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Rare and syndromic tumours in South African children: A novel report from Sub-Saharan Africa

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ABSTRACT

Background and Aims: There is a paucity of literature available on the prevalence of paediatric rare and syndromic tumours in Sub-Saharan Africa, furthered by a lack of consensus on the definition of a "rare" tumour. The aim of this study was to describe the types, incidence, management, and overall survival of rare and syndromic tumours in South Africa to improve future management and outcomes.

Methods: A retrospective review of patients below 18 years of age presenting to Chris Hani Baragwanath Academic Hospital, South Africa, from the period of 1st January 2004 to 31st December 2017, with rare or syndromic tumours was conducted. Tumours were classified according to criteria described by international literature. (Ethics: M190920)

Results: One hundred and eighty-six tumours were identified, with an average incidence of 10 %. The mean age of presentation was 8.3 years. Ten anatomical regions were identified: soft tissue ($N = 68$, OS= 62 %), head and neck ($N = 35$, OS= 77 %), renal ($N = 19$, OS=74 %), skin ($N = 17$, OS=47 %), hepatic ($N = 16$, OS=38 %), adrenal ($N = 10$, OS= 80 %), female reproductive system ($N = 8$, OS=75 %), pulmonary, chest wall and mediastinum ($N = 7$, OS=86 %), gastrointestinal ($N = 4$, OS=75 %) and male reproductive system ($N = 2$, OS=100 %). The 10 most common variants included: malignant peripheral nerve sheath tumours ($N = 15$, 8 %, OS=47 %), nasopharyngeal carcinoma ($N = 14$, 8 %, OS=64 %), malignant melanoma ($N = 14$, 8 %, OS=43 %), Ewings sarcoma ($N = 13$, 7 %, OS=54 %), clear cell sarcoma of the kidney ($N = 9$, 5 %, OS=67 %), hepatocellular carcinoma ($N = 9$, 5 %, OS=22 %), desmoplastic small round cell tumour ($N = 7$, 4 %, OS=57 %), synovial sarcoma ($N = 7$, 4 %, OS=71 %), undifferentiated sarcoma ($N = 6$, 3 %, OS=66 %), infantile fibrosarcoma ($N = 6$, 3 %, OS=66 %). Treatment modalities included: surgery ($N = 24$, 13 %, OS=79 %), palliation ($N = 21$, 11 %, OS=0 %), surgery and chemotherapy ($N = 19$, 10 %, OS=58 %), and surgery, chemotherapy, and radiation ($N = 16$, 9 %, OS=75 %). Thirteen (7 %) were associated with the syndromes: Xeroderma pigmentosa ($N = 4$, 2 %), Neurofibromatosis ($N = 3$, 2 %), Tuberous Sclerosis ($N = 2$, 1 %), Giant congenital nevus syndrome ($N = 2$, 1 %), Li-Fraumeni ($N = 1$, 0.5 %) and 31q Deletion syndrome ($N = 1$, 0.5 %). Overall, there was a 66 % survival rate.

Conclusion: The diagnosis of rare tumours in the paediatric population is rising but are rarely associated with a syndrome. Most require definitive surgical treatment; others required the addition of adjuvant chemotherapy and radiation. Overall, although lower than that reported in higher income countries, the prognosis of these tumours remains good.

Level of evidence: IV

Abbreviations: ACC, Adrenocortical Carcinoma; CCSK, Clear Cell Sarcoma of the Kidney; CHBAH, Chris Hani Baragwanath Academic Hospital; DSRCT, Desmoplastic Small Round Cell Tumour; GCNS, Giant Congenital Nevus Syndrome; GIT, Gastrointestinal; HCC, Hepatocellular Carcinoma; MIBG, Meta-iodobenzylguanidine; MPNST, Malignant Peripheral Nerve Sheath Tumour; NF, Neurofibromatosis; NPC, Nasopharyngeal Carcinoma; OS, Overall Survival; PCC, Phaeochromocytoma; PGL, Paraganglioma; SA, South Africa; SCC, Squamous Cell Carcinoma; STT, Soft Tissue Tumours; TS, Tuberous Sclerosis; XP, Xeroderma Pigmentosa.

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Introduction

The literature on rare childhood tumours, their treatment and prognosis, remains minimal with a lack of international collaboration between researchers. Furthermore, the definition of a "rare" childhood tumour varies globally, making it challenging for South African researchers and doctors to rely on international literature for guidance. A tumour is considered rare if there is: (1) no consensus on its management protocol, (2) it is considered an adult type presenting in children, (3) it presents atypically at the extremes of the expected age group, (4) if considered rare but typical to childhood, (5) if it is a common paediatric tumour occurring in a rare location [1], (6) if it presents with either an unusually differentiated histology or a histological variant of a defined rare tumour [2], or (7) if the tumour's incidence is <15 per 100,000 persons/year [3].

Previous research into the topic suggests that rare paediatric tumours account for 10 % of all childhood cancers [4]. Currently, worldwide data and treatment standards are being applied to rare and syndromic tumours presenting in South African. Through reviewing the: incidence, type, treatment, and overall survival rates of rare and syndromic tumours presenting to the Chris Hani Baragwanath Academic Hospital (CHBAH) paediatric oncology and surgery departments between 2004 and 2017, this research aims to contribute to the body of literature whilst providing valuable information on the treatment and epidemiological data of this population. CHBAH's paediatric oncology department is the largest in South Africa with a referral base that extends across South Africa and includes countries of the Southern African Development Community [5].

Method

A retrospective review of patients below 18 years of age presenting to CHBAH paediatric oncology and surgery departments in South Africa (SA) was conducted. Cases were selected using a set of criteria that had been previously described in the literature of rare tumours. This review included all paediatric patients, presenting with a rare/syndromic tumour between 1st January 2004 and 31st December 2017.

Data was obtained using the CHBAH paediatric oncology and surgery registries and the associated patient files. Variables collected included: patient demographics, anatomical distribution, histological classification, predisposing syndromes, treatment modalities and overall survival (OS).

Average tumour incidence was calculated using the total number of rare tumour cases divided by the total number of oncology cases that presented to the paediatric oncology and surgery centres during the study period. The annual incidence trend and yearly overall survival rates were depicted using line graphs. Rare tumour types were expressed as a proportion of both the total number of rare tumours and the total number per anatomical region. Descriptive variables were interpreted using frequencies and percentages. Age was described using mean and standard deviation values. Data was represented using line graphs and frequency tables. Human Research Ethics Committee Clearance: M190920

Results

Seven percent ($N = 186$) of all paediatric malignancies ($N = 2747$) were deemed rare or syndromic. Yearly incidence rates (Fig. A.1) fluctuated over the fourteen years resulting in an average of 10 %. The greatest number of rare tumours was identified in 2013 ($N = 23$). Tumours presented twice more commonly in males with a mean age of 8.3 years 95 % CI (7.6–9.0). Anatomical distribution, histological variants, treatment modalities and survival rates are depicted in Table B.1.

Rare tumours occurred in ten anatomical regions: soft tissue (STT) ($N = 68$, 37 %), head and neck ($N = 35$, 19 %), renal ($N = 19$, 10 %), skin ($N = 17$, 9 %), hepatic ($N = 16$, 9 %), adrenal ($N = 10$, 5 %), female reproductive ($N = 8$, 4 %), pulmonary, chest wall and mediastinum ($N = 7$, 4 %), gastrointestinal (GIT) ($N = 4$, 2 %) and male reproductive ($N = 2$, 1 %). The 10 most common histological variants were: malignant peripheral nerve sheath tumours (MPNST) ($N = 15$, 8 %, OS=47 %), nasopharyngeal carcinoma (NPC) ($N = 14$, 8 %, OS=64 %), malignant melanoma ($N = 14$, 8 %, OS=43 %), Ewings sarcoma ($N = 13$, 7 %, OS=54 %), clear cell sarcoma of the kidney (CCSK) ($N = 9$, 5 %, OS=67 %), hepatocellular carcinoma (HCC) ($N = 9$, 5 %, OS=22 %), desmoplastic small round cell tumour (DSRCT) ($N = 7$, 4 %, OS=57 %), synovial sarcoma ($N = 7$, 4 %, OS=71 %), undifferentiated sarcoma ($N = 6$, 3 %, OS=66 %) and infantile fibrosarcoma ($N = 6$, 3 %, OS=66 %).

One percent ($N = 27$) of all paediatric malignancies ($N = 2747$) were associated with a genetic syndrome. Seven percent ($N = 13$) of rare tumours were associated with a concurrent syndrome, namely: Xeroderma Pigmentosa (XP) ($N = 4$, 2 %), Neurofibromatosis (NF) ($N = 3$, 2 %), Tuberous Sclerosis (TS) ($N = 2$, 1 %), Giant congenital nevus syndrome (GCNS) ($N = 2$, 1 %), Li-Fraumeni ($N = 1$, 0.5 %) and 31q Deletion syndrome ($N = 1$, 0.5 %). Whilst the literature states 3 % of all

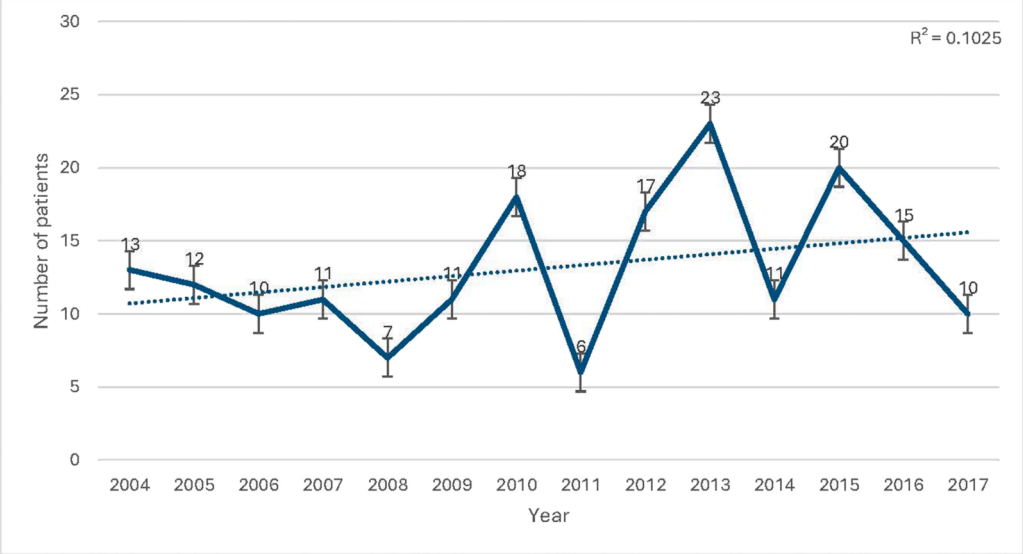

Fig. 1. A Line Graph Showing the Yearly Incidence Rates of Rare and Syndromic Tumours Presenting to CHBAH Paediatric Oncology and Surgery Departments from 2004 to 2017.

Table 1
Rare Tumours Presenting to the CHBAH Paediatric Oncology and Surgery Departments for the Period of 2004–2017; the Respective Treatment Modalities and Overall Survivals Represented per Anatomical Region.

Tumour location and number (%)	Mean age of population (years)	Tumour Histology Subtype	Tumour number per subtype (%)	Survival per subtype (%)	Treatment modalities per anatomical region **			Overall survival per anatomical region (%)
					Type	Number (%)	Survival (%)	
Total: 186 (100)	8.3							66
Soft Tissue N=68 (37%)	8.3	Malignant Peripheral Nerve Sheath Tumour [NF: N=2 (13%)] *	15 (22)	47 [100] *	Trimodal Therapy:	10 (15)	80	62
		Ewings Sarcoma	13 (19)	54	Dual Therapy:			
		Synovial Sarcoma	7 (10)	71	- S/C	4 (6)	25	
		Desmoplastic Small Round Cell Tumour	7 (10)	57	- S/R	1 (1)	100	
		Undifferentiated Sarcoma	6 (9)	66	- C/R	1 (1)	100	
		Infantile Fibrosarcoma	6 (9)	66	Monotherapy:			
		Embryonal Rhabdomyosarcoma [13q: N=1 (25%)] *	4 (7)	75 [100] *	- S	11 (16)	73	
		Leiomyosarcoma	3 (5)	33	- C	2(3)	0	
		Giant Cell Fibroblastoma	3 (5)	66	Palliation:	7(10)	0	
		Dermatofibrosarcoma Protuberans	1 (1)	100				
		Myoepithelioma of the Breast	1 (1)	100				
		Angiosarcoma	1 (1)	100				
		Myofibrosarcoma	1 (1)	100				
Head and Neck N=35 (19%)	8.2	Nasopharyngeal Carcinoma	14 (40)	64	Dual Therapy			77
		Mucoepidermoid Carcinoma	5 (13)	100	- S/R	4(11)	100	
		Acinic Cell Carcinoma	4 (11)	75	- S/C	2(6)	50	
		Pleomorphic Adenoma	3 (9)	100	- C/R	2(6)	100	
		Inflammatory Myofibroblastic Tumour	3 (9)	100	Monotherapy:			
		Thyroid Carcinoma	3 (9)	66	- S	6(17)	67	
		Immature Thyroid Teratoma	1 (3)	100	- C	1(3)	100	
		Olfactory Neuroblastoma	1 (3)	0	Palliation:	2(6)	0	
		Thyroid Cystic Teratoma	1 (3)	100				
Renal N=19 (10%)	7.7	Clear Cell Sarcoma	9 (47)	67	Trimodal Therapy:	5 (28)	80	74
		Nephroblastoma (Age>10 years)	6 (32)	83	Dual Therapy:			
		Angiomyolipoma [TS: N= 2 (100%)] *	2 (11)	[100] *	- S/C	3 (17)	67	
		Renal Cell Carcinoma	1(5)	100	Monotherapy:			
					- S	1(6)	100	
		Plexiform Neurofibroma [NF: N=1 (100%)]*	1(5)	0[0]*	Palliation:	1 (6)	0	
Skin N=17 (9%)	8.2	Malignant Melanoma [XP : N=4 (29%) / GCNS : N=2 (14%)]*	14 (82)	43 [75/50] *	Trimodal Therapy:	1 (6)	0	47
		Squamous Cell Carcinoma [XP : N=1 (33%)] *	3 (18)	66 [0] *	Dual Therapy:			
					- S/R	1 (6)	0	
					Monotherapy:			
					- R	2 (12)	100	
					- S	1 (6)	100	
					Palliation:	6 (35)	0	
Hepatic N=16 (9%)	8.4	Hepatocellular Carcinoma	9 (56)	22	Dual Therapy:			38
		Mesenchymal Hamartoma	3 (19)	66	- S/C	2 (13)	100	
		Rhabdomyosarcoma	3 (19)	33	Monotherapy:			
		Undifferentiated Sarcoma	1 (6)	100	- C	1(6)	0	
					Palliation	4 (25)	0	
Adrenal	7.9	Pheochromocytoma	5 (50)	100	Dual Therapy:			80
N=10 (5%)		Neuroblastoma (Age > 10 years)	2 (20)	50	- S/C	4(40)	75	
		Adrenocortical Carcinoma [LFS : N=1 (50%)] *	2 (20)	50 [0] *	Monotherapy:			
		Extra-adrenal Pheochromocytoma/ Paraganglioma	1 (10)	100	- C	1(10)	0	
					- S	1(10)	100	
Female Reproductive System N=8 (4%)	8.9	Ovarian N=6 (75%) — Juvenile Granulosa Cell	2 (25)	50	Dual Therapy			75
		Ovarian N=6 (75%) — Mucinous Cystadenoma	1 (12)	100	- S/C	2(25)	50	
		Ovarian N=6 (75%) — Fibrosarcoma	1 (12)	0	Monotherapy			
		Ovarian N=6 (75%) — Leydig Cell	2 (25)	100	- S	2(25)	100	
		Vaginal N=2 (25%) — Adenocarcinoma	1 (12)	100				
		Vaginal N=2 (25%) — Germ Cell Tumour	1 (12)	100				
Pulmonary/ Chest Wall/Mediastinal N=7 (4%)	9.3	Pulmonary N=4 (57) — Mucoepidermoid Carcinoma of the Bronchus	3(44)	100	Dual Therapy:			86
		Pulmonary N=4 (57) — Bronchoalveolar Carcinoma	1(14)	0	- S/C	1(14)	100	
		Chest Wall N=1 (14) — Plexiform Neurofibroma	1(14)	100				
		Mediastinal N=2 (29) — Thymolipoma	1(14)	100				
		Mediastinal N=2 (29) — Teratoma	1(14)	100				
Gastrointestinal System N=4 (2%)	8.2	Kaposiform Haemangioendothelioma of the Pancreas	1 (25)	100	Dual Therapy:			75
		Pancreatic Gastrinoma	1 (25)	0	- S/C	1(25)	100	
		Signet Ring Adenocarcinoma of Sigmoid Colon	1 (25)	100	Monotherapy:			
		Solid Pseudopapillary Carcinoma of the Pancreas	1 (25)	100	- S	1(25)	100	
					- C	1(25)	100	
					Palliation	1(25)	0	
Male Reproductive System N=2 (1%)	15	Leydig Cell	1 (50)	100	Monotherapy:			100
		Seminoma	1 (50)	100	- S	2 (100)	100	

NF- Neurofibromatosis, TS-Tuberous Sclerosis, XP- Xeroderma Pigmentosa, GCNS- Giant Congenital Nevus Syndrome, LFS - Li Fraumeni Syndrome, 13q- 13q Deletion Syndrome, Trimodal Therapy- Surgery and Adjuvant Chemotherapy and Radiation, S- Surgery, C- Chemotherapy, R- Radiation, S/C- Surgery and Chemotherapy, S/R- Surgery and Radiation, C/R- Chemotherapy and Radiation.
*Represents a rare tumour associated with a concurrent syndrome.
**Treatment modalities were described, in 53 % of cases.

paediatric malignancies as being associated with a genetic syndrome [6], this proportion was less (1 %) of which only 0.4 % of cases were considered rare. These associations are depicted in Table B.1.

Treatment modalities were specified in 53 % ($N = 98$) of cases. Eight common modalities were identified: definitive surgery ($N = 24$, 13 %, OS= 66 %); palliative care ($N = 21$, 11 %, OS= 0 %); surgery and chemotherapy ($N = 19$, 10 %, OS=58 %); surgery, chemotherapy, and radiation ($N = 16$, 9 %, OS=75 %); chemotherapy ($N = 6$, 3 %, OS=33 %); surgery and radiation ($N = 6$, 3 %, OS=83 %); chemotherapy and radiation ($N = 3$, 2 %, OS= 100 %) and radiation alone ($N = 2$, 1 %, OS=100 %). Four (2 %) patients defaulted treatment and 2 (1 %) demised prior to receiving treatment. Rare tumours had an average OS

rate (Fig. A.2) of 66 % (*N* = 122).

Discussion

Soft tissue tumours

Soft tissues (*N* = 68, 37 %) were the commonest site for rare tumours and formed 2 % of the total number of paediatric malignancies. This was lower than the 6 % documented internationally [7]. The mean age of presentation of 8.3 years 95 % CI (6.3–9.4) was older than 5 years with a female predilection (*N* = 38, 56 %) [8]. Thirteen histological variants were identified (Table B.1). Of these, synovial sarcoma (10 %), infantile fibrosarcoma (9 %) and undifferentiated sarcoma (9 %) presented less commonly than in the European population (19 %, 33 %, 19 %) [7,8,9]. Conversely, DSRCTs (10 %) and MPNSTs (22 %) occurred more frequently [7,8,9]. MPNSTs formed the largest proportion of STTs (*N* = 15, 22 %) of which 13 % (*N* = 2) were associated with NF. This is a greater association than that found in the United Kingdom (1–2 %) [10]. One (25 %) embryonal rhabdomyosarcoma (*N* = 4, 7 %) was associated with 13q deletion syndrome. The most frequent treatment modalities were surgical excision (*N* = 11, 16 %, OS=73) and trimodal therapy (*N* = 10, 15 %, OS=80 %). Fifteen percent (*N* = 10) of rare STT were treated using the recommended method of trimodal therapy for which the overall survival (80 %) was higher than the 70 % reported [11]. Rare STTs had an average OS of 62 % (*N* = 42) of which leiomyosarcoma had the poorest prognosis (OS=33 %, *N* = 1).

Tumours of the head and neck region

Rare tumours of the head and neck constituted 1 % of all paediatric malignancies and 19 % (*N* = 35) of rare tumours. The mean age of presentation was 8.2 years 95 % CI (6.5–9.9) with 66 % (*N* = 23) being female in gender. Contrary to the literature, malignant tumours (77 %) were more prevalent than benign (23 %) [12]. Of the 9 variants identified (Table B.1), NPC (*N* = 14, 40 %) was the most common with an average incidence of 0.5 %. This is below the international incidence (1–5 %) but is in keeping with South Africa not being an endemic country [13]. Rare thyroid tumours also had an overall incidence (0.2 %) lower than previously stated (6 %) [14]. Surgical excision (*N* = 6, 17 %, OS=67 %) was the most common treatment modality. Tumours had an average OS of 77 % (*N* = 27). NPC had the poorest prognosis (OS=64 %, *N* = 9) which was below the 77 % reported. The literature describes: (1) presenting age older than 14 (*N* = 7, 50 %), (2) male gender (*N* = 6, 43 %) and (3) stage 3 disease (*N* = 2, 14 %) as being unfavourable for NPC survival [15]. These factors were present in 79 % (*N* = 11) of NPC cases of which 36 % (*N* = 4) demised.

Renal tumours

Rare renal tumours (*N* = 19, 10 %) had a lower incidence rate (1 %) than common renal tumours in the same population group (5 %) [16]. The age of presentation (7.7 years) was older than that of common tumours (3.7 years), with an equal gender distribution [16]. Of the five variants (Table B.1), CCSK (*N* = 9, 47 %) was the most common and occurred more frequently than is internationally recognised (19 %) [17]. The prevalence of angiomyolipoma (11 %) and renal cell carcinoma (5 %) was equal to and less than previously reported values (11 %, 11 %) [18]. Both (100 %) cases of angiomyolipoma (*N* = 2, 11 %) were associated with TS. One (100 %) plexiform neurofibroma (*N* = 1, 5 %) was associated with NF. The most common treatment modality was trimodal (*N* = 5, 28 %, OS= 80 %). Rare renal tumours had an OS of 74 % (*N* = 14), with CCSK having the poorest prognosis (OS=67 %, *N* = 6). Literature states a 5-year OS of 90 % for early-stage CCSK treated with intensive chemotherapy [19,20]. Fifty six percent of cases were diagnosed at stage 3 or higher with 45 % having undergone a surgical nephrectomy with adjuvant chemotherapy or radiation.

Tumours of the skin

Skin malignancies had an average incidence in keeping with the 1 % described [21]. Previous studies on the epidemiology of paediatric melanomas describe a higher rate of presentation in older children and females [22]. Conversely, 57 % of this predominantly male (*N* = 9, 53 %) population were below the age of 10 with a mean age of presentation of 8.2 years 95 % CI (5.8–10.6). Seventeen (9 %) rare tumours were identified namely: malignant melanoma (*N* = 14, 82 %) and squamous cell carcinoma (SCC) (*N* = 3, 18 %). Six (35 %) tumours were associated with a concurrent syndrome. Of the melanoma cases, 4 (29 %) were associated with XP and 2 (14 %) with GCNS. One tumour (25 %) showed histology of both malignant melanoma and SCC and was also associated with XP. The literature describes that 22 % of paediatric melanomas have a non-modifiable risk factor like the above-mentioned syndromes (36 %) [22]. Treatment commonly involved the use of radiation (*N* = 2, 12 %, OS= 100 %) however, despite intervention, 6 (35 %) progressed to palliation. Skin Tumours had an average OS of 47 % (*N* = 8). The OS (87–95 %) for paediatric melanoma has improved worldwide [22],

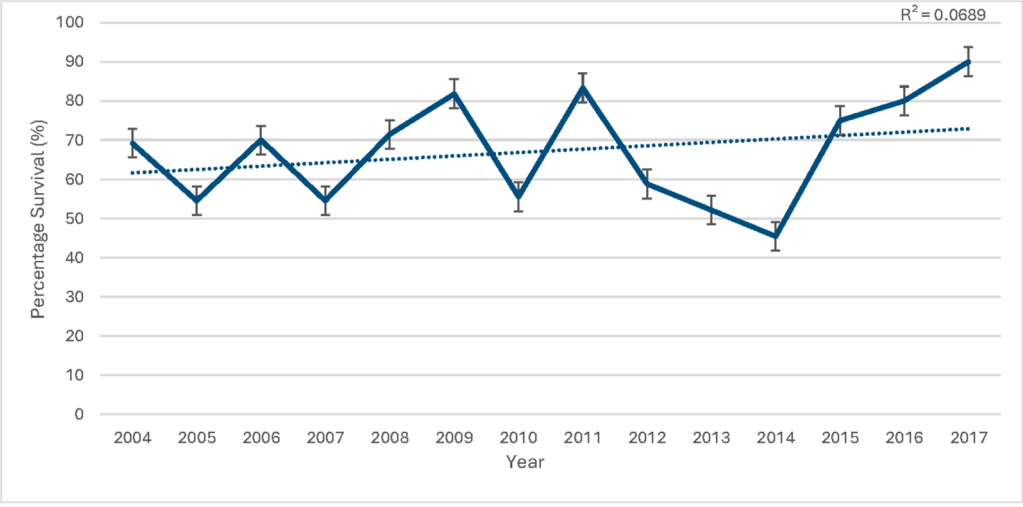

Fig. 2. A Line Graph Showing the Yearly Overall Survival Rates Associated with Rare and Syndromic Tumours presenting to CHBAH Paediatric Oncology and Surgery Departments from 2004 to 2017.

however, the prognosis in SA children is poor (OS=43 %).

Hepatic tumours

Rare hepatic tumours had an overall incidence of 1 % with a total number of sixteen (9 %). This frequently male ($N = 10$, 63 %) population had a mean age of 8.4 years 95 % CI (5.9–10.9). Of the 4 variants (Table B.1), HCC ($N = 9$, 56 %) was the most common with an overall incidence of 0.3 %. This is below the 1 % incidence rate previously reported [23]. In the Sub-Saharan paediatric population, HCC had previously occurred at a mean age of 13 years [24]. Rare tumours of the liver had an average OS of 38 % ($N = 6$) with HCC having the poorest prognosis (OS=22 %, $N = 2$). The combination of aggressive chemotherapy regimens and surgical resection is reported to be the most successful in the treatment of paediatric HCC [23]. Globally, the OS of HCC is 28 % with the presence of metastases being the strongest predictor for poor prognoses [24]. Of the HCC cases that demised ($N = 7$, 78 %), 3 (43 %) had distant metastases at the time of presentation.

Adrenal tumours

Five percent of rare paediatric tumours originated in the endocrine system; this is higher than is previously reported (3 %) [1]. Ten (5 %) adrenal tumours were identified. Whilst Adrenocortical carcinoma (ACC) was thought to be the most common, phaeochromocytoma (PCC) presented in 50 % ($N = 5$) of cases (Table B.1) [25]. The reported age of presentation for PCC and paraganglioma (PGL) is 11–13 years with a male predominance [26]. Patients were found to present much younger [7.9 years 95 % CI (5.2–10.7)] with an equal gender distribution. The following genetic syndromes: multiple endocrine neoplasia type 2, Von Hippel–Lindau type 2 and NF-1 have been associated with PCCs and PGLs [26]. Only 1 (50 %) ACC ($N = 2$, 20 %) was found to be associated with Li-Fraumeni syndrome. The common treatment modality was surgical excision and adjuvant chemotherapy ($N = 4$, 40 %, OS= 75 %). One (10 %) PCC was treated with adrenalectomy and Meta-iodobenzylguanidine (MIBG) (OS =100 %). When treated with the recommended methods of surgical resection, chemotherapy and/or radiation, 100 % ($N = 6$) of PCC and PGLs survived. Adrenal tumours had a good OS of 80 % ($N = 8$), with the two mortalities being an ACC associated with Li-Fraumeni syndrome and a neuroblastoma. This OS is higher than the 78 % reported [26].

Tumours of the female reproductive system

It is estimated that gynaecological malignancies account for 4 % of all malignancies in girls aged 0–18 years [27]. This population differed with an average incidence of 0.3 %. These females (100 %) had a mean age of 8.9 years 95 % CI (6.5–11.3). Of the 8 (4 %) rare tumours identified, 6 (75 %) were ovarian and 2 (25 %) were vaginal (Table B.1). In keeping with international literature, germ cell tumours of the ovary were the most common [27,28]. Two (25 %) females presented with an ovarian tumour histologically diagnosed as a Leydig cell tumour. When considering treatment for these patients, surgical procedures that preserve future fertility and endocrine function should be favoured [28]. Four (50 %, OS=75 %) cases underwent surgical excision, 2 (50 %, OS=50 %) of which required adjuvant chemotherapy. Rare gynaecological malignancies have a good prognosis (OS=96 %) worldwide, however, this (OS=75 %) was less evident in SA [27].

Pulmonary, chest wall and mediastinal tumours

Pulmonary malignancies in children are considered extremely rare [29].This finding was supported by an average incidence of 0.2 %. This female (100 %) population presented at a mean age of 9.3 years 95 % CI (5.7–12.9). Of the 7 (4 %) tumours identified, 4 (57 %) were pulmonary in origin, 1 (14 %) originated in the chest wall and 2 (29 %) in the mediastinum (Table B.1). Of the pulmonary tumours, 75 % are malignant with the most common variants being: plasma cell granulomas, pleuro-pulmonary blastomas, mucoepidermoid carcinoma and endobronchial fibrosarcoma [30]. Only two pulmonary tumours were identified namely: mucoepidermoid carcinoma of the bronchus (75 %) and bronchoalveolar carcinoma (25 %). The mainstay of treatment is surgical excision [29]. The only ($N = 1$, 14 %, OS=0 %) treatment modality identified in this population was the combination of surgical excision and adjuvant chemotherapy for a bronchoalveolar carcinoma. The prognosis (OS=86 %) for pulmonary tumours was found to be higher than previously reported (43 %) [30].

Tumours of the gastrointestinal system

Rare GIT tumours had an overall incidence rate of 0.1 %. The mean age of presentation was 8.2 years 95 % CI (3.3–13.1) with an equal gender distribution. Of the variants identified, 75 % occurred in the pancreas: solid pseudopapillary carcinoma ($N = 1$, 25 %), metastatic gastrinoma ($N = 1$, 25 %) and kaposiform haemangioendothelioma ($N = 1$, 25 %). One tumour was a signet ring adenocarcinoma ($N = 1$, 25 %) of the sigmoid colon. The literature describes an increased risk of pancreatic cancers with TS syndrome [31]. This was not evident. The pseudopapillary carcinoma of pancreas was treated surgically via Whipple's procedure, the pancreatic kaposiform haemangioepithelioma with prednisone and alpha interferon, and the signet ring adenoma with surgical excision and adjuvant chemotherapy. The OS was 75 % ($N = 3$) with the only mortality being the metastatic pancreatic gastrinoma. This reinforces the literature stating a long-term survival for malignant paediatric pancreatic tumours that undergo surgical resection [32].

Tumours of the male reproductive system

Rare tumours of the male reproductive system had an incidence rate of 0.07 %, below the 2–4 % described [33]. Tumours of the male reproductive system are found to have a bimodal incidence, with yolk sac tumours presenting commonly below the age of 2 and stromal tumours between 5 and 10 years [33]. This trend was not evident as the mean age of this male (100 %) population was 15 years 95 % CI (12.0–18.0). Two (1 %) tumours were identified, namely a Leydig cell tumour ($N = 1$, 50 %) and Seminoma ($N = 1$, 50 %) (Table B.1). Stromal Leydig cell tumours (10 %) are typically less common than yolk sac tumours (15 %) [33]. Orchidectomy ($N = 2$, 100 %) was the primary treatment and resulted in an OS of 100 % ($N = 2$). This is in keeping with international literature [34].

Conclusions

The diagnosis of rare tumours in the paediatric population in South Africa is rising but are rarely diagnosed with an associated syndrome. Most require definitive surgical treatment along with adjuvant chemotherapy and radiation and have a good overall prognosis albeit lower than that reported in high income countries. Mortality was higher in those types with known aggressive behaviour.

Authors' contributions

Dr. Alessia Pisapia (Corresponding Author and Principal Investigator) and Dr. Guy Shemesh (Principal Investigator) wrote up the research proposal and collected and analysed data pertaining to this manuscript. Dr. Alessia Pisapia wrote up the manuscript while Dr. Guy Shemesh collated all graphical content. Both investigators played a role in the editing process which was overseen by Dr. Derek Harrison (Main Supervisor). Dr. Derek Harrison provided direction and leadership throughout the course of this review.

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Disclaimer

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CRediT authorship contribution statement

Alessia Pisapia: Investigation. **Guy Shemesh:** Investigation, Writing – review & editing, Writing – original draft. **Derek Harrison:** Supervision.

Declaration of competing interest

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References

[1] H.A. Heij, Rare Tumors, The Surgery of Childhood Tumors, 2nd ed., Heidelberg, Berlin, 2008.
[2] N. Boyd, J.E. Dancey, C.B. Gilks, G.Huntsman D, Rare cancers: a sea of opportunity, Lancet Oncol. 17 (2016) 52–61, https://doi.org/10.1016/S1470-2045(15)00386-1.
[3] D.T. Schneider, I.B. Brecht, T.A. Olson, A. Ferrari, Rare Tumors in Children and Adolescents, 2nd ed., Springer Nature, Cham, 2022.
[4] A.S. Pappo, W.L. Furman, K.A. Schultz, A. Ferrari, Helman L, M.D. Krailo, Rare tumors in children: progress through collaboration, J. Clin. Oncol. 33 (2015) 3047–3054, https://doi.org/10.1200/JCO.2014.59.3632.
[5] Discovery South Africa, Early detection is key to curing childhood cancer. https://www.discovery.co.za/corporate/understand-cancer-early-detection-is-key, 2019 (accessed 01 September 2024).
[6] D.P. Pruteanu, D.E. Olteanu, R. Cosnarovici, E. Mihut, V. Nagy, Genetic predisposition in pediatric oncology, Med. Pharm. Rep. 93 (2020) 323–334, https://doi.org/10.15386/mpr-1576.
[7] A. Hayes-Jordan, Recent advances in non-rhabdomyosarcoma soft-tissue sarcomas, Semin. Pediatr. Surg. 21 (2012) 61–67, https://doi.org/10.1053/j.sempedsurg.2011.10.006.
[8] M.X. Cai, C. Pan, Q.D. Ye, M. Zhou, Y.J. Gao, W.T. Hu, et al., Clinical analysis of 51 cases with rare childhood soft tissue sarcomas, Chin. J. Pediatr. 54 (2016) 917–922, https://doi.org/10.3760/cma.j.issn.0578-1310.2016.12.009.
[9] A.I. Skene, L. Barr, M. Robinsond, C. Fisher, J.M. Thomas, Adult type (non-embryonal) soft tissue sarcomas in childhood, Med. Pediatr. Oncol. 21 (1993) 645–648, https://doi.org/10.1002/mpo.2950210907.
[10] D.G.R. Evans, M.E. Baser, J. McGaughran, S. Sharif, E. Howard, A. Moran, Malignant peripheral nerve sheath tumours in neurofibromatosis 1, J. Med. Genet. 39 (2002) 311–314, https://doi.org/10.1136/jmg.39.5.311.
[11] A. Ferrari, B. Brennan, M. Casanova, N. Corradini, P. Berlanga, R.A. Schoot, et al., Pediatric non-rhabdomyosarcoma soft tissue sarcomas: standard of care and treatment recommendations from the european paediatric soft tissue sarcoma study group (EpSSG), Cancer Manag. Res 23 (2022) 2885–2902, https://doi.org/10.2147/CMAR.S368381.
[12] N.D. Dombrowski, N.E. Wolter, A.L. Irace, M.J. Cunnigham, S.O. Vargas, A. R. Perez-Atayde, et al., Pleomorphic adenoma of the head and neck in children: presentation and management, Laryngoscope 129 (2019) 2603–2609, https://doi.org/10.1002/lary.27590.
[13] E. Ozyar, U. Selek, S. Laskar, O. Uzel, Y. Anacak, M. Ben-Arush, et al., Treatment results of 165 pediatric patients with non-metastatic nasopharyngeal carcinoma: a rare cancer network study, Radiother. Oncol. 81 (2006) 39–46, https://doi.org/10.1016/j.radonc.2006.08.019.
[14] V. Poorten, G. Hens, P. Delaere, Thyroid cancer in children and adolescents, Curr. Opin. Otolaryngol. Head Neck Surg. 21 (2013) 135–142, https://doi.org/10.1097/MOO.0b013e32835e15d9.
[15] Z.J. Qian, M.C. Jin, K.D. Meister, U.C. Megwalu, pediatric thyroid cancer incidence and mortality trends in the United States, 1973-2013, JAMA Otolaryngol. Head Neck Surg. 145 (2019) 617–623, https://doi.org/10.1001/jamaoto.2019.0898.
[16] S. Mushunje, G. Naidu, D.S. Harrison, A 10-Year retrospective review of paediatric surgical oncology at Chris Hani Baragwanath academic hospital, S. Afr. J. Oncol. 3 (2019) a87, https://doi.org/10.4102/sajo.v3i0.87.
[17] K. Nakata, M. Colombet, C.A. Stiller, K. Pitchard-Jones, E. Stellarova-Foucher, et al., Incidence of childhood renal tumours: an international population-based study, Int. J. Cancer. 147 (2020) 3313–3327, https://doi.org/10.1002/ijc.33147.
[18] E. Ayaz, H.N. Ozcan, B. Oguz, M. Haliloglu, Beyond Wilms tumor: imaging findings and outcomes of rare renal tumors in children, Pediatr. Radiol. 52 (2022) 2557–2567, https://doi.org/10.1007/s00247-022-05422-7.
[19] N.L. Seibel, Y.Y. Chi, E.J. Perlman, J. Tian, J. Sun, J.R. Anderson, et al., Impact of cyclophosphamide and etoposide on outcome of clear cell sarcoma of the kidney treated on the national Wilms tumor study-5 (NWTS-5), Pediatr. Blood Cancer. 66 (2019) e27450, https://doi.org/10.1002/pbc.27450.
[20] J.A. Kalapurakal, E.J. Perlman, N.L. Seibel, M. Ritchey, J.S. Dome, P.E. Grundy, Outcomes of patients with revised stage i clear cell sarcoma of kidney treated in national wilms tumor studies 1-5, Int. J. Radiat. Oncol. Biol. Phys. 85 (2013) 428–431, https://doi.org/10.1016/j.ijrobp.2012.04.023.
[21] H. Hamm, P.H. Höger, Skin tumors in childhood, Dtsch. Arztebl. Int. 108 (2011) 347–353, https://doi.org/10.3238/arztebl.2011.0347.
[22] F.K. Saiyed, E.C. Hamilton, M.T. Austin, Pediatric melanoma: incidence, Treatment, and Prognosis, Pediatr. Health Med. Ther. 18 (2017) 39–45, https://doi.org/10.2147/PHMT.S115534.
[23] G.B. Chavhan, I. Siddiqui, K.M. Ingley, A.A. Gupta, Rare malignant liver tumors in children, Pediatr. Radiol. 49 (2019) 1404–1421, https://doi.org/10.1007/s00247-019-04402-8.
[24] P. Czauderna, G. Mackinlay, G. Perilongo, J. Brown, E. Shafford, D. Aronson, et al., Hepatocellular carcinoma in children: results of the first prospective study of the international society of pediatric oncology group, J. Clin. Oncol. 20 (2002) 2798–2804, https://doi.org/10.1200/JCO.2002.06.102.
[25] R. Mihai, Rare adrenal tumors in children, Semin. Pediatr. Surg. 23 (2014) 71–75, https://doi.org/10.1053/j.sempedsurg.2014.03.004.
[26] R. Bholah, T.E. Bunchman, Review of pediatric pheochromocytoma and paraganglioma, Front. Pediatr. 13 (2017) 155, https://doi.org/10.3389/fped.2017.00155.
[27] C. Woolmuth, I. Woolmuth-Wieser, Gynecologic malignancies in children and adolescents: how common is the uncommon? J. Clin. Med. 10 (2021) 722, https://doi.org/10.3390/jcm10040722.
[28] F.E. al Jama, A.A. al Ghamdi, T. Gasim, et al., Ovarian tumors in children and adolescents—a clinical study of 52 patients in a university hospital, J. Pediatr. Adolesc. Gynecol. (2011) 25–28, https://doi.org/10.1016/j.jpag.2010.06.005.
[29] B.W.R. Balzer, C. Loo, C.R. Lewis, et al., Adenocarcinoma of the lung in childhood and adolescence: a systematic review, Journal of Thoracic Oncology (2018) 1832–1841, https://doi.org/10.1016/j.jtho.2018.08.2020.
[30] M.C. Cohen, R.O.C. Kaschula, Primary pulmonary tumors in childhood: a review of 31 years' experience and the literature, Pediatr. Pulmonol (1992) 222–232, https://doi.org/10.1002/ppul.1950140405.
[31] P. Francalanci, F. Diomedi-Camassei, C. Purificato, et al., Malignant pancreatic endocrine tumor in a child with tuberous sclerosis, Am. J. Surg. Pathol. (2003) 1386–1389, https://doi.org/10.1097/00000478-200310000-00012.
[32] N.A. Shorter, R.D. Glick, D.S. Klimstra, et al., Malignant pancreatic tumors in childhood and adolescence: the memorial Sloan-Kettering experience, 1967 to present, J. Pediatr. Surg. (2002) 887–889.
[33] C. Sangüesa, D. Veiga, M. Llavador, et al., Testicular tumours in children: an approach to diagnosis and management with pathologic correlation, Insights. ImAging (2020) 74, https://doi.org/10.1186/s13244-020-00867-6.
[34] M. Hendricks, A. Cois, A.L. Geel Jet, Sex cord stromal tumors in children and adolescents: a first report by the south african children's cancer study group (1990-2015), J. Pediatr. Hematol. Oncol. (2021) 619–624, https://doi.org/10.1097/MPH.0000000000002076. PMID: 33560080.