Special issue: “FOCUS ON PEDIATRIC NEPHROLOGY”

In this special issue, Researchers and Specialist Registrars of University of Catania, Catanzaro and Messina (ITALY) focused on nephron-urological abnormalities in children, ranging from glomerular (nephrotic and Alport syndrome, chronic glomerulonephritis) and urologic diseases (multicystic dysplastic kidney, obstructive pathologies and stones).

Particular attention was paid to congenital syndrome, such as Vacterl, Fabry and Goldenhar syndrome and acquired conditions such as Schoenlein-Henoch disease potentially leading to renal impairment.

In addition, oxidative stress in newborns is involved in the progression of renal failure. When associated to congenital renal anomalies a dialysis treatment might be needed.

Dialysis is a treatment option for children who are experiencing kidney failure. We treated about the differences between adult and pediatric dialysis concerning physical and staffing requirements.

In this regards we reported a clinical case of a child in dialytic treatment who was used innovative topical ozone therapy for infantile atopic dermatitis.

In conclusion, aim of this report was to discuss about pediatric nephro-urological issues by reporting literature reviews and clinical cases.

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Diabetes insipidus (DI) is characterized by hypoosmotic polyuria related to deficiency of arginine-vasopressin (AVP) secretion (central diabetes insipidus, CDI) or renal insensitivity to AVP (nephrogenic diabetes insipidus, NDI). We report a case of a child with congenital NDI.
The purpose of this article is to review the main congenital anomalies of kidneys and urinary tract that can be diagnosed prenatally and postnatally by imaging technique. The incidence of congenital anomalies of the kidney and urinary tract during the past decade has been estimated to be 0.4 to 4.0 cases per 1000 births. Congenital kidney disease can evolve in chronic disease in childhood and in adulthood. A diagnostic imaging of the various congenital renal and urological conditions allows pediatricians to make a correct diagnosis and treatment. Because of the concerns about long-term effects of ionizing radiation, the most commonly and first used imaging modality for evaluation of the urinary system is ultrasound.
NEPHROTIC SYNDROME: IMMUNOLOGICAL MECHANISMS

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Nephrotic Syndrome (NS) is a rare disease (around 2-7 cases per 100,000 children per year) characterized by proteinuria ≥50 mg/kg/day (or ≥40 mg/m²/h) or a proteinuria/creatininuria ratio >2 (mg/mg); hypoalbuminaemia< 25 g/l and edema. The protein leakage, with the consequent hypoalbuminaemia and edema, due to podocyte alterations may be caused by genetic diseases, immunological mechanisms, infections, toxins or malignancy. However, most commonly the exact etiology is unknow. The idiopathic NS may be classified based on response to corticosteroid therapy or the histological appearance. The first classification identifies steroid-resistant NS (no response after 4 weeks of steroid therapy); frequently relapsing NS (≥2 relapses in first 6 months or ≥4 relapses in 1-year); steroid dependent NS (relapses during steroid decalage or within 2 weeks from steroid therapy interruption). The histological classification is based on light and electron microscopy after renal biopsy, which is indicated in case of onset disease before 1 year or after 12 years of age. Macroscopic hematuria: persistent hypertension and/or microscopic hematuria and/or low plasma C3 renal failure not related to hypovolemia; steroid resistance: secondary or related-syndromes NS. Minimal change disease (MCD) is the most common form of idiopathic NS in children, with good response to steroid treatment, and it is characterized by normal glomerular appearance on light microscopy and evidence of podocyte foot alterations on electron microscopy, due to immunological related damage. Focal segmental glomerulosclerosis (FSGS) is described in idiopathic NS, particularly in steroid-dependent or steroid-resistant forms, and is characterized by evidence of focal glomerular damage with secondary sclerosis and adhesion with Bowman’s capsule; the electron appearance is the same of MCD one. Recent authors hypothesize that the FSGS is an evolution of MCD. These 2 idiopathic NS forms may be expression of the same immunological disease, with 2 different severity grades; so they may be considered different moments of the same disease spectrum. Less common idiopathic NS forms are membranoproliferative glomerulonephritis; membranous nephropathy; IgM-nephropathy; C1q nephropathy and thin basement membrane disease (1, 2, 3).
Alport’s syndrome (AS, OMIM 301050) is a hereditary disorder characterized by progressive renal failure, hearing impairment and ocular changes. It is clinically and genetically heterogeneous and in its natural history, renal disease progresses from microscopic haematuria to proteinuria, and finally to progressive renal insufficiency. AS is caused by an inherited defect in a type IV collagen, a structural material, expressed in many tissues that is essential for the normal function of different parts of the body. In most cases, about the 85%, Alport’s syndrome is X-linked and is originated by mutations in the \textit{COL4A5} gene. In the remaining cases, it may be inherited in either an autosomal recessive, or rarely in an autosomal dominant manner. Mostly, the condition is caused by mutations in the \textit{COL4A3} or \textit{COL4A4} genes. Coexisting mutations in \textit{COL4A3}, \textit{COL4A4}, \textit{COL4A5} or \textit{COL4A6} were found to cause an Alport’s syndrome phenotype with digenic inheritance. Diagnosis of the condition is based on family history, clinical signs, and specific procedures such as a kidney biopsy. The diagnosis can be confirmed by genetic testing. Treatment may include use of a hearing aid, hemodialysis, and peritoneal dialysis to treat those with end-stage renal failure, and, as the last step, kidney transplantation. Firstly described by Arthur C. Alport’s, in 1927, over the years it has become a pathology of high scientific interest. At the moment, thanks to advances in diagnostic techniques, it is possible to make an early diagnosis avoiding irreversible damages and life-threatening complications.
CLINICAL COURSE OF A PEDIATRIC SERIES OF MULTICYSTIC DYSPLASTIC KIDNEY


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CONSERVATIVE MANAGEMENT IN CONGENITAL SEVERE BILATERAL HYDRONEPHROSIS RELATED TO URETERO-PELVIC JUNCTION OBSTRUCTION

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We report our experience in conservative management of patients with prenatal and neonatal diagnosis of severe bilateral ureteropelvic junction obstruction (UPJO), focusing on the actual predictors of renal function impairment or spontaneous resolution. Between 1996 and 2006, 20 patients with bilateral severe hydronephrosis related to UPJO were included in the study. Indications for surgery were an increased hydronephrosis, decreased renal function, onset of symptoms. Conservatively treated patients were followed up for 3 months to 10 years with renal ultrasound, DTPA diuretic, urine culture. At first renal scan, 22 out of 40 renal units had a poor, 10 an intermediary and 8 a good drainage. Pyeloplasty was required in 10 of the 40 kidneys, while 30 out of 40 kidneys were followed conservatively. At the end of follow up, sieric normalized creatinine and estimated glomerular filtration rate were normal in all patients. Our data showed that bilateral severe hydronephrosis related to UPJO can be safely managed in a similar manner of a unilateral case. A poor drainage could be considered a negative predictive factor in the feasibility of a conservative management.
Urolithiasis is a well-known condition that can affect any part of the urinary tract. With a rate of 3-5% the incidence of upper urinary tract for long has been higher in adults (1-3), but recently it has increased among children reaching 3.3%. Indeed, more than 1% of all urinary stones are seen in patients aged < 18 years (4). Pediatric urolithiasis is endemic in Turkey and Far East and it is probably due to malnutrition and racial factors (5). The spontaneous stone passage is more likely in children than in adults, indeed ureteral calculi spontaneously pass into 41-63% of children (1). Rate of stone passage depends on size and stone location in the urinary system. Stones sized <5 mm have a passage rate ranging from 40% to 98%, whilst stones >5 mm have between 55% and 50% (6). In the last decade, the use of alpha blockers has proven well efficacious in helping spontaneous passage of distal ureteric stones in adults (7-9). The latest EAU guidelines support their use in adults while remain vague about their use in children because of unclear safety and efficacy (4). In search of evidence supporting or not the use of medical expulsive therapy in children we reviewed the literature dealing with the management of urolithiasis in pediatric patients. The primary aim of the present study was to evaluate the efficacy of medical expulsive therapy (MET), defined as stone expulsion rate, with α-blockers compared to a control group. The secondary aim was to assess the safety, defined as side effects rate, of MET compared to a control group.
Nocturnal enuresis (NE) was defined by the World Health Organization (ICD-10) and the American Psychiatric Association (DSM-5) as bed-wetting in children aged >5 years. In cases of mental retardation, the developmental age may be equivalent to 5 years. In this review, we focus on the current knowledge about the etiology of enuresis and the most recent therapeutical options. Both non-pharmacological and pharmacological therapies are included, although the relative effectiveness of each remains uncertain. To date, motivational, alarm and drug therapies are the mainstay of treatment. Alarm therapy remains the first-line treatment modality for NE, while desmopressin is the most commonly used medical treatment.
RENAL ANOMALIES IN NEWBORNS WITH VACTEREL ASSOCIATION:
CASE SERIES AND LITERATURE REVIEW

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Anderson-Fabry Disease (AFD) is a rare, X-linked inborn error of glycosphingolipid catabolism caused by a deficient or absent activity of the lysosomal enzyme, α-galactosidase A, resulting in the progressive multisystem lysosomal accumulation of glycosphingolipids, mainly globotriaosylceramide (Gb3). Among the wide spectrum of clinical signs and symptoms and the life-threatening complications of Fabry disease, renal failure causes significant morbidity and mortality. Various evidence shows that the accumulation of Gb3 in different renal cells is present since the first years of life, many years and usually decades before manifest symptoms and signs of renal involvement. Early renal damage can be demonstrated by clinical signs as microalbuminuria and proteinuria, developing as early as in the second decade of life. A decline in GFR is uncommon at paediatric ages but may be seen as early as adolescence. Renal biopsy is rarely used in paediatric patients with Fabry disease although evidence shows that it may be considered a valid tool for the diagnosis of early and potentially reversible nephropathy, as well as for the evaluation of the effectiveness of enzyme replacement therapy (ERT). Although there is consensus in considering the early initiation of ERT as the only tool able to prevent the progression of nephropathy, the issue on the correct timing for the onset of ERT in pediatric age remains open in the management of this chronic and progressive disease.
URETEROCYSTOPLASTY (BLADDER AUGMENTATION) IN A 16 YEAR-OLD BOY WITH GOLDENHAR SYNDROME

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The use of the dilated ureter for bladder augmentation is universally accepted for its lower rate of complications compared to the use of gastrointestinal segments. We report the case of a 16-year-old boy affected by Goldenhar syndrome who presented with neurogenic bladder with small-capacity, 5° grade vesico-ureteral reflux (VUR) with megaureter and bilateral hydronephrosis. Bladder augmentation using the distal dilated ureter, transuretero-ureterostomy left to right and Mitrofanoff’s appendicovesicostomy were performed. Six months after surgery voiding cystourethrogram (VCUG) revealed a compliant bladder with a functional capacity of 400 ml. Ureterocystoplasty is a safe and effective method of augmenting small capacity urinary bladder. We suggest using the ureter, when available, instead of using gastrointestinal segments.
UNUSUAL PRESENTATION OF HENOCH-SCHÖNLEIN PURPURA

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Henoch Schonlein Purpura (HSP) is a systemic IgA-mediated vasculitic disease that affects the small vessels of the skin, the joints, the gastrointestinal tract and the kidneys (1). It is the most common childhood vasculitis, with an incidence estimated at 3-26 per 100,000 children, and with a male-to-female ratio of 2:1 (2-6). The 90% of patients are under 10 years of age, with a mean age of 4 years (4). It seems to be most common in fall and winter in children, and summer and winter in adults (7). Recent studies suggested a strong genetic predisposition in individuals with immunoglobulin Avasculitis (IgA V) associated to HLA class II region. Clinically, the non-thrombocytopenic purpura often located on lower extremities and buttocks is the essential element for the diagnosis of HSP. Treatment is supportive, because the disease is usually benign and self-limited. Indeed, in children, the prognosis is good, with a self-limited course and without any complications and after a median follow-up of 12 months, complete recovery was obtained in 83% of the IgAV patients (4, 8). The aim of our study is to describe some atypical presentations of the HSP in children.
RENAL OXIDATIVE INJURY IN NEWBORNS

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Obesity in children has been recognized as a major underlying factor of the pathogenesis of several diseases and a reduced life expectancy. This study aims to verify if clinical parameters, such as waist circumference and/or body mass index and biohumoral and inflammatory parameters can help predict cardiac structural and functional alterations, through an echocardiogram test in obese children and adolescents. Children were prospectively enrolled at the AUOC outpatients’ department of Emergency Paediatrics, University Hospital, Messina, from June to December 2017. Clinical, metabolic parameters and an inflammation marker (HMGB1) were evaluated and a transthoracic echocardiogram was carried out. Twenty-two obese subjects were prospectively enrolled. HMGB1 values were 12.6 ± 2ng/ml, significantly higher compared to a previously studied healthy control group. A significant positive correlation was found both between total cholesterol levels and HMGB1 values (r=0.846, p=0.000) and between LDL cholesterol and HMBG1 values (r=0.663, p=0.001). No correlation was found between clinical, biohumoral and echocardiograph parameters. In obese children cardiac parameters obtained from echocardiogram tests may be in the normal range. However, other parameters may be altered in the early phase, showing that infantile obesity can compromise myocardial functions, even in the absence of comorbidities. Furthermore, the evaluation of concentrations of HMBG1 could explain how an initial inflammation can trigger the condition of meta-inflammation.
HEMODIALYSIS IN CHILDREN: HOW, WHEN AND WHY

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End-stage renal diseases requiring chronic dialysis are rare in childhood and adolescence, but they are associated with high mortality and impaired quality of life (1, 2). The most common disease that causes chronic kidney disease (CKD) is primary glomerular disease (GD), followed by congenital abnormalities of the kidney and urinary tract, cystic, hereditary or congenital disorders and, more rarely, secondary GD. However, patients with secondary GD, urologic disorders, and metabolic diseases have greater mortality risk than patients with primary GD (3). Here, we focused on the different options of treatment available, and specifically we compared peritoneal dialysis and hemodialysis, showing pros and cons between them.
LOCAL THERAPY WITH OZONE IN THE MANAGEMENT OF THE EXIT SITE IN A PATIENT UNDERGOING PERITONEAL DIALYSIS


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The natural history of children with end stage renal disease is dialysis until a transplant can be done. There are two types of dialysis: hemodialysis and peritoneal dialysis (1). Peritoneal dialysis is preferred in young children because getting the vascular access for hemodialysis is challenging (2). Catheters should be surgically placed in a paramedian or lateral abdominal region with an extremity located in Douglas’ pouch.
LAPAROSCOPIC NEPHRECTOMY IN CHILDREN WITH WILMS TUMOR. CONSIDERATIONS AFTER 10 YEARS OF EXPERIENCE

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Despite laparoscopy in children is considered safe and is routinely used for several procedures, even in neonates and in pediatric oncology, its role in the treatment of pediatric renal tumors is still controversial. This study analyzes the results of laparoscopic nephrectomy for Wilms Tumor (WT) in pediatric age compared with open nephrectomy after 10 years of experience in a single centre. From 1993 in our center of reference for pediatric oncology, 30 patients with WT have been treated. We performed 21 open nephrectomy and in the last 10 years 9 laparoscopic nephrectomy. In all patients treated laparoscopically, the same technique made by the same equip was used. Compared with patients treated by open surgery, we did not find a significant difference in terms of outcome and survival. In the open surgery group, two patients had lung relapse while in the other group there was one local relapse. These three children obtained and maintained a second complete remission with chemotherapy. Open surgery complications were a tumor rupture in two cases, and an episode of pancreatitis 10 days after surgery. In the laparoscopic group, there were two conversions to open surgery not considered as complications but a surgical choice for cystic areas present in the tumor. As far as complications and oncologic outcomes are concerned, both techniques showed similar results. In experienced hands, laparoscopy proves to be an attractive alternative to open surgery for pediatric renal tumors.
Pelviureteric junction obstruction (PUJO) due to intrinsic or extrinsic causes is a common problem in childhood. Extrinsic compression by a lower pole-crossing blood vessel can present symptomatically in older children. In these cases, laparoscopies Vascular Hitch can represent a valid alternative to pyeloplasty dismembered. We analyzed the data of 4 children affected by extrinsic PUJO treated at our institution with the laparoscopic Vascular Hitch procedure modified by Chapman. Surgical indications included presence of clinical symptoms, worsening of intermittent hydronephrosis, signs of obstruction on the MAG-3 scan, clear or suspected images of polar crossing vessels on CT scan or Uro-MRI. All procedures were completed laparoscopically. No complications occurred. Mean follow-up was 13 months with resolution of symptoms and PUJ obstruction and significant improvement of hydronephrosis in all cases. When blood vessels crossing lower pole represent the pure mechanical cause of UPJ obstruction the laparoscopic Vascular Hitch procedure represents an excellent alternative to dismembered pyeloplasty. It is less technically demanding then pyeloplasty and is associated with a lower complication rate. The main challenge is to intraoperatively ascertain the absence of associated intrinsic stenosis.