INTRODUCTION

Renal tumors occurring in children comprise a spectrum of morphologic subtypes, including some with benign histopathology. Wilms' tumor (also called nephroblastoma or renal embryoma) is by far the most common form of malignant renal tumor in children ***(Geller et al., 1997).***

Other rare forms of childhood renal tumors include clear cell sarcoma of the kidney, rhabdoid tumor of the kidney, congenital mesoblastic nephroma, multilocular cystic renal tumor, renal cell carcinoma, and angiomyolipoma ***(Geller et al., 1997)***.

Malignant renal tumors represent 6.3% of tumors diagnosed among children younger than 15 years of age (incidence 7.9 per million) ***(Bernstein et al., 1995).***

Wilm's tumor is the most common form of renal cancer in children younger than 15 years of age, representing approximately 95% of renal cancer in children ***(Bernstein et al., 1995).***

Much less common forms include rhabdoid tumors of the kidney (1% of renal cancers) and clear cell sarcoma of the kidney (1.6% of renal cancers) ***(Bernstein et al., 1995).***

Renal carcinomas are the most common form of renal cancer in adults, represented only in 2.6% of renal cancers

in children younger than 15 years old ***(Bernstein et al., 1995).***

The diagnosis of these pediatric renal tumors can be suggested by their unique clinical history, such as age at presentation and distinctive imaging features. Knowledge of these lesions can help suggest a specific diagnosis, which in turn has implications for preoperative planning and prognosis ***(Lowe et al., 2000).***

The goal of therapy is to provide the highest possible cure rate with the lowest treatment related morbidity. Significant improvement in survival rates for children with pediatric renal tumors have been achieved by an improved understanding of the disease and multimodality approach to therapy, through the incorporation of surgery, radiotherapy and chemotherapy ***(Green et al., 1998).***

AIM OF THE WORK

The aim of this study is to discuss renal tumors in pediatric age group and to review the recent trends in the lines of management.

WILMS' TUMOR

Epidemiology

Wilms' tumor, or nephroblastoma, is the most common primary malignant renal tumor of childhood. This embryonal tumor develops from remnants of immature kidney ***(Ritchy and Shamberger, 2007)*** and accounts for 80% of genitourinary cancer in children under 15 years ***(Govender; 2000).***

The annual incidence rate of Wilms' tumor in children younger than 15 years is about 7 to 10 cases per million, and it accounts for 6% to 7% of all childhood cancers ***(Bernstein et al., 1999)*** or about 450 to 500 new cases annually in the United States ***(Breslow et al., 1988).***

These tumors are uncommon in neonates and most cases occur in children of between 1 and 3 years of age ***(Govender, 2000).***

Over 90% of cases in the National Wilms' Tumor Study Group (NWTS) occurred in patients under 6 years of age. Although the peak incidence is in childhood, nephroblastomas have been reported in adults ***(Murphy et al., 1994).***

Wilms' tumor typically affects young children (median age, 3.5 years), with more than 80% of cases

occurring in those younger than 5 years ***(Kalakapural et al., 2004).***

The median age at diagnosis is highest for unilateral unicentric cases and lowest for bilateral cases. Wilms' tumor occurs at an earlier age in males, with the mean age at diagnosis for those with unilateral tumors being 41.5 months versus 46.9 months in females. The mean age at diagnosis for those with bilateral tumors is 29.5 months for males and 32.6 months for females ***(Breslow et al., 1993).***

The overall mean age for females and males is 42.5 months and 36.5 months respectively ***(Murphy et al., 1994).***

There is no consistent gender preponderance although some series have reported a slight female predominance, but the frequency is slightly higher among girls in the United States ***(Breslow et al., 1993).***

In general, nephroblastomas occur with equal frequency in both kidneys. Five to 6% of cases are bilateral ***(Govender, 2000).***

With regard to ethnicity, the incidence of Wilms' tumor is lower in East Asian populations and higher in black populations than in the North American and European white populations ***(Fukuzawa et al., 2004).***

In the USA the age-standardized rate of nephroblastomas is 8.5 cases per million Caucasian children per year. The corresponding figure for American black children is 10.9 ***(Stiller et al., 1991).***

In the UK, the relative incidence rates in Asians are about half those in Caucasians, while West Indians have rates more than twice those of Caucasian rates ***(Govender, 2000).***

Several epidemiologic studies have investigated occupational, environmental, and lifestyle issues as risk factors for Wilms' tumor ***(Breslow et al., 1993).***

Evidence of a consistent association of Wilms' tumor with any parental environmental exposure has not been provided ***(Ritchey, 2002).***

Associated syndromes:

A number of recognizable syndromes are associated with an increased incidence of Wilms' tumor (Table 1) ***(Clericuzio, 1993).***

Table (1): Incidence of Congenital Anomalies in Patients with Wilms' Tumor Reported to the National Wilms' Tumor Study Group:

Anomaly	Rate (per 1000)
Aniridia	7.6
Beckwith-Wiedemann syndrome	8.4
Hemihypertrophy	33.8
Genitourinary anomalies	
Hypospadias	13.4
Cryptorchidism	37.3
Hypospadias and cryptorchidism	12.0

These may be divided into those characterized by overgrowth and those lacking overgrowth. Syndromes with overgrowth features include hemihypertrophy, which may occur alone or as part of the Beckwith-Wiedemann syndrome (BWS) ***(Ritchey, 2002).***

BWS is a rare disorder consisting of developmental anomalies characterized by excess growth at the cellular, organ, (macroglossia, nephromegaly, hepatomegaly) or body segment (hemihypertrophy) levels ***(Wiedemann, 1983).***

Although most cases of BWS are sporadic, up to 15% exhibit heritable characteristics with apparent autosomal-dominant inheritance. The incidence of tumor development in BWS is 10% to 20% including Wilms' tumor, adrenocortical

neoplasms, and hepatoblastoma. The risk of Wilms' tumor development in patients with hemihypertrophy and BWS is estimated to be approximately 4% 10 % ***(Beckwith, 1996).***

Children with BWS found to have nephromegaly (kidneys greater than or equal to the ninety-fifth percentile of age-adjusted renal length) are at the greatest risk for the development of Wilms' tumor ***(DeBaun et al., 1998).***

Other overgrowth syndromes, Perlman, Soto's, and the Simpson-Golabi-Behmel syndromes, also are associated with the development of Wilms' tumor ***(Neri et al., 1998).***

With or without the stigmata of BWS, 3% of patients who develop Wilms' tumor also may be affected by hemihypertrophy ***(Breslow et al., 1988).***

The risk of Wilms' tumor development in patients with hemihypertrophy is estimated to be on the order of 3% to 5% ***(Tank and Kay, 1980).*** Isolated involvement of the leg is the most common manifestation in these patients ***(Green et al., 1992)*** and may not become clinically apparent until after the diagnosis of Wilms' tumor. Hemihypertrophy may be ipsilateral or contralateral to the tumor. The mean age at diagnosis of Wilms' tumor in patients with BWS and hemihypertrophy is similar to that of the general Wilms' tumor population ***(Breslow et al., 1988).***

Genitourinary anomalies (renal fusion anomalies, cryptorchidism and hypospadias) are present in 4.5% of patients with Wilms' tumor ***(Ritchey, 2002).***

These disorders are common in children, and prospective evaluation for the onset of Wilms' tumor is not necessary in most children with genital anomalies. However, one specific association of male pseudohermaphroditism, renal mesangial sclerosis, and nephroblastoma is the Denys-Drash syndrome (DDS) ***(Dome et al., 1999).***

The majority of these patients progress to end-stage renal disease. Nephropathy usually develops early in life, and renal biopsy demonstrates mesangial sclerosis ***(Mc Taggart et al., 2001).***

A specific mutation of the 11p13 Wilms' tumor gene has been identified in these children ***(Coppes et al., 1993).*** Although XY individuals have been reported most often, DDS has been found in genotypic/phenotypic females ***(Mc Taggart et al., 2001).***

The incidence of aniridia in Wilms' tumor patients is 1.1%. Aniridia and Wilms' tumor are most commonly associated in patients with the Wilms' tumor, aniridia, genital anomalies, and mental retardation (WAGR) syndrome ***(Choyke et al., 1999).***

Aniridia is caused by an abnormality of the *PAX6* gene located adjacent to the WT1 gene. Aniridia patients

with deletions that include WT1 are more prone to the development of Wilms' tumor ***(Muto et al., 2002).*** Wilms' tumor will develop in approximately 40% of aniridia patients with deletions of WT1. Conversely, Wilms' tumor does not develop in aniridia patients with normal WT1 ***(Grenskov et al., 2001).***

WAGR patients are more likely to have bilateral tumors and the condition is diagnosed at a younger age. They are more prone to the development of renal failure if they survive into puberty ***(Breslow et al., 2003).***

An association between Wilms' tumor and horseshoe kidney has been noted. A review of National Wilms' Tumor Study Group (NWTSG) patients found a sevenfold increased risk for Wilms' tumor in patients with a horseshoe kidney ***(Mesrobian et al., 1985).*** The diagnosis of horseshoe kidney can be missed on preoperative imaging because of the location of the tumor ***(Neville et al., 2002).***

Wilms' tumor has been reported in patients with multicystic dysplastic kidney, but there is not sufficient evidence that it occurs at an incidence greater than that in children with two normal kidneys ***(Narchi, 2005).***

There is an increased risk for müllerian duct anomalies in girls with Wilms' tumor ***(Byrne and Nicholson, 2002).*** Approximately 10% of girls will have

abnormalities such as duplication of the cervix or uterus or a bicornuate uterus ***(Ritchy and Shamberger, 2007).***

Screening with serial renal ultrasonography has been recommended in children with aniridia, hemihypertrophy, and BWS. Review of most studies suggests that 3 to 4 months is the appropriate screening interval. Tumors detected by screening will generally be of lower stage ***(Choyke et al., 1999).***

There were not enough patients in these retrospective reviews to determine whether early detection had an impact on patient survival. Two recent reports have called attention to the increased incidence of nonmalignant renal lesions in children with BWS ***(Ritchey, 2002).***

Nonmalignant lesions included medullary renal cysts in 13% of patients, hydronephrosis in 12%, and nephrolithiasis in 4%. In two patients, nephrectomy was performed for benign disease due to false-positive screening ***(Ritchey, 2002).***

Pathology:

A. Favorable-Histology Wilms' Tumor:

Macroscopic appearance:

Nephroblastoma usually are large, well circumscribed, rounded, solitary renal masses that push against and distort the adjacent renal parenchyma ***(Zhou and Galluzzi, 2007)*** forming a pseudo capsule composed of

compressed, atrophic renal tissues ***(Schmdt and Beckwith, 1995).***

Wilms' tumor often is greater than 5 cm in diameter and more than 30% are larger than 10 cm ***(Jennette et al., 2007).*** They tend to bulge above the cut surface and are soft, fleshy, and gray-white to tan with a texture and appearance resembling brain tissue ***(Grignon and Staerkel, 2006).***

Cysts are common, as are foci of haemorrhage and necrosis ***(Jennette et al., 2007).*** This consistency increases the risk for intraoperative tumour rupture. Most Wilms' tumor is unicentric, but 12% are multicentric unilateral tumour ***(Breslow et al., 1993).***

Depending on the stromal content of the tumor, a lobulated appearance may be seen ***(Zhou and Galluzzi, 2007).***

Predominantly cystic Wilms' tumor that contains blastema and other Wilms' tumor tissues in its septa is called cystic partially differentiated nephroblastoma ***(Jennette et al., 2007).***

Microscopic appearance:

Nephroblastoma are a group of very heterogenous neoplasms, to the degree that one nephroblastoma may have a little in common with another, depending on the cell

composition and architectural patterns observed ***(Zhou and Galluzzi, 2007).***

The tumor is composed of elements that resemble normal fetel tissue including (1) Metanephric blastema, (2) Immature stroma (mesenchymal tissue), (3) Immature epithelial element ***(Jennette, 2005).***

Triphasic tumors are distinctive, but biphasic and monophasic tumors are not uncommon ***(Zhou and Galluzzi, 2007).***

Blastema consists of densely packed small cells randomly arranged in sheets ***(Grimes et al., 1982).***

The cells of the blastemal pattern are small, round to oval, and have high nuclear / cytoplasmic ratios ***(Zhou and Galluzzi, 2007).*** With hyper chromatic nuclei and scanty cytoplasm ***(Grignon and Staerkel, 2006).***

The chromatin is usually course and evenly distributed with inconspicuous small nucleoli; mitotic activity is brisk ***(Magee et al., 1987).***

Like small cell carcinoma of the lung, they show prominent nuclear overlapping. Several blastemal patterns have been described. The diffuse blastemal pattern is characterized by a fairly uniform population of noncohesive cells and uniquely infiltrative margins. In contrast, the cells of other blastemal patterns tend to be

more cohesive and border less infiltrative and more sharply defined ***(Zhou and Galluzzi, 2007).***

The organized blastemal pattern may be seen in the form of nodules (Nodular blastema), anastomosing cords (Serpentine blastema), or even palisaded arrangements (Blasmoid blastema) embedded in loose, myxoid, or fibromyxoid stroma ***(Zhou and Galluzzi, 2007).***

The epithelium of the Wilms' tumor usually consists of small tubules or cysts lined by columnar or cubiodal cells. Occasionally, it forms structures resembling glomeruli or has mucinous, squamous, neural, or endocrine differentiation ***(Beckwith, 1983).***

The stroma of Wilms' tumor is variable and may differentiate toward almost any type of soft tissue ***(Jennette et al., 2007).***

In most cases, this is composed of immature myxoid and spindled mesenchymal cells; however, essentially any type of stromal differentiation, including smooth muscle, skeletal muscle, fat, bone, cartilage, and neuroglial tissue, may be observed ***(Zhou and Galluzzi, 2007).***

When diffuse differentiation toward skeletal muscle occurs, the term fetal rhabdomyomatous' nephroblastoma is applied ***(Jennette et al., 2007).***

Fetal rhabdomyomatous nephroblastoma is a rare variant of nephroblastoma, a predominantly monophasic mesenchymal variant, composed of fetal skeletal muscle. This variant was first recognised by Eberth ***(Govender, 2000)*** but Wigger coined and defined the term fetal rhabdomyomatous nephroblastoma in 1976 ***(Wigger, 1976).***

Although nephroblastomas in general show an even gender distribution or slight female preponderance, fetal rhabdomyomatous nephroblastoma has a male preponderance ***(Mahoney and Saffos, 1981).***

The patients usually present earlier, with a mean age of 19.5 months ***(Eble et al., 1983).*** The frequency of bilateral tumours is much higher with fetal rhabdomyomatous nephroblastomas than for nephroblastomas in general-a rate of 30% against 5.4% respectively.The cut section of this variant has a whorled and lobulated appearance similar to uterine leiomyomas in the majority of cases ***(Govender, 2000).***

Complex combinations of differentiated epithelium and stroma are sometimes present. The term teratoid Wilms' tumor has been applied to these ***(Kotiloglu et al., 1994).***

Initial reports of teratoid nephroblastomas described a tendency for bilaterality ***(Govender, 2000),*** but later reports have described unilateral cases ***(Kotiloglu et al., 1994).***