access to care for patients with Rb, or patients traveling to another country for treatment caused the lower incidence as the Ministry of Health hospitals and private hospitals have excellent referral systems for care of Rb patients who are directed to KKESH, and all requests for care outside the Kingdom are processed through the Ministry of Health.

In our study, the proportion of bilateral Rb was 30%. Another study from KSA in 2002 reported that 75% of children with Rb aged 5-12 years had unilateral Rb, and 25% had bilateral Rb.¹⁵ Bilateral cases are typically hereditary, and the decrease in the rate of bilateral Rb compared with the report from 1997 is a better sign as mortality has been reported to be higher among children with bilateral disease.¹⁶ It may reflect better awareness of the genetic transmission among families with Rb.¹⁴ The proportion of bilateral Rb cases in our study was slightly higher than that reported in Central America (24%) in

2012,¹¹ and 24.6% in the USA (1975-1995),¹⁷ and was lower than that reported in UK in 1963-2002 (36.3%).¹⁸ The ratio of unilateral versus bilateral Rb in children less than one year was significantly higher than among children of more than one year of age in our study. Karcioğlu et al¹⁵ also reported the ratio of unilateral to bilateral Rb cases in children aged less than one year as 2.8:1, and in older children as 4:1. Bilateral Rb is often hereditary, and these children often present earlier than unilateral cases.¹⁹

The incidence of SCC was 200/100,000 and 50/1000,000 for BCC in our study. The highest reported incidence for BCC was 299/100,000 and for SCC was 118/100,000 both from New Zealand.²⁰ A study in southwestern KSA also noted that 70% of skin cancer was due to SCC and BCC, and 90% of BCC were located in the head and neck areas.²¹ It is surprising that the incidence is relatively low in our study despite the exposure of the Saudi population to extreme heat and sunlight throughout the year, which are known risk factors for skin cancers.²² The incidence of skin cancers from the Saudi cancer registry has not been reported. However, non-melanotic skin cancer in 2000 accounted for 3.6% (369/10,152) of all cancer cases in adult Saudis, and in 2004 it was 4.05% (259/6,380).²³ The incidence of skin cancers in this study is, however, comparable to that reported from neighboring Jordan, where the rates of SCC were reported as 23.3/100,000 in females and 19.7 in males.²⁴

The low incidence of periocular skin cancers in the Saudi population compared with countries with similar arid and sunny climates could be due to the use of traditional garments that cover the head, face, and neck providing protection from direct sunlight in both genders.²⁵ Additionally, legally banned alcohol, lower human papillomavirus infection rates (HPV), and possible genetic factors among the Saudi population may contribute to the lower rates of SCC.²⁶ Although the number of cases of SCC seen at KKESH remained stable over time, BCC significantly increased over time in both the male and female population. The reasons for selective increase in BCC cases are unclear. The BCC is a slow growing tumor of the elderly. It is possible that earlier diagnosis by referring physicians, or the increased life expectancy among Saudis could have contributed to this increase.²⁷ A study from Iran suggested that there was a rising trend of skin cancer in 6 provinces.²⁸

In this study, we used age-gender standardized World Health Organization population in the year 2000 and 2005 to compare the trend by time. Therefore, comparison of the Iranian results with our

study outcomes, which is based on the data over 3 decades, and without using global population as an index should be carried out with caution. The rates of skin cancer are significantly greater in males compared to females globally.²⁹ A previous study in KSA described a higher risk of non-melanotic skin cancer among males compared with females.²⁵ The results reported from this TR were comparable to this previous study.²⁵ The gender difference in periocular skin related malignancies as observed in our study could be due to the additional protection conferred by the traditional use of a face cover (veil), and infrequent participation in outdoor activities by females.²² The incidence of uveal melanoma among the adult Saudi population was similar to the low incidence reported in India.³⁰ However, the mean age of patients with malignant melanoma in an Indian population was lower (45.9±14.8 years) than that reported in our study (53.1±17.3 years), and in a study on a Western population (60±16 years).^{30,31}

One limitation of this study related to melanomas is that the TR only included cases that were diagnosed and treated by enucleation, or biopsy at the hospital. It did not include cases of small and medium-sized tumors that might have been treated by other modalities (brachytherapy), and without tissue diagnosis. There were 5 cases of early uveal melanomas that were conservatively treated with plaque therapy in the same period (personal communication from data obtained from the KKESH operating room log book). Therefore, the registry may under represent the incidence of uveal melanoma in KSA in the last few years. The data from the KKESH TR concurs with observations reported by Al-Suhaibani et al³² who highlighted the low incidence of uveal melanoma in KSA compared with Western populations.

The SGC of the eyelid is a rare malignant tumor that can be associated with high mortality unless treated aggressively.³³⁻³⁵ The higher incidence of SGC in females is worth noting in our study. Exposure to dust and prolonged use of Kohl, an indigenous herbal mascara applied to the lids is frequent among females in the Middle Eastern countries, and may be a contributing factor in SGC.³⁶ Further research is recommended to study the biological and clinical behavior of SGC, and survival rates of patients within the Saudi population.

Orbital and adnexal lymphomas in our study were evenly distributed over the last 3 decades. This is in contrast to a report of a rising trend of the incidence of non-Hodgkin's ocular lymphomas in the United States.³⁷ The mean age of 52.7 years when non-Hodgkin's ocular lymphomas was detected in our study appeared to be

lower than that reported in the West, where the average age for the onset of ocular and adnexal lymphomas is in the 60's.³⁸ Most patients had non-Hodgkin's type lymphoma, which is similar to that reported from the West.³⁷

In summary, the analysis of the TR at KKESH presents a 30-year overview of malignant neoplasms seen at this institution. The incidence of ocular malignant neoplasms calculated from this hospital-based registry provides a reasonable estimate for the Kingdom because of the nature of ocular oncology practices, and referral in the Kingdom. The data is robust for intra-ocular, orbital, and ocular surface malignancies, since specialized treatments are available only at KKESH. For eyelid and periocular malignancies, the registry may slightly under represent the incidence of skin cancers, since more oculoplastic specialists provide surgical care in the Kingdom in the last 5 years. The registry however, showed stable rates of SCC, but a significant increase in BCC over the last 3 decades.

One potential weakness of the TR is that the data for malignant neoplasms is mainly derived from cases that had histopathologic diagnosis at KKESH (other than Rb). However, we believe that the registry captured most of the cases of malignant neoplasms, other than those rare cases with malignant tumors that were unfit for treatment, and were referred to a general hospital for treatment after initial evaluation.

In summary, the study describes malignant ocular neoplasms in KSA. All cancers remained stable over 3 decades except BBC.

Acknowledgment. *The authors gratefully acknowledge Mr. Rich Bains for assisting in English editing of the manuscript.*

References

- Bai S, Ren R, Shi J, Xu X, Zhao J, Gao F, et al. Retinoblastoma in the Beijing Tongren Hospital from 1957 to 2006: clinicopathological findings. *Br J Ophthalmol* 2011; 95: 1072-1076.
- Shields CL, Demirci H, Karatza E, Shields JA. Clinical survey of 1643 melanocytic and nonmelanocytic conjunctival tumors. *Ophthalmology* 2004; 111: 1747-1754.
- MacCarthy A, Bunch KJ, Fear NT, King JC, Vincent TJ, Murphy MF. Paternal occupation and retinoblastoma: a case-control study based on data for Great Britain 1962-1999. *Occup Environ Med* 2009; 66: 644-649.
- Alkatan HM, Al-Arfaj KM, Maktabi A. Conjunctival nevi: Clinical and histopathologic features in a Saudi population. *Ann Saudi Med* 2010; 30: 306-312.
- Alfawaz AM, Al-Hussain HM. Ocular manifestations of xeroderma pigmentosum at a tertiary eye care center in Saudi Arabia. *Ophthalm Plast Reconstr Surg* 2011; 27: 401-404.
- About KKESH. King Khaled Eye Specialist Hospital. [Accessed 2012 December 29]. Available from: <http://www.kkesh.med.sa>
- Research Department. King Khaled Eye Specialist Hospital. [Accessed 2012 December 29]. Available from: <http://rd.kkesh.med.sa>
- Malignant and benign neoplasm of eye in 'The International Statistical Classification of Diseases and Related Health Problems. 10th revision, Australian Modification (ICD-10-AM). National Centre for Classification in Health. Lidcombe (AUS): ISCDRHP; 2008. p. 45-58.
- Dean AG, Sullivan KM, Soe MM. OpenEpi: Open Source Epidemiologic Statistics for Public Health version 2.3. [updated 20 May 2009. accessed 29 January 2012] Available from: www.OpenEpi.com
- Huaman A, Cavender JC. Tumors of the eye in Saudi Arabia. *Ann Saudi Med* 1991; 11: 675-680.
- Young JL, Smith MA, Roffers SD, Liff JM, Bunin JR. Retinoblastoma in Cancer Incidence and Survival among Children and Adolescents: United States SEER Program 1975-1995. SEER Pediatric Monograph. Bethesda (MD): National Cancer Institute; 1999. p. 73-78.
- Jaradat I, Yousef YA, Mehyar M, Sultan I, Khurma S, Al-Rawashded K, et al. Retinoblastoma in Jordan: an epidemiological study (2006-2010). *Hematol Oncol Stem Cell Ther* 2011; 4: 126-131.
- Khandekar R, Ganesh A, Al Lawati J. A 12-year epidemiological review of retinoblastoma in Omani children. *Ophthalmic Epidemiol* 2004; 11: 151-159.
- Gatta G, Capocaccia R, Coleman MP, Ries LA, Berrino F. Childhood cancer survival in Europe and the United States. *Cancer* 2002; 95: 1767-1772.
- Karcioglu ZA, Abboud EB, Al-Mesfer SA, Al-Rashed W, Pilapil DH. Retinoblastoma in older children. *J AAPOS* 2002; 6: 26-32.
- Shinohara ET, DeWees T, Perkins SM. Subsequent malignancies and their effect on survival in patients with retinoblastoma. *Pediatr Blood Cancer* 2014; 61: 116-119.
- Luna-Fineman S, Barnoya M, Bonilla M, Fu L, Baez F, Rodríguez-Galindo C. Retinoblastoma in Central America: report from the Central American Association of Pediatric Hematology Oncology (AHOPCA). *Pediatr Blood Cancer* 2012; 58: 545-550.
- MacCarthy A, Birch JM, Draper GJ, Hungerford JL, Kingston JE, Kroll ME, et al. Retinoblastoma in Great Britain 1963-2002. *Br J Ophthalmol* 2009; 93: 33-37.
- Zafar SN, Ahmad SQ, Zafar N. Retinoblastoma in an adult. *BMC Res Notes* 2013; 6: 304.
- Brougham ND, Dennett ER, Tan ST. Changing incidence of non-melanoma skin cancer in New Zealand. *ANZ J Surg* 2011; 81: 633-636.
- Al-Maghrabi JA, Al-Ghamdi AS, Elhakeem HA. Pattern of skin cancer in Southwestern Saudi Arabia. *Saudi Med J* 2004; 25: 776-779.
- Mason RS, Reichrath J. Sunlight vitamin D and skin cancer. *Anticancer Agents Med Chem* 2013; 13: 83-97.
- Al-Eid HS, Arteh SO, editors. Adult Cancers in Saudi Arabia. Cancer Registry Report Kingdom of Saudi Arabia - 2004. Riyadh (KSA): Ministry of Health; 2005. p. 22.
- Omari AK, Khammash MR, Matalka I. Skin cancer trends in northern Jordan. *Int J Dermatol* 2006; 45: 384-388.

25. Al Aboud KM, Al Hawsawi KA, Bhat MA, Ramesh V, Ali SM. Skin cancers in Western Saudi Arabia. *Saudi Med J* 2003; 24: 1381-1387.
26. Wang XI, Thomas J, Zhang S. Changing trends in human papillomavirus-associated head and neck squamous cell carcinoma. *Ann Diagn Pathol* 2012; 16: 7-12.
27. World Health Organization. Life Expectancies at Birth. In: Statistics of Saudi Arabia 2011. [Accessed 2013 July 29] Available from: <http://www.who.int/countries/sau/en/>
28. Heidari M, Najafi F. Trends of skin cancer incidence in 6 geographical regions of the Islamic Republic of Iran, 2000-2005. *East Mediterr Health J* 2013; 19: 59-65.
29. Lomas A, Leonardi-Bee J, Bath-Hextall F. A systematic review of worldwide incidence of nonmelanoma skin cancer. *Br J Dermatol* 2012; 166: 1069-1080.
30. Dhupper M, Biswas J, Gopal L, Kumar SK, Khetan V. Clinicopathological correlation of choroidal melanoma in Indian population: A study of 113 cases. *Oman J Ophthalmol* 2012; 5: 42-45.
31. Singh AD, Turell ME, Topham AK. Uveal melanoma: trends in incidence, treatment, and survival. *Ophthalmology* 2011; 118: 1881-1885.
32. Al-Suhaibani A, Chaudhry IA, Al-Harathi E, Abboud EB. Uveal melanoma in Saudi Arabia. *Ophthalmology* 2007; 114: 194.
33. Mulay K, Aggarwal E, White VA. Periocular sebaceous gland carcinoma: A comprehensive review. *Saudi J Ophthalmol* 2013; 27: 159-165.
34. Kale SM, Patil SB, Khare N, Math M, Jain A, Jaiswal S. Clinicopathological analysis of eyelid malignancies - A review of 85 cases. *Indian J Plast Surg* 2012; 45: 22-28.
35. Shields JA, Demirci H, Marr BP, Eagle RC Jr, Shields CL. Sebaceous carcinoma of the ocular region: a review. *Surv Ophthalmol* 2005; 50: 103-122.
36. Al-Ashban RM, Aslam M, Shah AH. *Kohl (surma)*: a toxic traditional eye cosmetic study in Saudi Arabia. *Public Health* 2004; 118: 292-298.
37. Moslehi R, Devesa SS, Schairer C, Fraumeni JF Jr. Rapidly increasing incidence of ocular non-hodgkin lymphoma. *J Natl Cancer Inst* 2006; 98: 936-939.
38. Ferry JA, Fung CY, Zukerberg L, Lucarelli MJ, Hasserjian RP, Preffer FI, et al. Lymphoma of the ocular adnexa: A study of 353 cases. *Am J Surg Pathol* 2007; 31: 170-184.

Related Articles

Aldebasi YH, Mohieldein AH, Almansour YS, Almutairi BL. Dyslipidemia and lipid peroxidation of Saudi type 2 diabetics with proliferative retinopathy. *Saudi Med J* 2013; 34: 616-622.

Elbably A, Mousa A, Osman EA. Selective laser trabeculoplasty after canaloplasty improves the efficacy of intraocular pressure reduction in eyes with open angle glaucoma. *Saudi Med J* 2013; 34: 544-546.

Gedik S, Gonul S, Koktekir BE, Bakbak B. In vivo confocal microscopy of corneal endothelium in patients with retinitis pigmentosa. *Saudi Med J* 2012; 33: 1330-1333.