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DIALYSIS THERAPY - IMPLICATIONS AND COMPLICATIONS. STUDY AND CLINICAL ALGORITHM

PhD thesis abstract

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Introduction

Paediatric nephrology is the specialty concerned with the investigation, diagnosis and management of acute and chronic kidney disease and the prescription of renal replacement therapy.

Dialysis therapy required for both patients with severe acute kidney injury (AKI) and patients diagnosed with chronic kidney disease dialysis stage (CKD G5) is lifesaving.

Through the use of special procedures and equipment, dialysis removes excess fluids and toxic and nitrogen-retaining products, ensuring the survival of the chronic patient until renal transplantation and saving the life of the AKI patient in whom supportive measures have proven insufficient.

Over the years, paediatricians in Paediatric Nephrology Departments have cared for and monitored these patients, actively participating in better understanding renal replacement techniques, optimising these procedures and minimising associated complications.

AKI remains an important contributor to mortality and morbidity in the paediatric population. AKI management consists of supportive measures, effective in some patients. However, there are also situations when renal replacement therapy becomes necessary and can be achieved by acute intermittent haemodialysis, acute peritoneal dialysis or continuous dialysis therapy (haemodialysis/ haemodiafiltration/ haemofiltration - HDF).

The indication for dialysis, the optimal time to initiate dialysis, and the choice of dialysis modality for which category of patient continue to raise controversy and remain targets for future study.

A severe AKI episode requiring a dialysis procedure has prognostic implications. Although until recently, the condition was considered to be self-limiting and reversible, numerous studies have shown that after an episode of severe AKI requiring acute dialysis, in many cases recovery is not complete and long-term impairment of renal function occurs. Thus, severe AKI becomes a risk factor for the development of CKD with all its complications and implications, as well as an important risk factor for the progression of existing chronic disease.

From the need for life-saving acute dialysis therapy it can lead over time to CKD with the need for renal replacement therapy through dialysis and renal transplantation.

At the Maria Sklodowska Curie Children's Emergency Clinical Hospital, in the Paediatric Nephrology Department and the Haemodialysis Centre, patients requiring acute or chronic dialysis are constantly cared for. The care of these patients as well as their regular monitoring led to the idea of this study which aims to follow the prognostic implications of the patient who required acute dialysis, as well as the complications associated with the chronically dialyzed patient. The type of dialysis chosen, depending on patient characteristics and other socio-economic factors , was also a point of interest.

The scientific hypotheses formulated will be supported by studies carried out on groups of patients admitted to the Paediatric Nephrology Department and the Haemodialysis Centre of the "Maria Sklodowska Curie" Children's Emergency Clinical Hospital in the period 2016-2020.

The aim of the study is to identify early patients at risk of developing CKD after an episode of severe AKI requiring dialysis, identify risk factors and correctly manage these patients.

Also, proper diagnosis and treatment of complications associated with chronic kidney disease aims to improve the life of the chronically dialyzed patient until kidney transplantation.

I. GENERAL PART

1. ACUTE DIALYSIS

1.1 Acute kidney injury (AKI)

1.1.4 Definition. Staging

Acute kidney injury (AKI) defines a sudden, potentially reversible loss of kidney function characterised by a decrease in glomerular filtration rate and the inability of the kidney to maintain fluid homeostasis and acid-base and water-electrolyte balance(1).

Several definitions and staging of AKI have been proposed, based on clinical studies, the most important being: pRIFLE (2,4,5), IRAN criteria (1,6,7), KDIGO criteria (8,9). The KDIGO criteria have general applicability to both the paediatric and adult patient (13).

It remains an issue for future study in an attempt to establish a definition and staging of AKI that has the best clinical applicability and is universally used, as AKI remains an

important cause of mortality and morbidity in the critically and non-critically ill paediatric patient and an important risk factor for the development of long-term CKD (10, 11, 12).

1.1.5. Aetiology

Studies in paediatric patients have concluded that (15, 16, 17, 18):

- In developed countries, the aetiology is more frequently related to primary glomerular disease, nephrotoxic factors, AKI acquired during hospitalisation of a critical, post-surgical, oncological patient;

- In developing countries, the most common causes remain dehydration, sepsis, typical haemolytic uraemic syndrome with prodromal diarrhoea.

1.1.6 Indications for renal replacement therapy in acute kidney injury

Renal replacement therapy (RRT) is indicated in children with severe AKI at high risk of mortality due to associated complications: volemic overload, severe disturbances of water-electrolyte and acid-base balance, symptomatic uraemia.

The recommendation to initiate acute dialysis may be made in urgent situations (volemic overload of more than 10-15%, complications of uremia, hydroelectrolytic and acid-base disturbances not correctable by treatment, in intoxications, in tumour lysis syndrome) and in "non-urgent" situations, when an unfavourable evolution of the patient with AKI is predicted.

1.2. Renal replacement therapy in AKI

Dialysis can be performed safely for paediatric patients at any age. There are three ways to perform renal replacement therapy: peritoneal dialysis (PD), haemodialysis (HD), continuous dialysis therapy (RRT - continuous haemodialysis, haemofiltration, haemodiafiltration).

A very important issue and controversy is the choice of the type of dialysis to be used in the patient with severe AKI. There are many elements to be considered: existing resources in the clinic (necessary equipment, technology, specialised staff), clinician preference/experience, patient characteristics (age, weight, comorbidities, haemodynamic status, main purpose of dialysis -ultrafiltration or removal of retained substances). There are advantages and disadvantages associated with all dialysis procedures.

1.2.1 Acute peritoneal dialysis

1.2.2.2. General. Definition. Principles

Peritoneal dialysis is an intracorporeal method of dialysis, it does not require an extracorporeal circuit or anticoagulation. The operating principle is based on physiological processes that allow fluid exchange and elimination of toxic substances. The abdominal cavity is the dialyser, the peritoneal membrane is the dialysing membrane and the dialysis solution is the dialysate.

It is a simple, safe and cost-effective dialysis procedure that is used worldwide in both high-income and developing countries: in North America (31)-in high-income countries 72% HD and 24% HDF, in middle/low-income countries: 68% PD; in Europe (32) 39.4% PD, 38.2% HDF, 22.4% HD.

There are still poor regions in the world where dialysis is not available for severe paediatric AKI, and the impact is devastating, with very high child mortality (30).

1.2.2.1. Indications

There are some situations where peritoneal dialysis is indicated in preference to other modalities: infants and children weighing < 15 kg , cardiovascular instability in whom there are no HDF circuits suitable for small extracorporeal volumes, presence of coagulation disorders that contraindicate placement of a central venous catheter, in very low birth weight neonates/infants in whom it is difficult to obtain a central venous approach to initiate an extracorporeal dialysis procedure (29, 36, 37, 38), is preferred post cardiovascular surgery in the neonatal period and in infants, has excellent cardiovascular tolerance because it achieves removal of excess fluid and toxic products gradually and continuously without risking hemodynamic instability (29, 33, 34, 35, 39, 40).

1.2.2.1. Contraindications

Absolute contraindications to peritoneal dialysis are related to conditions affecting the integrity of the abdominal cavity or peritoneal cavity: gastroschisis, omphalocele, bladder exstrophy, diaphragmatic hernia, pre-existing peritoneal adhesions, malignant disease involving the peritoneum, necrotic ulcerative enterocolitis in new-borns, sepsis with digestive entry point, recent intra-abdominal surgery.

Relative contraindications to peritoneal dialysis are related to impending abdominal surgery.

The following medical conditions are not contraindications for peritoneal dialysis: vesicostomy, ureterostomy/ureterostomy, gastrostomy, colostomy, ventriculoperitoneal shunt.

1.2.2.1. Access routes.

The surgical route (laparoscopic or abdominal dissection) with placement of the flexible Tenckhoff catheter is the optimal choice.

1.2.2.1 Equipment

After peritoneal catheter insertion, peritoneal dialysis is performed using a manual, closed delivery system based on the principle of gravity. Fluid balance can be monitored using a graduated device, which allows easy calculation of the amounts of fluid introduced into the peritoneum or evacuated at the end of a shift.

1.2.2.1 Dialysis solutions

Dialysis solutions are marketed in preformed, sterile bags containing glucose solutions of varying concentrations, physiological electrolyte levels, and a buffer substance.

1.2.2.1 Prescription

The prescription of acute peritoneal dialysis should take into account the child's age and weight or body surface area. The amount of peritoneal dialysis fluid used for dialysis exchanges is calculated according to these parameters: start with 10ml/kgc/cycle and increase progressively to a maximum of 35-40ml/kgc/cycle or a maximum of 600-800ml/m2 b.s. in children <2 years and 1000-1200ml/m2 b.s. in children >2 years; the increase should be progressive.

There are three times of dialysis prescription: "*In-flow time*" (the time it takes for the peritoneal dialysis fluid to enter the abdomen) with an average duration of 10 minutes; "*Dwell time*" (the time the peritoneal dialysis fluid stays in the abdomen) with an average duration of 40 minutes; "*Drain time*" (the time the peritoneal dialysis fluid drains from the abdomen) with an average duration of 20 minutes.

1.2.2.1 Patient monitoring

During dialysis cycles, patients require very close monitoring of their fluid balance. The following are also monitored daily: weight, diuresis, vital function parameters, acid-base and water-electrolyte balance, dialysis exchange performance, appearance of dialysis fluid, appearance of catheter insertion port, cultures and smears of dialysis fluid are taken daily.

1.2.2.1 Complications

- Infectious complications: acute peritonitis, the most common complication associated with acute peritoneal dialysis.

- Non-infectious complications: abdominal pain, loss of protein with need for increased protein intake, loss of immunoglobulins with decreased intra-infectious defences, hyperglycaemia, electrolyte disturbances, complications related to peritoneal dialysis catheter failure, hydrothorax, abdominal hernia.

1.2.3. Acute intermittent haemodialysis

1.2.3.1. General. Definition. Principle.

It is a very effective way of extra-renal cleansing, used especially for older children, children weighing > 15-20kg. Currently, most haemodialysis machines available on the market can be used in children weighing > 15-20 kg (21).

Acute haemodialysis and chronic haemodialysis operate according to the same principles: excess water is removed by ultrafiltration; nitrogen retention products and toxins are removed by convection and diffusion.

1.2.3.2. Indications for acute haemodialysis

Acute intermittent haemodialysis is particularly recommended in paediatric patients with AKI in the following situations (21, 47, 48, 49, 50, 51, 52): tumour lysis syndrome, severe hyperkalaemia, ingestion of dialysable toxins, iatrogenic AKI secondary to contrast media, nephrotoxic drugs (NSAIDs, vancomycin, aminoglycosides, ACE inhibitors, acyclovir, etc.).), hyperammonemia from liver failure and inborn metabolic diseases, AKI associated with hypercatabolic states (burns), significant volemic overload with acute pulmonary oedema.

1.2.3.3.Contraindications

There are some situations in which acute haemodialysis cannot be performed (21, 53): neonatal paediatric patients and infants in whom vascular access cannot be achieved; children weighing < 15-20 kg, haemorrhagic diathesis, haemodynamically unstable patients, critical patients in whom HDF is preferred.

1.2.3.4 Access routes

It is generally considered that these patients will require haemodialysis for a short period of time. For this reason, a temporary, non-unsealed, two-lumen central venous catheter is preferred to ensure adequate flow for dialysis with minimal risk of complications.

1.2.3.5. Equipment

With haemodialysis, the patient's blood comes into contact with a dialysis solution through a semi-permeable membrane belonging to the haemodialysis machine.

1.2.3.6. Prescription

To prescribe haemodialysis, the following factors must be taken into account: blood flow rate, dialysis solution flow rate, dialyser dimensions (dialysis membrane, extracorporeal circuit tubing dimensions, dialysis solution composition, dialysis solution temperature, ultrafiltration, anticoagulation, duration of haemodialysis session.

1.2.3.7 Complications of acute intermittent haemodialysis

Complications that may be encountered in patients with AKI and HD are: hypotension, central venous catheter infection, complications related to the timing of central venous catheter insertion (pneumothorax, haemothorax, pulmonary embolism), imbalance syndrome, haemolysis, anaphylaxis.

2. CHRONIC DIALYSIS

2. 1. Chronic kidney disease

2.2.1. Definition. Staging

Chronic kidney disease (CKD) is defined by the presence over a period of at least 3 months of abnormalities of renal structure or function with implications for the patient's health status (19, 61).

Table 2.1 CKD classification according to eGFR(19,61)

eGFR	Staging	Degree of renal function impairment
>90	G1	Normal or increased GFR
89-60	G2	slightly low GFR
59-45	G3a	Slightly to moderately low GFR
44-30	G3b	Moderate to severely low GFR
29-15	G4	Severely low GFR
<15	G5	Kidney failure

2.2.2. Etiology

In children, the most common causes of CKD and CKD G5 are: congenital anomalies of the kidneys and urinary tract (CAKUT). Other causes: hereditary diseases, acquired glomerular diseases, metabolic diseases, neoplasia, tumours, unidentified causes.

2.1.1.Indications for initiation of renal replacement therapy in chronic kidney disease

According to KDOQI (Kidney Diseases Outcomes Quality Initiative) and European guidelines it is recommended (43): at GFR <=15 ml/min/1.73m2 dialysis initiation should

be considered; at GFR <=8 ml/min/1.73m2 dialysis should be initiated even if the patient is still asymptomatic.

2.2. Renal replacement therapy in CKD G5

2.2.1. Peritoneal dialysis in CKD G5

Peritoneal dialysis is considered the ideal modality for renal replacement in children with CKD G5, especially for those diagnosed in the first decade of life. Over time it has proven to be an effective modality of dialysis worldwide.

2.2.1.1 . Advantages and disadvantages of chronic peritoneal dialysis (CPD)

Advantages: ideal for young children and infants, simple and easy to learn technique, performed at the patient's home, fewer dietary and fluid restrictions, better preservation of residual renal function, lower risk of bacteraemia and septicaemia, lower cardiovascular risk, less need for blood transfusions.

Disadvantages: risk of 'burnout' for carers, risk of non-adherence to dialysis prescriptions and therefore ineffective treatment, risk of depression, infectious risks (peritonitis, catheter exit tract infection/tunnel infections), risk of abdominal hernias, risk of decreased appetite with reduced nutritional intake due to abdominal pressure.

2.2.1.2. Types of chronic peritoneal dialysis :

- continuous ambulatory peritoneal dialysis (CAPD)

- automatic peritoneal dialysis (APD): intermittent nocturnal, continuous cycling, adapted automatic, Tidal peritoneal dialysis

2.2.1.3. Patient preparation prior to initiation of chronic dialysis. Principles.

Before starting CPD, both patient and family should be informed about the dialysis procedure through information materials (written and video). It is also necessary: a clinical assessment and laboratory tests, screening for chronic nasal carriage of Staphylococcus aureus , pre-operative assessment to identify signs of umbilical or inguinal hernia, to plan the catheter exit site.

The principle of chronic peritoneal dialysis is the same as in acute peritoneal dialysis.

2.2.1.6. Prescribing chronic peritoneal dialysis

Before determining the dialysis prescription, it must be determined which type of chronic peritoneal dialysis the patient will undergo: CAPD or APD. As a rule, in CAPD 3 to 5 shifts are performed in 24 hours. In APD: in intermittent night-time dialysis, rapid

exchanges are performed only during the night, and in automatic dialysis with continuous cycles, rapid exchanges are performed at night and only one exchange during the day.

2.2.1.5 Monitoring the CKD G5 patient on peritoneal dialysis

Patients on chronic peritoneal dialysis require constant monitoring, both to estimate appropriate dialysis and to modify dialysis parameters according to required regimens, and through regular clinical and biochemical assessments.

2.2.1.6 Complications of chronic peritoneal dialysis (CPD)

CDP may associate complications: infectious (peritonitis, tunnel infection), non-infectious (mechanical complications caused by increased intra-abdominal pressure or related to catheter malfunction), sclerosing peritonitis, pain.

2.2.1. Haemodialysis in CKD G5 with the need for RRT

2.2.1.1.Advantages and disadvantages of haemodialysis (HD) in CKD G5

In Europe, the ratio of peritoneal dialysis patients to haemodialysis patients is 2:1 (118).

Advantages of HD: rapid way to rebalance the body by removing excess fluid and correcting hydro-electrolyte imbalances, haemodialysis sessions are organised 3 times/week, the rest of the time remains free, the patient is constantly monitored by medical staff during dialysis, if FAV (arteriovenous fistula) is used for vascular access, risks of infection and complications are lower.

Disadvantages: most haemodialysis machines are authorised for operation in patients weighing > 15 - 20kg, requires presence in hospital to perform the operation 3 times/week, haemodialysis schedule must be strictly adhered to, requires vascular access for operation, requires specialised equipment and team, cannot be performed in haemodynamically unstable patients, requires more food and fluid restrictions, involves infectious risks, involves increased need for blood transfusions.

2.2.1.2. Principles. Prescription

The operating principles of haemodialysis have been discussed previously. There are some aspects of technique and haemodialysis prescription in CKD that are different in the paediatric patient.

AVF (arteriovenous fistula) is the general recommendation for vascular access, but among paediatric patients it is not always feasible, especially in young children. The central venous catheter (CVC) is another option for vascular access, most commonly used in the young child, in whom the performance of AVF is difficult.

Generally , for the CKD G5 patient with a RRT requirement: 3 dialysis sessions/week are performed, lasting about 4 hours, use anticoagulation of the circuit with heparin, use different blood flow rates, different volumes of blood adapted to the patient's weight to ensure good clearance and ultrafiltration to keep the patient cardiovascular stable, the patient's pre-dialysis weight is established in order to determine the need for ultrafiltration.

2.2.1 Complications associated with the CKD G5 patient requiring chronic dialysis

2.2.1.1.Bone and mineral metabolism disorders (CKD MBD)

It is characterised by the presence of one or more of the following: abnormalities of calcium, phosphorus, parathormone and Vitamin D3; changes in bone structure and composition; calcifications in vessels or other soft tissues.

2.2.1.2. Stunting

There are many factors involved in growth impairment in the CKD patient with or without RRT:

low caloric intake, established caloric protein malnutrition, metabolic acidosis, chronic anaemia, impaired mineral and bone metabolism, growth hormone resistance; prior corticosteroid treatment, genetic factors, associated comorbidities

2.2.1.3.Chronic anaemia

Anaemia is common in dialysis patients and is associated with increased risk of mortality, cardiac damage through left ventricular hypertrophy, a factor involved in growth impairment. The main cause is decreased endogenous production of erythropoietin

2.2.1.4. Cardiovascular complications

Risk factors associated with the development of cardiovascular disease are hypertension, ventricular hypertrophy, dyslipidaemia and disorders of mineral and bone metabolism.

Compared to the general population, mortality associated with cardiovascular risk is 1000 times higher (129).

2.2.1.5. Complications related to neuropsychiatric development

Neurodevelopmental deficits have been observed over time in children requiring chronic dialysis therapy. They are also thought to be influenced by: school absenteeism, social environment which may or may not provide learning opportunities, fatigue, need for daytime sleep, effects of uraemia or other toxic metabolites on a developing brain. Another

important aspect frequently encountered in the CKD G5 patient, is the risk of depression, with decreased self-image

2.2.1.6. Infectious complications

Infectious complications are another important cause of mortality associated with children on dialysis, whether peritoneal dialysis or haemodialysis. In peritoneal dialysis, infectious complications are acute peritonitis and catheter infection (tunnel infection or catheter exit site infection). For patients requiring HD, infectious complications are related to central venous catheter infection. Therefore, in these patients, FAV is preferred, if possible, as it is associated with a much lower risk of complications.

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II. SPECIAL PART - PERSONAL CONTRIBUTIONS

3. Working hypothesis and general objectives

In the Children's Emergency Clinical Hospital "Maria Sklodowska Curie" in the Paediatric Nephrology Ward and Haemodialysis Center patients diagnosed with severe AKI with acute dialysis need were cared for annually for different periods of time, as well as children diagnosed with CKD G5. Patients received peritoneal dialysis or haemodialysis, acute or chronic.

Monitoring of these patients during re-evaluations in the clinic generated the idea of a clinical trial on the long-term implications of severe AKI requiring dialysis. In these patients, the presence of hypertension, proteinuria, elevated serum creatinine values and decreased eGFR >= 90 days after the AKI episode are long-term consequences and risk factors for the development of CRB and the need for some form of renal replacement therapy (RRT). An important objective of the study is to optimise the identification of patients at risk by appropriate monitoring and to institute therapeutic measures that may influence modifiable risk factors (e.g. high blood pressure), so that the rate of progression to chronic disease decreases.

Another objective of the study is to monitor complications associated with children with CKD. These children often require long periods of dialysis (months or years) before kidney transplantation. The aim of the study is to optimise monitoring and early diagnosis of these complications and to administer appropriate treatment, so as to improve the patient's quality of life in the pre-transplant period and to reduce the morbidity and mortality rate due to CKD.

The development of a clinical algorithm for choosing renal replacement therapy according to patient characteristics was another focus of this study.

4 Prognostic implications of severe acute kidney injury requiring renal replacement therapy: risk factors for progression to chronic kidney disease

4.1. Working hypothesis and specific objectives

In the study we followed patients admitted to the "M.S.Curie" Children's Emergency Clinical Hospital in Bucharest, Paediatric Nephrology Department, with a diagnosis of Acute Kidney Injury requiring Dialysis, over a period of 5 years (1 January 2016-31 December 2020).

A large proportion of patients included in the study, were personally cared for, both in the episode of AKI that required the choice and institution of renal replacement therapy, and subsequently, for periodic evaluations post severe AKI and dialysis.

To carry out the study we used data taken from the patients' observation sheets and data from the hospital's computer system: :history of the disease, pathological, physiological and heredo-collateral history, clinical data related to the patient's condition on admission, laboratory investigations.

Objectives: number of cases of severe acute kidney injury requiring renal replacement therapy, type of dialysis therapy chosen according to patient characteristics, complications associated with dialysis therapy, long-term implications of a Severe AKI episode requiring dialysis-identification of risk factors for progression to CKD.

4.2. Materials and methods

Longitudinal, retrospective, observational study of cases of severe acute kidney injury requiring renal replacement therapy. Forty-four patients with AKI and acute dialysis were included in the study.

Inclusion criteria: age between 3 months and 18 years, patients diagnosed with AKI who underwent acute dialysis.

Exclusion criteria: patients in the neonatal period or in the age range 1-3 months (this age group was managed in the NICU-Neonatal Intensive Care Unit department), patients diagnosed with AKI but who did not require acute dialysis.

4.3.Results

The data obtained from the analysis of the patients included in the group had the following results and conclusions:

• Forty-four patients who had suffered an episode of AKI requiring dialysis were included in the study. The number of patients admitted to the clinic with the diagnosis of AKI during this time frame was much higher (151 patients), but as observed most responded to conservative treatment and did not require dialysis. These patients were not excluded from the study.

• Of the total 44 patients included, female dominance (68.2%) was noted both in the group of patients who developed severe AKI and in the group of patients who developed "de novo" CRB: of the 23 patients who presented with proteinuria, 16 were girls; of the 8 patients who presented with eGFR < 60ml/min/1.73m2sc, 5 were girls; of the 14 patients included in the risk group for developing CRB, 11 were girls. Previous studies have not shown an association between the severity of AKI and patient sex, in some studied groups the male sex predominated, in others the female sex, or gender equality was noted in this pathology. Neither in our group, the statistical analysis did not identify a significant value of this variable for the development of a severe episode of AKI with the need for dialysis and progression to CKD.

• The age of the patients included in the study had a median age of 1 year, both for those who progressed to CKD and for those who recovered renal function post AKI. It is noted that patients who did not progress to CKD had an interquartile interval between 7 months and 1 year, compared to those who progressed to CKD and who had an interquartile interval between 9 months and 2 years. It is thus concluded that those with younger age recovered better renal function after the AKI episode.

• The weight of the patients was a significant variable in the study, with a median value of 10 kg. This variable was an important criterion in the choice of the RRT modality performed on the patients in the group. Of the total of 44 patients, 42 underwent peritoneal dialysis, all weighing < 15 kg. In our clinic, haemodialysis machines , with extracorporeal circuits and venous lines are approved for operation in patients weighing > 15 kg. Only 2 patients underwent haemodialysis.

• The most common aetiology of AKI was typical HUS , accounting for 95% of cases. This correlates with the young age of the patients, as HUS is known to occur frequently in children < 5 years of age, but also with the complicated course of this pathology, with the majority of HUS patients developing severe forms of AKI requiring dialysis.

• The majority of patients in the group were anuric (84.1%) . Anuria requires restricted fluid administration, so in order to be able to administer the necessary treatment to

patients without risk of volemic overload, it is necessary to initiate RRT. The period of anuria was variable and the longer it was, the longer the period of need for RRT, the longer the patient's hospitalization period, the more complicated the course and the unfavourable long-term prognosis.

• The water-electrolyte and acid-base balance disturbances characteristic of AKI were present in the group of patients: 66% had hyponatraemia, more than 50% had hyperkalaemia and uncompensated metabolic acidosis. All these imbalances were corrected after initiation of RRT.

• The majority of patients showed significant nitrogen retention since admission to hospital. In the group of patients who developed RRT post AKI, on admission to hospital, serum creatinine had a median value of 3.1 mg/dl, with an interquartile interval of 2.4 mg/dl to 4.36 mg/dl. Serum urea had a median value of 125 mg/dl, with an interquartile interval of 81-157 mg/dl)

• Peritoneal dialysis was the dialysis modality of choice, with patient weight being one of the most important factors in the choice of method. It proved effective in all patients, succeeding in correcting the imbalances that had been established and was maintained until patients resumed diuresis. The minimum number of dialysis days was 3 days and the maximum number of days was 33 days.

• The median number of days of dialysis required was 14 days, with interquartile interval of 6-20. The two patients with the most days of dialysis (33 days, 25 days), required prolonged hospitalization(71 days, 34 days respectively), had a complicated course of AKI, with rapid progression to RRT and death.

• Statistical analysis identified that the number of patient days in hospital was the main predictor of progression to CKD, with a cut off value of 23 days. Patients hospitalized >= 23 days have an increased risk of developing CKD post AKI.

• Complications suffered by patients during the performance of RRT were infectious and/or mechanical: 5 patients were complicated with peritonitis requiring intraperitoneal and systemic antibiotic therapy, 6 patients had difficulty performing peritoneal dialysis due to mechanical causes and required catheter replacement, 1 patient had both complications.

• Monitoring of patients at 90 days post AKI is essential for early identification of patients who develop "de novo" CKD or patients who are "at risk" of developing CKD.

Persistence of proteinuria at 3 months post AKI and/or a fall in eGFR <60ml/min/1.73m2sc defines CKD.

Presence of hypertension at 3 months post AKI and/or eGFR decrease 89-60 ml/min/1.73m2sc or hyperfiltration with eGFR>150ml/min/1.73m2sc are risk factors for progression to CKD.

In the studied group, 23 patients (52%) had proteinuria at 3 months post AKI, meeting the defining criteria for CKD.

In the studied group, the patients included were of young age, mostly under 2 years, the eGFR value was used as a guideline to assess renal function and no staging of renal disease was performed using it. However, previous studies have shown that a decrease in eGFR greater than 1 standard deviation from normal for age and sex is significant and those patients should be carefully monitored and further investigated.

4.4. Discussion. Conclusions

Several important conclusions emerged from this study:

- Acute kidney injury affects a large number of children and is associated with a high risk of morbidity and mortality.
- Renal replacement therapy is an extremely important life-saving treatment for children who suffer an episode of acute kidney injury. Acute peritoneal dialysis was the first modality of RRT used in children, being simple, safe, cost-effective and proven effective in ensuring adequate clearance, good ultrafiltration and correction of hydro-electrolyte and acid-base imbalances. In Europe it is used extensively in both high socio-economic and developing countries. And in our clinic it is a widely used dialysis modality for both AKI and chronic patients.
- All patients going through a severe episode of AKI are at risk of developing chronic kidney disease. **They should be monitored at 1,3, 6,12 months after the episode of acute kidney injury**, then annually. As part of this assessment, the following are required: measurement of BP, performing urine summary and urinary protein/creatinine ratio, determination of serum urea and creatinine and Bedside Schwartz eGFR calculation. KDIGO recommends an evaluation of the patient 90 days after the episode of ARF(165).
- In addition to eGFR determination, proteinuria has been shown to be closely related to progression to chronic kidney disease regardless of eGFR value(161,162). Determination of the urinary protein/creatinine ratio, performed from a urine sample, is a simple investigation to perform and should become a constant investigation present in the work-up performed in these patients.

- Increased proteinuria and elevated blood pressure values are risk factors for progression of kidney disease that can potentially be modified by instituted treatment and thus slow or stop disease progression.
- ACEs (angiotensin-converting enzyme inhibitors) and ARBs (angiotensin receptor blockers) have been shown to be much more effective in decreasing proteinuria and progression of coronary kidney disease than other antihypertensive agents(156).
- Maintaining blood pressure values around the 50th percentile for age has been shown to slow the rate of progression of kidney disease(136). Determination of BP values at home is necessary for these patients both for monitoring and for tracking the effectiveness of treatment (155).
- These classes of antihypertensives have also been shown to be effective as antiproteinurics (137), but not in all patients. In some of these patients, proteinuria remained at elevated levels despite instituted treatment and thus maintained the risk of progression of chronic kidney disease (136,138).
- Early identification of patients who develop CKD or are at risk of developing CKD, allows early institution of the necessary therapeutic measures to decrease disease progression and progression to dialysis. According to international studies, it has been found that there is an annual decline in eGFR for patients diagnosed with chronic kidney disease developed after a severe episode of acute kidney injury, whether or not requiring dialysis therapy.
- The European Study Group of Nutritional Treatment of Chronic Renal Failure in Childhood reported in a study of a group of patients diagnosed with CKD a mean decline in eGFR of approximately 4.5 ml/1.73m2/min over 2 years(134).
- CKiD (Chronic Kidney Disease in Children) reported in another study a mean annual decrease in eGFR of 1.8ml/1.73m^2/min(135).
- The Acute Kidney Injury - Chronic Kidney Disease association is complex and remains a focus for future studies. It is still unclear, which patients are more likely to develop chronic kidney disease. Future studies will be needed to establish the causal relationship between AKI and the subsequent development of CKD.
- Studies in adult patients have shown that the severity and duration of AKI episodes increase the risk of developing CKD (163).
- It should be determined whether:
  - The cause of acute kidney injury might be related to a higher risk of later developing chronic kidney disease;

• Whether certain treatments, could help decrease the severity of the acute injury or prevent it from setting in, and thus decrease the risk of kidney disease. Furosemide given at a dose of 1 mg/kgc/dose, helps to maintain kidney flow and has a kidney protective effect in the early stages of AKI;

• If new biomarkers, KIM-1, IL-18 , N-GAL and L-FABP can be used both for early detection of acute kidney injury and in assessing the risk of progression to chronic kidney disease. Some studies have shown that 5 years after the episode of AKI, patients who developed CKD showed increased levels of some of these biomarkers. A clear correlation could not be established so far and future studies are needed.

5. Complications associated with the patient with chronic kidney disease dialytic stage: monitoring, diagnosis and treatment

5.1 Working hypothesis and specific objectives

In the study we followed patients admitted to the Children's Emergency Clinical Hospital "Maria Sklodowska Curie", Bucharest, in the Paediatric Nephrology Department and in the Haemodialysis Centre, with the diagnosis of Chronic Kidney Disease stage G5 (CKD), under chronic dialysis program (haemodialysis or peritoneal dialysis), in the period 2016-2020.

To conduct the study we used data taken from the patients' hospitalization records and the hospital's information system: history of disease, pathological history, comorbidities, clinical data related to the patient's condition and anthropometric data, laboratory investigations, results of imaging and interdisciplinary assessments.

Objectives:

- Diagnosis and management of complications associated with the chronic dialysis patient: anaemia, bone and mineral metabolism disorders, water-electrolyte and acid-base balance disorders and cardiovascular impairment;
- Complications of the vascular approach required to perform haemodialysis and its implications for changing the type of RRT from HD to CPD.

5.2 Material and method

Retrospective study of patients diagnosed with Chronic Kidney Disease stage G5 (CKD) on chronic dialysis program at the Emergency Clinical Hospital for Maria Slodowska Curie Children's Hospital, in the Pediatric Nephrology Department and the Hemodialysis Center, from 2016 to 2020. 25 patients were included in the study, 9 of whom are still undergoing renal replacement therapy in our clinic.

Inclusion criteria: patients with CKD G5, age < 18 years, follow-up of at least 3 months in the clinic.

5.3 Results / 5.4 Discussion. Conclusions

a. In the period 2015-2020 in the Dialysis Center of the Children's Emergency Clinical Hospital "M.S.Curie", 25 patients diagnosed with CKD G5 and in need of dialysis were cared for. The age of the patients ranged from 9 to 18 years, with female dominance (60%).

All these patients were initially included in the HD program. The decision to perform HD as a modality of RRT was made based on several factors:

- Patient characteristics(age, weight, waist, hemodynamic status at the time of initiation of RRT).
- Preference/experience of clinicians and patient/carers at the time

b. The most common **aetiology** of the patients in the study group was congenital and hereditary diseases - 17 patients (68%). Acquired causes of CKD were found in 20% of cases (5 patients), while in 3 patients the aetiology remained uncertain.

According to studies conducted by CkiD (Chronic Kidney Disease in Children), ESCAPE (The Effect of Strict Blood Pressure Control and ACE inhibition on the Progression of CRF in Paediatric Patients), in Europe by the ItalKid Project and in North America by NAPRTCS (the North American Paediatric Renal Trials and Collaborative Studies), in the aetiology of chronic kidney disease, non-glomerular diseases - congenital abnormalities of the kidneys and urinary tract have an increased prevalence compared to glomerular diseases. (131,132,133).

The data also coincide with the conclusion of our study, 68% of the patients in our group have nonglomerular aetiology. This could also be explained by the fact that congenital renal anomalies can remain asymptomatic for a long time in evolution and patients do not performs routine medical check-ups, while glomerular pathology is accompanied by clinical manifestations that require immediate medical evaluation and thus a prompt diagnosis.

c. Vascular access of patients included in the HD program was achieved in 80% of cases (20 patients) by the establishment of a CVC. Only 5 patients (20%) of the group received functional AVFs.

Although the universal recommendation for vascular approach is FAV, this is not always achievable among paediatric patients. It is estimated that, despite these recommendations, the majority of CKD G5 children with RRT requirement perform HD via central venous catheter: 78% in the United States and 60% in Europe(43)

This result is also found in our study.

Therefore, CVC remains the most commonly used vascular access route for the young child in whom performing FAV is not feasible.

For the future, FAV should be encouraged for all patients in whom immediate renal transplantation is not expected and should be encouraged even for patients with small venous diameters (<3 mm).

d. **Complications of vascular access**

In CVC the most common complication was thrombosis encountered in 7 patients(28%), followed by catheter infection encountered in 4 patients(16%).

In the case of catheter infections, a significant reduction of catheter infections was observed in the group of patients studied with strict adherence to certain rules:

- sterilisation of healthy carriers of intranasal staphylococcus aureus
- strict compliance with the protocol for hand washing and disinfection
- performing sterile CVC manoeuvres.

The last catheter infection was reported at the end of 2020- 1 patient, thereafter no further catheter infections were reported.

For patients receiving FAV, fistula aneurysm was the most common complication, followed by fistula thrombosis. These patients were converted to PD.

The aim would be to achieve better control of AH in the case of aneurysms and to avoid intradialytic hypotension in the case of thrombosis.

e. Complications associated with the patient diagnosed with CKD G5 with RRT requirement

- Stunting , defined as height and weight below the 3rd percentile for age and sex, was found in 13 patients (52%) of the group. Another 4 patients (16%) had a weight below the 3rd percentile with normal waist.

A multitude of factors are involved in affecting the growth of the CKD patient. Modifiable factors are those of interest to clinicians. Maintaining adequate nutrition, correcting anaemia, correcting imbalances related to phosphocalcic metabolism, maintaining parathormone at values up to 3-5 times normal, correcting acidosis are the goals. By monitoring patients during monthly assessments, adjustments are made to the background treatment according to the needs of each patient in order to achieve the best possible control of these imbalances.

-Chronic anaemia was present in all patients of the studied group. The main cause is a decrease in endogenous erythropoietin production and to a lesser extent other factors (iron deficiency, blood loss in HD, chronic inflammation, etc).

All patients were evaluated by the following investigations: complete blood count, reticulocytes, sideremia, ferritin, transferrin saturation, total iron-binding capacity, as well as occult bleeding test and vitamin B12 and folic acid. Other causes of anaemia can thus be identified: iron deficiency (microcytic anaemia) or folate/vitamin B12 deficiency (macrocytic).

After identifying the causes, treatment consisted of iron supplementation (if necessary) and erythropoiesis-stimulating agents (erythropoietin).

For erythropoietin treatment, either eopoietin (80-120 IU/kg/week in 3 doses) or darbeopoietin (0.25-0.25 microg/kg/week) was used, subcutaneously for peritoneal dialysis and intravenously for haemodialysis patients (via vascular access), until obtaining a haemoglobin value of 11-12g/dl, according to the recommendations in the literature (128,152,153).

Values < 10-11g/dl increase the risk of heart damage

Values > 13g/dl are associated with cardiovascular events in adults; retrospective studies in the paediatric population have not demonstrated this risk in children(128,151).

The introduction of erythropoietin in the treatment of anaemia (in 1986) revolutionised the treatment of CKD, as symptoms erroneously attributed to uraemia disappeared with the correction of anaemia: improved appetite, improved exercise tolerance, increased intelligence test scores and quality of life(128,149).

- Altered mineral metabolism and impaired bone structure and composition are consistently seen in patients undergoing renal replacement therapy(139). Abnormalities of calcium, phosphorus, PTH and Vitanin D3 were found in patients.

It appears that elevated PTH may itself be a risk factor for myocardial fibrosis, thickening of arterial walls and a risk factor for hypertension(141).

Vitamin D treatment was necessary to control parathormone levels and was given to all patients in the form of Calcitriol or alpha- calcidol. Studies show increased survival in dialysis patients receiving Vitamin D3 treatment(146).

The majority of patients experienced secondary hyperparathyroidism responsive to treatment. Current European guidelines recommend maintaining a PTH level of 3-5 times normal for the dialysis patient.

Only one patient required parathyroidectomy in the context of unresponsive secondary hyperparathyroidism.

- The patients in the study group showed hyperphosphoremia, with a median serum phosphorus value of 6.1 mg/dl. Increased serum phosphorus levels are strongly correlated with increased PTH, increased renal fibrosis, ventricular hypertrophy and increased risk of mortality(140).

The phosphorus chelator used in the treatment of the patients in the group was Sevelamer- phosphorus chelator without calcium. It proved to be very effective in lowering phosphorus, phosphorus x calcium product, parathormone without causing hypercalcemia.

It has been shown to slow the progression of cardiovascular disease, the occurrence of vascular calcifications and decrease mortality rates (147,148).

- Cardiovascular complications

- Hypertension was present in 80% of patients . These patients received antihypertensive monotherapy or combination regimen with 2,3 or 4 antihypertensives. Control of hypertension was achieved in 68% of patients (17 patients). Lack of compliance with treatment was one of the reasons for lack of response to treatment. Fluid overload was another cause, corrected by prolonging dialysis time.
- HVS was found in 60% of the patients in the group, with varying degrees of severity, in 52% of cases (13 patients) being concentric and in 16% of cases (4 patients) being eccentric.
- Vascular involvement - vascular calcifications were found in 3 patients (12%).

According to studies in the literature, a child or young individual on renal replacement therapy has the same risk rate of cardiovascular death as an 80-year-old individual in the general population (142).

The following are cited as risk factors for cardiovascular disease:

- hypercalcaemia, hyperphosphatemia, elevated phosphorus x calcium values. However, there have been studies demonstrating the presence of calcifications in the vessels and thickening of the carotid walls, without yet evident changes in mineral metabolism, demonstrating that CKD "per se" plays a role in the development of these lesions (143,144).
- Uremia favors calcifications in the tunica media, with decreased vessel elasticity. Measurement of carotid IMT (intima-media thickness) by cardiac ultrasound is the method of assessing cardiac damage and its increase is associated with a poor prognosis(145).
- Disorders in lipid metabolism are frequently seen in patients with CKD representing another risk factor for cardiovascular disease. (157).

The goal for these patients is to slow the progression of cardiovascular disease through effective control of hypertension, correction of anaemia and phosphocalcic metabolism imbalances.

Through clinical follow-up of patients, laboratory tests, regular cardiac ultrasound and monitoring of BP values, we can detect early these modifiable risk factors with appropriate treatment.

6. RRT

All patients included in the study initially underwent HD. Vascular access was obtained by CVC in 80% of cases or by AVF in 20% of cases.

Following these patients during the study, it was found that some of them were converted to PD, this RRT modality being used more and more frequently in our clinic for the chronic patient. Its advantages have been previously discussed, the most important being related to the fact that the residual renal function is better preserved, it is associated with a lower cardiovascular risk and does not require a venous approach - a very important aspect for the chronic patient, who needs to protect the venous capital, while waiting for the transplant renal.

In the case of the studied group, 7 patients were converted to DP. This decision was made due to the complications associated with vascular access (aneurysm / fistula thrombosis, CVC infections), due to associated comorbidities (Hereditary thrombophilia), as well as due to the patient's choice (the convenience of performing DP at home).

In the future, the aim is to propose PD as the first option for RRT in patients in whom renal transplantation cannot be performed quickly, and HD as the second option for patients in whom PD cannot be performed.

HD remains a rapid way to rebalance the body by removing excess fluid and correcting hydro-electrolyte imbalances.

Although general recommendations are to choose PD as the RRT modality for the chronically ill patient, there is a recent downward trend in its prescription. NAPRTC(The North American Paediatric Renal Trials and Collaborative Studies),USRDS(United States Renal Data System) and COR(Canadian Organ Replacement Registry) reported a decrease in the number of patients performing PD and an increase in those performing HD (43).

6. Clinical algorithm for choosing the type of dialysis according to the clinical characteristics of the patient

Another objective of the study was to develop a clinical algorithm for the choice of the type of dialysis for the paediatric patient with severe AKI and the paediatric patient with CKD stage V. This algorithm is based on the current recommendations of international guidelines, adapted to the existing resources of the "M.S.Curie" Children's Emergency Hospital and Romania..

1. Dialysis therapy for children diagnosed with AKI can be achieved by three modalities: peritoneal dialysis, acute intermittent haemodialysis and continuous dialysis therapy (continuous haemodialysis, continuous haemofiltration, continuous haemodiafiltration).

When deciding on the modality of dialysis for AKI patients, the characteristics of the patient and the resources available in the clinic (human and technical) must be taken into account.

- for patients weighing <15 kg, for those with haemodynamic instability or coagulation disorders, PD or continuous dialysis therapy (HDF) should be chosen.
- HD is used in children weighing more than 15-20 kg, hemodynamically stable, as the critical patient cannot tolerate rapid changes in flow, and most HD machines are approved for use in patients weighing < 15 kg;
- HDF requires a special machine and is performed on intensive care units.

PD is much easier to perform compared to HD or HDF, does not require sophisticated equipment and the technique is easy to learn and perform, it can be performed at all ages from neonatal to adolescence. It has proven effective in ensuring adequate clearance, effective ultrafiltration , and in correcting hydro-electrolyte and acid-base imbalances, even in the critically ill patient. In Europe, PD remains the most widely used method in both developed and developing countries.

2. Patients diagnosed with stage 4 CKD require frequent monitoring and preparation of both the patient and caregivers, through discussion with the patient and caregivers, provision of information materials, about the progression of the disease to stage 5, the need for dialysis and/or renal transplantation, and the performance of necessary procedures (such as AVF).

3. For the BRC G5 patient:

- CDP is the ideal modality of renal function replacement for the paediatric patient with stage 5 CKD. It is performed by continuous ambulatory peritoneal dialysis or automated peritoneal dialysis. Can be performed in both young patients and adolescents

- HD is the type of dialysis that can be performed in children weighing >15-20 kg, and most haemodialysis machines are approved for operation in patients above this weight limit.

- The idea of preventive renal transplantation from a living related donor is accepted by most clinicians, but a small number of patients benefit from this form of renal replacement.

7. Conclusions and personal contributions

This paper aimed to:

a. The clinical study of patients admitted to the Children's Emergency Clinical Hospital "M.S. Curie" Bucharest , Pediatric Nephrology Department, with the diagnosis of AKI requiring dialysis, over a period of 5 years (2016-2020). A large proportion of the patients included in the study were personally cared for, both in the episode of acute kidney injury requiring the choice and institution of dialysis therapy, and in post-episode AKI evaluations.

The study objectives included analysis of these cases, the type of ESRD chosen and associated complications , as well as the long-term implications of a severe AKI episode requiring dialysis and identification of risk factors for progression to CRB.

b. Clinical study of patients admitted to the Children's Emergency Clinical Hospital "M.S.Curie "Bucharest, in the Paediatric Nephrology Department and in the Haemodialysis Center, diagnosed with G5 RBC, with the need for RRT (peritoneal dialysis or haemodialysis), over a period of 5 years (2016-2020). The objectives of the study included the diagnosis and management of complications associated with the patient on chronic dialysis, and complications associated with the vascular approach required to perform HD , their implications on the decision to convert the patient to PD.

c. Development of an algorithm for the choice of the type of dialysis required for the patient with AKI, but also for the CKD G5 patient, based on the recommendations of international guidelines and adapted to the existing resources in our hospital and in Romania.

Study limitations:

- In the studied group, the most common cause of AKI was typical HUS , with prodromal diarrhoea, with predominance of young age. Future studies should include cases of AKI with more varied aetiological substrate, in patients of all ages

- Given that any episode of AKI carries a risk of progression to CRB, a study including all patients diagnosed with AKI with or without the need for RRT could achieve more statistically significant correlations to identify risk factors for progression to CRB in these patients.

- Monitoring of patients could not be performed in all cases, as one patient did not present for follow-up.

- In the case of CKD G5 patients, all patients were initially included in the HD program and in the evolution, some of them were converted to PD. It will be interesting to follow the BRC G5 patient included in the PD program as an initial dialysis modality: how long will the peritoneum retain its dialysis membrane qualities, whether cardiovascular damage is slowed down in these patients as shown in other studies, the degree of patient and caregiver compliance over long periods of time to this dialysis modality, etc.

Disadvantages of the study:

- For patients who did not show signs of CKD at the 3-month post-AMI evaluation, progression was not followed after 1 year. It is considered that even for those in whom recovery appears complete, a further assessment 1 year after the episode of AKI is required. The assessment should include: clinical examination, BP determination (ambulatory monitoring is recommended and the patient presents with diary performed at home), serum creatinine determination, eGFR, urinalysis and urinary protein/creatinine ratio. A protocol for monitoring the patient post AKI should be established.

- For the BRC G5 patient with associated complications due to loss of renal function, each of these should be monitored in dynamic detail, by means of laboratory analyses performed periodically, over long periods of time, following the evolution according to the treatment administered in a given period, the results obtained under an instituted treatment, the measures taken following these results, conclusions.

Advantages of the study:

- The study was conducted on batches of patients admitted and cared for in the "M.S.Curie" Children's Clinical Hospital, where there is a Paediatric Nephrology Department and a Haemodialysis Centre, with multidisciplinary teams and technical facilities necessary for the care of these patients. This has allowed the analysis in one place of a significant number of patients with complex pathology, requiring dialysis procedures, complex treatments, investigations and monitoring.

- PD was the most commonly used form of acute dialysis. The study proves that it is an effective treatment modality for severe AKI that does not respond to supportive therapy.

- Provides clinically important information about patient follow-up post AKI.

- Identifies the presence of risk factors for progression to CKD in post ARF patients and thus

- Enables therapeutic measures to be instituted to slow disease progression.

- Supports the usefulness of establishing a monitoring protocol for the post-AKI patient.

- Supports the idea of initiating PD as the primary modality of RRT for the CKD G5 patient.

Personal contributions:

- The practical aim of the study was to compose a clinical algorithm useful in the choice of dialysis modality for the patient diagnosed with AKI or CKD.

- Establishment of a monitoring protocol for the post AKI patient, for early identification of risk factors and patients who develop "de novo" CKD.

- The conversion of patients from HD to PD and their favourable outcome under PD has changed the choice of RRT for the CKD patient. It encourages the initiation of PD in the chronic patient, thus protecting the vascular capital so important for these patients awaiting renal transplantation. A project is also underway to obtain automated home peritoneal dialysis machines;

- From this study, it appears that future research is needed to determine whether :

• Therapeutic measures to prevent AKI, or those that decrease the severity of the AKI episode, may impact the future development of chronic disease.

• Analysis of new biomarkers (KIM-1, N-GAL, IL-18) will help to identify early in the evolution of renal tissue damage before renal function is impaired and their values could be correlated with the severity of the AKI episode or the risk of progression to CKD.

•Innovative treatments will be able to better control complications associated with BRC G5 patient. Currently, despite proper management and treatments, they continue to affect these patients.

Several important conclusions emerge from this study:

1. AKI affects a large number of children and is associated with high risk of morbidity and mortality.
2. The number of children who have had an episode of AKI responsive to supportive treatment without the need for dialysis is much higher than the number of children who have had a severe episode of AKI requiring dialysis.
3. All patients who experience an episode of AKI, with or without dialysis, are at risk of developing CRB.
4. According to the study, younger patients recovered better renal function after the episode of AKI.
5. The most common aetiology of AKI was HUS- glomerular causes. The study also included patients affected by the wave of typical HUS illnesses with prodromal diarrhoea , from 2016-2017.
6. Dialysis therapy is lifesaving. Acute peritoneal dialysis has been the preferred modality of dialysis in AKI patient and has proven its effectiveness.
7. The number of days of hospitalization of dialysis patients was positively correlated with the risk of progression to CKD. The duration of hospitalization was identified as the main predictor of progression to CKD, with a cut-off value of 23 days.
8. Monitoring of patients at 90 days post AKI is essential for early identification of patients who develop de novo CKD.
9. Persistence of proteinuria at 90 days post AKI and/or eGFR decrease <60ml/min/1.73m^2 b.d. defines CKD
10. Persistence of hypertension at 90 days post AKI and/or decrease in eGFR <89-60ml/min/1.73m2s.c. or hyperfiltration with eGFR >150 ml/min/1.73m2s.c. are risk factors for progression to CKD.
11. Early identification of patients who develop CRB or have risk factors for developing CRB allows early measures to be put in place to slow the progression of kidney disease and dialysis.
12. The number of CKD G5 patients is increasing. Studies show that the number of children with CKD G5 has almost tripled in the last 30 years(43).

13.Dialysis(HD, PD) remains the most common modality of RRT until renal transplantation.

14. The management of patients with G5 CRB has been much improved in recent times, but nevertheless mortality among them has remained high, their life expectancy being 30-40 years less than that of healthy individuals with the same age, race and sex characteristics(84,85,86).

15. In CKD G5 patients, the most common aetiology was non-glomerular causes, namely congenital abnormalities of the kidney and urinary tract.

16. The most used dialysis modality for the chronic patient was HD.

17. Vascular access was achieved in 80% of cases by setting up a CVC. Performing FAV was possible in only 20% of cases.

18. Complications of vascular access were found in both CVC and FAV and was one of the factors determining the conversion of patients to PD.

19. Patients converted to PD had a favourable outcome.

20. All patients with CKD G5 had associated complications of chronic disease: anaemia, bone and mineral metabolism disorders, growth retardation, cardiovascular impairment . Although attempts are being made to manage these imbalances as correctly as possible by detecting them early and administering treatments to correct them, these complications continue to be present, which raises future challenges in identifying innovative treatments.

21. According to studies in the literature, a child or young individual on dialysis has the same risk of cardiovascular death as an 80-year-old individual in the general population.

22. RRT in patients diagnosed with AKI can be achieved by PD, HD and HDF

23. The choice of dialysis modality must take into account medical and socio-economic aspects.

24. Patient characteristics: age, weight, aetiology of AKI, associated comorbidities, haemodynamic status of the patient are essential in the choice of RRT.

25. The clinician's experience, the patient's preference, the existing resources in the clinic (multidisciplinary team, necessary equipment, technology) are also very important for the choice of the RRT modality.

26. HD is the nodal modality chosen for the haemodynamically stable patient weighing > 15 kg.

27. PD can be performed in hemodynamically stable or unstable patient regardless of weight. The only absolute contraindications are related to pre-existing pathology of the abdominal and/or peritoneal cavity.

28. HDF is reserved for the critically ill patient and is performed in intensive care units.

29. Patients diagnosed with CKD G4 (eGFR Bedside Schwarz= 29-15ml/min/1.73m^2bs) should be included in an education program about available RRT modalities, renal transplantation and the steps required to enroll the patient in the National Renal Transplant Registry.

30. For CKD G4 patients in whom HD is expected to be initiated within 5-6 months and renal transplantation is not anticipated within this timeframe, it is recommended to perform FAV.