

**Sudan University of Sciences and Technology**

**College of Graduate Studies**

**Evaluation of The Role of  $^{99m}\text{Tc}$ -DMSA Scan In  
Diagnosis of UTI Of Sudanese Children Patients**

**تقويم دور التصوير بالتكنيشيوم دى.ام.اس.أي في تشخيص إلتهاب القناة  
البولية للمرضى الأطفال السودانيين**

**Research Submitted for partial fulfillments of the requirements of the  
M.Sc. degree of Nuclear Medicine**

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**2015**

## ***Abstract:***

This study include 77 patients in different age, sex, center of origin and type of food and drink intake. To study the relationship between thyroid function test and thyroid uptake using  $^{99m}\text{Tc}$ . The study was also designed to help in determination of the normal range of the thyroid uptake in Sudanese as well as the possibility of replacing the TFT test by thyroid uptake. The study was conducted at RICK; nuclear medicine department (gamma camera and RIA) for five months From MAY to AUG 2009. the level of thyroid hormones T4, T3 and TSH in the subject's blood were measured using sensitive RIA method against the thyroid uptake value in the gamma camera (mediso).the result of this study showed that, there was a direct relationship between thyroid uptake and the level of the thyroid related hormones(for individual). The percentage of thyroid uptake for the subjects included in the study was ranging between 1.2 and 8.0. also the study indicated that There were possibilities of using thyroid uptake only as a diagnostic tool for thyroid activity without TFT due to the ability of thyroid uptake in giving sufficient information concerning thyroid status.

## الخلاصة

أجريت هذه الدراسة على 77 مريض من مختلف الأعمار و الولايات و نوع الطعام و الشراب لديهم، الغرض من الدراسة معرفة العلاقة بين مستوى هرمونات الغدة الدرقية بطرق القياس المناعية الإشعاعية و مسح تشبع الغدة و مقارنة الفحصين من حيث ضبط نتيجة الفحص، وأيضا لحساب المعدل الطبيعي و المقبول للسودانيين و أخيرا إبراز إمكانية إجراء المريض لفحص مسح تشبع الغدة الدرقية فقط إذا كانت نتيجة الفحص تغني عن نتيجة فحص الهرمونات في الدم.

أجريت هذه الدراسة في المعهد القومي للعلاج بالأشعة والطب النووي بالخرطوم (إلقاما كاميرا، معمل قياس المناعة الإشعاعية ) لمدة خمسة أشهر وذلك عن طريق فحص هرمونات الغدة في معمل النظائر المشعة، وفحص تشبع الغدة بقسم الطب النووي حيث إلقاما كاميرا، وقد خلصت الدراسة علي الآتي:

(1) ارتباط فحص مسح تشبع الغدة الدرقية بفحص الهرمونات بطرق القياس المناعية الإشعاعية بعلاقة طردية (فرديا).

(2) الإثبات المبدئي للمعدل الطبيعي لتشبع الغدة لعنصر التكنشيوم المشع وهو 1.2 \_ 8 %.

(3) إمكانية إجراء المريض لفحص مسح تشبع الغدة الدرقية فقط دون الحاجة الماسة لفحص الهرمونات في الدم، إذ أن فحص مسح تشبع الغدة الدرقية يعطي مؤشرات صحيحة لمستوي هرمونات الغدة في الدم إذا كان بالمعدل الطبيعي، الارتفاع أو النقصان

**Table of contents:**

<b>No</b>	<b>content</b>	<b>Page No</b>
	Abstract (English)	
	Abstract (Arabic)	
	Table of content	
	List of figures	
	Chapter one	
<b>1-1</b>	Introduction	
<b>1-2</b>	Problem of the study	
<b>1-3</b>	Purpose of the study	
<b>1-3-1</b>	General objective	
<b>1-3-2</b>	Specific objectives	
<b>1-4</b>	Significances of the study	
	Chapter two : Theoretical background and literature review	
<b>2-1</b>	Theory and Structure	
<b>2-1-1</b>	Scintillation Camera	
<b>2-1-2</b>	Collimators	
<b>2-1-2-1</b>	Parallel Hole	
<b>2-1-2-1-1</b>	Low-energy all-purpose collimators (LEAP)	
<b>2-1-2-1-2</b>	High-resolution collimators	
<b>2-1-2-1-3</b>	High- and medium-energy collimators	
<b>2-1-2-1-4</b>	Slant-hole collimators	
<b>2-1-2-2</b>	Nonparallel-Hole Collimators	
<b>2-1-2-2-1</b>	Pinhole	
<b>2-1-2-2-2</b>	Converging	
<b>2-1-2-2-3</b>	Diverging	
<b>2-1-2-2-4</b>	Fan-beam collimators	
<b>2-1-3</b>	Detector, NaI(Tl) Crystal	
<b>2-1-3-1</b>	Size and Thickness	
<b>2-1-3-2</b>	Energy Selection	
<b>2-1-3-3</b>	Automatic Peak Tracking	
<b>2-1-3-4</b>	Counting	
<b>2-1-4</b>	Position Determining Circuit (x, y Coordinates)	
<b>2-1-4-1</b>	Pulse-height Distribution among PM Tubes	

2-1-5	Intrinsic Spatial Resolution	
2-1-6	Display	
2-1-6-1	Cathode-ray Tube	
2-1-6-2	Display of Individual Interactions	
2-1-6-3	Integration on a Film	
2-1-6-3-1	Film Characteristics	
2-1-6-3-2	Film Exposure	
2-1-6-3-3	Multi format Recording	
2-1-7	Imaging with a Scintillation Camera	
2-1-8	Interfacing with a Computer or All-digital Camera	
2-1-9	Digitization in General	
2-1-9-1	Digitization in the Scintillation Camera	
2-2	Primary quality control Tests of Gamma Cameras	
2-2-1	Intrinsic Spatial Resolution	
2-2-2	Intrinsic Energy Resolution	
2-2-3	Intrinsic Flood Field Uniformity	
2-2-3-1	Integral Uniformity	
2-2-3-2	Differential Uniformity	
2-2-4	System Spatial Resolution without Scatter	
2-2-5	Whole body System Spatial Resolution without Scatter	
2-2-5-1	Resolution Parallel to the Direction of Motion	
2-2-5-2	Resolution Perpendicular to the Direction of Motion	
2-3	Secondary quality control tests of Gamma Camera Systems	
2-3-1	Intrinsic spatial linearity	
2-3-2	Multiple window spatial registration	
2-3-3	Intrinsic count rate performance in air	
2-3-4	System Count Rate Performance with Scatter	
2-3-5	Intrinsic Spatial Resolution at 75,000 Counts per Second	
2-3-6	Intrinsic Flood Field Uniformity at 75,000 Counts per Second	
2-3-7	System Spatial Resolution with Scatter	
2-3-8	System Planar Sensitivity and Penetration	
2-3-9	Detector Shielding	
2-3-10	system volume sensitivity	
2-4	previous studies	
	Chapter three	
3	Materials and methods	
3-1	Model one	
3-2	Model two	
3-2-1	Methods of data collection	
3-3	Model three	
3-3-1	Part one	
3-3-2	Part two	
3-3-3	Method of data collection	
	Chapter four	

<b>4</b>	Result and discussion	
<b>4-1</b>	Description of the independent programme	
<b>4-1-1</b>	Methods of LSF and MTF calculation by our program	
<b>4-2</b>	Resolution	
<b>4-3</b>	Uniformity and linearity	
<b>4-4</b>	Conclusion	
<b>4-5</b>	Recommendation	
	References	
	Appendix	

### List of figures:

<b>Fig No</b>	<b>Title</b>	<b>Page No</b>
<b>2-1</b>	Components of a standard nuclear medicine imaging system	
<b>2-2</b>	The diameter Vs the resolution	
<b>2-3</b>	The hole diameter Vs the resolution	
<b>2-4</b>	Angle of acceptance	
<b>2-5</b>	thicker septa are used to block high- and medium-energy photons	
<b>2-6</b>	Parallel-hole (A) and slant-hole (B) collimators	
<b>2-7</b>	Pinhole collimator	
<b>2-8</b>	Collimators used in a scintillation camera	
<b>2-9</b>	Converging collimators	
<b>2-10</b>	Diverging collimator	
<b>2-11</b>	(A) In a converging collimator, holes converge toward the patient in both planes and uniformly enlarge an image. (B) In a fan-beam collimator	
<b>2-12</b>	Collimated Source Geometry	
<b>2-13</b>	Determination of FWHM and FWTM	
<b>2-14</b>	source position for whole body resolution measurements	
<b>2-15</b>	Cylindrical source holder for multiple window spatial registration measurement showing liquid ga-67 source inside	
<b>2-16</b>	Source holder for count rate measurements	
<b>2-17</b>	volume sensitivity cylindrical phantom (acrylic)	
<b>3-1</b>	a camera shoot image represent the Perspex sheet with dimension of 42 X 42cm	
<b>3-2</b>	image showed a sheet of Perspex used for flood phantom fabrication	
<b>3-3</b>	image shows the whole liquid flood phantom, the holes for passage the water and radioactive material at the left side	
<b>3-4</b>	image show the lead within rubber sheet grooves of the bar quadrate phantom	

<b>3-5</b>	An X-Ray image showed the lead lines after exposed to 140KeV	
<b>3-6</b>	Image of the gamma camera used for experiments	
<b>3-7</b>	Image of the workstation of the gamma camera used for experiments	
<b>3-8</b>	Image show the flood phantom during filling with water (side view)	
<b>3-9</b>	Image show the flood phantom during filling with water (front view)	
<b>3-10</b>	Image show the flood phantom during filling with 99mTc (side view)	
<b>3-11</b>	Image show the flood phantom center during uniformity quality control test (side view)	
<b>3-12</b>	Image show the flood phantom center during uniformity quality control test (front view)	
<b>3-13</b>	Image show the workstation during uniformity quality control test acquisition	
<b>3-14</b>	Image show the bar quadrate phantom center during intrinsic linearity and resolution quality control test acquisition	
<b>3-15</b>	Image show the bar quadrate phantom center during intrinsic linearity and resolution quality control test acquisition	
<b>3-16</b>	Image showed the point source centered at floor during intrinsic linearity and resolution quality control acquisition	
<b>3-17</b>	Image show the workstation during linearity and resolution quality control test acquisition	
<b>3-18</b>	Image of the bar phantom	
<b>3-19</b>	Image of the liquid flood phantom	
<b>3-20</b>	Image of the bar quadrate phantom with CFOV and UFOV presented	
<b>3-21</b>	Image shows the Steel mold	
<b>3-22</b>	Image shows the par phantom with lead thickness presented	
<b>3-23</b>	Image shows the whole par phantom	
<b>3-24</b>	Image shows the nuclear medicine technologist during preparation of 99mTc for Flood phantom	
<b>3-25</b>	image shows the flood phantom after preparation	
<b>3-26</b>	Image shows $^{99}\text{Mo}$ - $^{99\text{m}}\text{Tc}$ generator used	
<b>3-27</b>	Image shows the plastic bags and absorbable material on gamma camera head	
<b>3-28</b>	Image shows the flood phantom center on the camera table with collimator inferior	
<b>3-29</b>	Image shows the work station computer during flood source image	
<b>3-30</b>	Image shows the par phantom centering over the flood	

	phantom (front view)	
<b>3-31</b>	Image shows the par phantom centering over the flood phantom (side view)	
<b>3-32</b>	Image shows the par phantom centering over the flood phantom (superior view)	
<b>3-33</b>	Image shows the par phantom centering over the camera table and head below the phantom without collimator (front view)	
<b>3-34</b>	Image shows the point source centering over the camera head at ceiling	
<b>3-35</b>	Image shows the par phantom centering between the camera head and point source on camera table	
<b>3-36</b>	Image shows the work station during intrinsic bar phantom image with 256 X 256 matrix size	
<b>3-37</b>	Image shows the work station during intrinsic bar phantom image with 512 X 512 matrix size	
<b>3-38</b>	Image of Flood phantom	
<b>3-39</b>	Image showed the 99Mo/99mTc generator	
<b>3-40</b>	Image showed the liquid flood phantom during acquisition	
<b>3-41</b>	Image show the slit phantom and flood phantom during acquisition	
<b>3-42</b>	Image show the slit phantom centred during intrinsic image	
<b>4-1</b>	Image shows the frontal part of the phantom made of Perspex (42×42×10 cm) that simulates the four quadrant bars phantom each one was 20×20 cm.	
<b>4-2</b>	Image shows the back part simulates the liquid flood phantom made of Perspex (42×42×1 cm) and has orifice 0.5 cm to be fill with a liquid radioactive material	
<b>4-3</b>	Image show example image of our fabricated phantom	
<b>4-4</b>	Image show our program result for measuring the resolution	
<b>4-5</b>	Image shows the resolution % vs. objects size for SPECT in RICK and Royal care hospitals-Khartoum Sudan using developed phantom	
<b>4-6</b>	Image shows the resolution % vs. objects frequency for SPECT in RICK and Royal care hospitals-Khartoum Sudan using developed phantom	
<b>4-7</b>	Image shows the comparison resolution% measured by phantom and the QA base line for Royal Care and RICK hospitals	
<b>4-8</b>	Image shows the comparison resolution% measured by phantom and the QA base line for Royal Care and RICK	
<b>4-9</b>	Image show the intensity of all lines of slit phantom at RICK	
<b>4-10</b>	Image show the intensity of all lines of slit phantom at RCIH	
<b>4-11</b>	Image shows the counts distributions in X and Y-axis	



	direction via phantom lead slits	
<b>4-12</b>	Image shows the counts difference in X and Y-axis direction via phantom lead slits	
<b>4-13</b>	shows the image uniformity of the developed flood phantom obtained from gamma camera SPECT	
<b>4-14</b>	Images A and B: shows the point spread function of flood field uniformity obtained by developed phantom and analyzed by IDL program	
<b>4-15</b>	Images A, B and C: image of Uniformity after applied of correction map	

# **Chapter one**

## **Introduction**

Over the past decade we have gained many new insights into the etiology and pathophysiology of urinary tract infections (UTIs) in children. The role of bacterial virulence in the etiology of UTIs has been emphasized by our infectious diseases colleagues. Several genetically coded bacterial virulence factors have been identified that enhance the potential of uropathogenic organisms to cause symptomatic disease, such as the ability of certain strains of bacteria to adhere or attach to human uroepithelium. Interacting with these virulence factors are a multitude of host defense factors operating at every level of the urinary tract, ranging from the perineum to the renal parenchyma. These complex host-parasite interactions determine an individual's susceptibility to urinary infection. Experimental studies combined with clinical observations have clearly demonstrated the critical role that infection plays in producing irreversible renal scarring, the most severe long-term sequelae of childhood

UTIs. This awareness has led to greater emphasis being placed on the nonsurgical management of conditions, such as vesicoureteral reflux (WR) and nonobstructive hydronephrosis. Meanwhile, the recognition of the important role of voiding and bowel dysfunction in the cause of recurrent UTIs has led to improved management of these children, who were previously subjected to unnecessary and usually ineffective cystoscopic procedures and urethral dilations. The imaging modalities involved in the evaluation of children with UTIs have also changed with replacement of intravenous pyelography (IVP) by sonography, renal cortical scintigraphy, or both. Sonography is a noninvasive, painless technique that has been shown to be as sensitive as IVP for the detection of significant structural abnormalities of the urinary tract. The use of technetium  $^{99m}\text{Tc}$  ( $^{99m}\text{Tc}$ )-labeled dimercaptosuccinic acid (DMSA) renal scans has allowed for accurate identification of acute pyelonephritis and the ability to document the extent and progression of renal parenchymal damage. This has led to further refinement of therapeutic regimens, such as outpatient management of children with acute pyelonephritis. The use of renal cortical scintigraphy has confirmed a higher than previously recognized incidence of nonreflux pyelonephritis in children. As documented

by DMSA scans, acute pyelonephritis damage can be reversed in many cases with prompt diagnosis and antibiotic therapy. In others, severe scarring results despite appropriate therapy (Rushton Gil 1997). Pediatrics is a specialized field of application of nuclear medicine and many centers are still reluctant to perform radionuclide tests in children. The practical aspects of conducting the examination undoubtedly constitute the main difficulty: preparation and information of patient and parents, the capacity to handle the natural anxiety related to the procedure, the creation of a friendly environment (waiting room and gamma camera room), adequate immobilization of the patient, adaptation of the acquisition to the size of the patient (zoom and pinhole views), and the administration of intravenous injections and blood sampling with minimal discomfort for the child. In addition, special attention should be given in this young age group to the problems of radiation protection and the variation in function of age of the biological distribution, uptake, and retention of radiopharmaceuticals. Similarly, numerous difficulties and pitfalls in the interpretation of images and functional parameters are evident during maturation. Finally, although many indications for nuclear medicine procedures are common to children and adults, there is a wide panel of specific pediatric indications of which the nuclear medicine physician should be aware. Nephro-urology is probably the best illustration of this specificity. Although generally not more than 5% of the workload of a nuclear medicine department is devoted to this sub specialty, more than 60% of the pediatric examinations are aimed at exploring the urinary tract. There are 2 main reasons for this difference. First, urinary tract infection is frequent in childhood, and approximately 80% of first infections occur before a child reaches 2 years of age. Association with structural abnormalities such as underlying vesico-ureteric reflux is not rare, and complications such as severe recurrent infections, scarring, loss of renal function and, in the long term, hypertension constitute a constant preoccupation for the pediatrician. Second, prenatal screening has led to the detection of a large number of uronephrological abnormalities. It is therefore understandable that the clinician is tempted to prevent further deterioration of the kidney. Nuclear medicine offers the possibility of evaluating, from the very early weeks, the function of the urinary tract, and the effect of any medical or surgical treatment. We are now at a point where many uncertainties related to the procedures have been clarified. Most of the uronephrological

techniques are now better understood and are almost standardized. Some pitfalls of interpretation are known, the levels of sensitivity and specificity have been largely evaluated, robustness in reporting on a test has been checked on many occasions and experimental studies have validated these procedures. However, there still is a long way to go, and we need much more rigorous work to evaluate the real utility of these examinations. Although we can identify the acute lesion of pyelonephritis, we still need to prove that the acute dimercaptosuccinic acid scintigraphy ( $^{99m}\text{Tc}$ -DMSA) can modify the strategy of treatment and follow-up. A renal scar can be shown much easier than with the classical intravenous Urography, but we still do not know what the consequence will be for the patient having 1, 2, or multiple scars. Are we forced to continue conducting the very unpleasant direct cystography in a 2-year-old child simply because of acute pyelonephritis, or, will a normal DMSA scan allow us to spare patients many unnecessary tests? Having the possibility of regularly evaluating the renal function of a hydronephrotic kidney by using renography already has completely changed the strategy of the surgeon and, although many uncertainties related to the criteria of surgery still remain, it is already very clear that only a minority of these children will now undergo surgery compared with the systematic surgical approach one generation earlier. The details of the radionuclide procedures used in pediatric uronephrology are presently described in detail in various American and European guidelines and will be cited within. However, guidelines generally are a compromise between different opinions, based or not on solid evidence. This review should be regarded as an opinion based on personal experience, clinical, and experimental studies and numerous debates with clinicians involved in this particular field of medicine. Several technical aspects related to these procedures will be examined, but it was our feeling that, at the present time, more attention should be paid to the potential impact these techniques may have in the strategy of pediatric uronephrology. (Piepsz Amy et.al (2006))

## **2-1 problem of the study:**

According to the information gained from central federal ministry of the health Sudan (2000-2002) the UTI affected 323 male patients and 68 female patient in the age group of less than one year. Urine culture state as standard test for evaluation of UTI

,but the urine culture can't distinguish between the acute pyelonephritis and lower UTI as two disease ,shows the same signs and symptoms . So the researcher want to evaluate the role of  $^{99m}\text{TC}$ -DMSA (Dimercaptosuccinic Acid) in detection of UTI regardless the signs and symptoms which may appear in the acute pyelonephritis.

## **2-2 objectives of the study:**

### **2-2-1 general objectives:**

The main general objective of this study is to evaluate the role of  $^{99m}\text{TC}$ -DMSA in detection of UTI in Sudanese children patients.

### **2-2-2 specific objectives:**

-to assess the diagnostic value of  $^{99m}\text{TC}$ -DMSA scintigraphy in detection the children with acute UTI Documented by positive urine culture.

-to visualize the extend of renal damage using  $^{99m}\text{TC}$ -DMSA scintigraphy.

## **2-3 Importance of the study:**

At the end of this study the researcher is predict that the  $^{99m}\text{TC}$ -DMSA scintigraphy shall give information about the present of UTI as well as information about the extend and severity of The disease which cannot be obtained from the result of urine culture test.

## **Chapter two**

### **Literature review**

#### **2-1 theoretical background:**

#### **2-1-1 Urinary Tract Infection:**

##### **2-1-1-1 Introduction:**

In 30% of children with urinary tract anomalies, urinary tract infection (UTI) can be the first sign (JBSastre,et.al2007). If we fail to identify patients at risk, damage to the upper urinary tract may occur. Up to 85% of infants and children with febrile UTI have visible photon defects on technetium  $^{99m}\text{Tc}$ -DMSA scanning, and 10–40% of these children have permanent renal scarring (B Jakobsson,et.al 1997) that may lead to poor renal growth, recurrent pyelonephritis, impaired glomerular function, early hypertension, end stage renal disease, and preeclampsia (R Fotter et.al 2001). Identifying children at risk of renal parenchymal damage and follow-up imaging after UTI is controversial. In these guidelines, we provide recommendations for the diagnosis, treatment, and imaging of children presenting with UTI based on evidence, and when this is lacking, based on expert consensus.

##### **2-1-1-2 Background:**

UTI is the most common bacterial infection in childhood (TL Stull, and AHoberman1991), and up to 30% of infants and children experience recurrent infections during the first 6–12 mo after initial UTI (P Mangiarotti et.al 2000). In very young infants, symptoms of UTI differ in many ways from those in older infants and children.

The prevalence is higher in the first age group, with a male predominance. Most infections are caused by *Escherichia coli*, although in the first year of life *Klebsiella pneumoniae*, *Enterobacter*, *Enterococcus*, and *Pseudomonas* are more frequent than later in life, and there is a higher risk of urosepsis compared with adulthood (N Shaikh et al 2008). The incidence of UTIs depends on age and sex. In the first year of life, UTIs are more common in boys (3.7%) than in girls (2%). This is even more pronounced in febrile infants in the first 2 mo of life, with an incidence of 5% in girls and 20.3% in uncircumcised boys, as demonstrated in one prospective study of >1000 patients using urine specimens obtained by catheterization (J Zorc, N Shaikh et al 2008). Later, the incidence changes, and about 3% of prepubertal girls and 1% of prepubertal boys are diagnosed with a UTI.

### **2-1-1-3 Methodology:**

Several guidelines on dealing with specific subgroups of UTI are currently available, some of which are driven by economic and health care issues (KB Roberts et al 1983). The recommendations in these guidelines were developed by the European Association of Urology (EAU)/European Society for Pediatric Urology (ESPU) Pediatric Guidelines Committee after a review of the literature and a search of PubMed and Embase for UTI and newborn, infants, preschool, school, child, and adolescent. A consensus decision was adopted when evidence was low. In these cases, all relevant papers and statements were discussed by all the authors until a consensus was achieved. The same criteria for the levels of evidence and grades of recommendation as in the EAU guidelines were used (LMD Shortliffe et al 2007).

### **2-1-1-4 Classification:**

The four widely used infection classification systems depend on the site, episode, symptoms, and complicating factors. For acute treatment, the site and severity are the most important.

#### **2-1-1-4-1 Classification according to site:**

Cystitis (lower urinary tract) is inflammation of the urinary bladder mucosa with symptoms including dysuria, stranguria, frequency, urgency, malodorous urine, incontinence, haematuria, and suprapubic pain. However, in newborns and infants, these symptoms are rarely diagnosed accurately. Pyelonephritis (upper urinary tract) is diffuse

pyogenic infection of the renal pelvis and parenchyma with symptoms including fever (>38 °C). But unlike adults, infants and young children may have nonspecific signs such as poor appetite, failure to thrive, lethargy, irritability, vomiting, or diarrhoea.

#### **2-1-1-4-2 Classification according to episode:**

Classifications are first infection and recurrent infection, which is subdivided into unresolved or persistent and reinfection (JC, Craig et al 1998).

#### **2-1-1-4-3 Classification according to symptoms:**

Asymptomatic bacteriuria (ABU) indicates attenuation of uropathogenic bacteria by the host or colonisation of the bladder by nonvirulent bacteria that are incapable of activating a symptomatic response (no leucocyturia or symptoms). In patients with significant bacteriuria, leucocyturia can be present without any symptoms. Symptomatic UTI includes irritative voiding symptoms, suprapubic pain (cystitis), fever, and malaise (pyelonephritis). In patients with a neurogenic bladder and malodorous urine, it is difficult to distinguish between ABU and symptomatic UTI.

#### **2-1-1-4-4 Classification according to complicating factors:**

Uncomplicated UTI is an infection in a patient with a morphologic and functional normal upper and lower urinary tract, normal renal function, and a competent immune system. Complicated UTI occurs in newborns, in most patients with clinical evidence of pyelonephritis, and in children with known mechanical or functional obstructions or problems of the upper or lower urinary tract (MW, Burnet et al 1987).

#### **2-1-1-5 Diagnostic work-up:**

##### **2-1-1-5-1 Medical history:**

The site, episode, symptoms, and complicating factors are identified by taking the patient's history. This includes questions on primary (first) or secondary (recurring) infection, febrile or nonfebrile UTIs; malformations of the urinary tract (eg, pre- or postnatal ultrasound [US] screening), previous operations, drinking, and voiding habits; family history; whether there is constipation or the presence of lower urinary tract symptoms; and sexual history in adolescents.

##### **2-1-1-5-2 Clinical signs and symptoms:**

Fever may be the only symptom of UTI, especially in young children (WA, Bonadio 1987 And M, Slater et al 1999) Newborns with pyelonephritis or urosepsis can present with



nonspecific symptoms (failure to thrive, jaundice, vomiting, hyperexcitability, lethargy, hypothermia, and sometimes without fever). (R. Beetz 2012 and NK, Biyikli et al. 2004) Septic shock is unusual, even with high fever (JC, Craig et al. 2010) unless obstruction is present or the child is otherwise compromised. In older children, lower urinary tract symptoms include dysuria, stranguria, frequency, urgency, malodorous urine, incontinence, haematuria, and suprapubic pain, and for the upper urinary tract, fever and flank pain. UTI in infancy may also be accompanied by a transient pseudohypoaldosteronism with profound hyponatraemia with or without hyperkalaemia (F Tutunculer et al. 2004 and R, Nandagopa et al. 2009).

#### **2-1-1-5-3 Physical examination:**

A complete paediatric physical examination is required to exclude any other source of fever, and especially if the fever has no apparent cause, UTI should be ruled out. Physical examination should search for signs of constipation, palpable and painful kidney, palpable bladder (stigmata of spina bifida or sacral agenesis spine and feet), for genital disorders (phimosis, labial adhesion, postcircumcision meatal stenosis, abnormal urogenital confluence, cloacal malformations, vulvitis, epididymo-orchitis), and measure temperature.

#### **2-1-1-5-4 Urine sampling, analysis, and culture:**

Before any antimicrobial agent is given, urine sampling must be performed. The technique used to obtain urine for urinalysis or culture affects the rate of contamination that in turn influences interpretation of the results, especially in early infancy (JC, Craig et al. 2010 and P, Whiting et al. 2005).

##### **2-1-1-5-4-1 Urine sampling:**

##### **2-1-1-5-4-1-1: Newborns, infants, and non-toilet-trained children:**

In newborns, infants, and non-toilet-trained children, there are four main methods for obtaining urine with varying contamination rates and invasiveness. A plastic bag attached to the cleaned genitalia is the technique used most often in daily practice. It is helpful when the culture result is negative. UTI can be excluded without the need for confirmatory culture if the dipstick is negative for both leukocyte esterase and nitrite, or microscopic analysis is negative for both pyuria and bacteriuria and (P, Whiting et al. 2005). As a result of the high contamination rate and high incidence of false-positive

results, urine bag culture alone is not sufficiently reliable for diagnosing UTI. For clean-catch urine collection, the infant is placed in the lap of a parent or nurse holding a sterile foil bowl underneath the infant's genitalia (IJ, Ramage et al 1999). This is time consuming and requires careful instructing of the parents. There seems to be a good correlation between the results of

a urine culture obtained by this method and by suprapubic bladder aspiration (SPA) (KB, Roberts et al 1983 And IJ, Ramage et al 1999). However, the contamination rates were 26% in clean-catch urine compared with 1% in the SPA group in a 2012 study (S, Tosifet al 2012), bladder catheterisation may be an alternative to SPA, although the rates of contamination are higher (BJ, Austin et al 1999). The risk factors for a high contamination rate using this technique are patients <6 mo of age, difficult catheterisation, and uncircumcised boys (S, Wingerter 2011). Therefore, in children <6 mo of age and uncircumcised boys, use of a new sterile catheter with each repeated attempt at catheterisation may reduce contamination (BJ, Austin and C. Bollard 1999). Otherwise, SPA should be the method of choice. Catheterisation is preferable in children with urosepsis when a permanent catheter may be considered in the acute phase. SPA is the most sensitive method for obtaining an uncontaminated urine sample. Using US to assess bladder filling simplifies the aspiration (H, Buys and SC, Kiernan 1994). Bladder puncture causes more pain than catheterisation in infants <2 mo of age (E, Kozar et al 2006). The Eutectic Mixture of Local Anesthetics, an emulsion containing a 1:1 mixture of lidocaine and prilocaine, can be used topically to reduce pain (S. Dutta 1996).

#### **2-1-1-5-4-1-2 Toilet-trained children:**

In toilet-trained children, a clean voided midstream urine sample has a good rate of accuracy. It is important to clean the genitalia beforehand to reduce the contamination rate. In this age group, clean catch voided urine, preferably midstream, has a sensitivity of 75–100% and a specificity of 57–100%, as shown in five studies using an SPA urine sample as the reference standard. If there is strong suspicion of upper UTI and for the differential diagnosis of sepsis, it is appropriate to obtain an adequate urine sample by catheterisation or SPA. In infants, the use of a bag is reliable only if the dipstick is negative; otherwise, the urine should be obtained through catheterisation or SPA. This is

also recommended for exclusion or confirmation of UTI in older children who are severely ill. (Raimund Stein et al. 2015)

#### **2-1-1-5-4-2 Urine analysis:**

Dipsticks and microscopy are commonly used for urinalysis. Some centres use flow imaging analysis technology. Most dipsticks test for nitrite, leukocyte esterase, protein, glucose, and blood. A dipstick test that is positive for leukocyte esterase and nitrite is highly sensitive for UTI. A test that is negative for leukocyte esterase and nitrite is highly specific for ruling out UTI. A few studies have suggested that glucose is also a useful marker. Only one study has looked at the diagnostic accuracy of a dipstick test for blood. It found that blood demonstrated poor sensitivity (25%) and high specificity (85%). Microscopy is used to detect pyuria and bacteriuria. Bacteriuria alone has a higher sensitivity than pyuria alone, although if both are positive, there is a high likelihood of UTI (P, Whiting M, Westwood L, Bojke et al. 2006). Flow imaging analysis technology is increasingly used to classify particles in uncentrifuged urine specimens. The numbers of white blood cells, squamous epithelial cells, and red cells correlate well with those found by manual methods. (Raimund Stein et al. 2015)

#### **2-1-1-5-4-3 Urine culture:**

In patients with negative results on dipstick, microscopic, or automated urinalysis, urine culture is unnecessary if there is an alternative cause of the fever or inflammatory signs. However, if the dipstick and/or urinalysis are positive, confirmation of UTI by urine culture is mandatory. The classical definition of  $>10^5$  CFU/ml of voided urine is still used to define significant UTI in adult women. However, the count can vary and be related to the method of specimen collection, diuresis, and the duration and temperature of storage between collection and cultivation. The recent American Academy of Pediatrics (AAP) Guidelines on UTI suggest that the diagnosis should be based on the presence of both pyuria and at least 50 000 CFU/ml in an SPA sample. However, some studies have shown that in voided specimens, 10 000 organisms may indicate significant UTI. If urine is obtained by catheterisation, 1000–50 000 CFU/ml is considered positive, and any counts obtained after SPA should be considered significant. Mixed cultures indicate contamination (Raimund Stein et al. 2015)

#### **2-1-1-5-5. Blood test:**

Serum electrolytes and blood cell counts should be obtained for monitoring ill patients with febrile UTI. C-reactive protein has a lower specificity for identifying patients with renal parenchymal involvement, whereas serum procalcitonin ( $>0.5$  ng/ml) can be used as a reliable serum marker. In a severely ill child, blood cultures should be taken as well as US imaging of the urinary tract. (Raimund Stein et al 2015)

#### **2-1-1-5-6. Ultrasound:**

Early US examination is indicated in children with febrile UTI and urosepsis to discriminate initially between complicated and uncomplicated UTI. It is also indicated if UTI is associated with pain or haematuria, or according to the preference of the treating physician/surgeon. (Raimund Stein et al 2015)

#### **2-1-1-6. Therapy:**

Before any antibiotic therapy is started, a urine specimen should be obtained for urinalysis and urine culture. In febrile children with signs of UTI (clinical signs, positive dipstick and/or positive microscopy), antibiotic treatment should be initiated as soon as possible to eradicate the infection, prevent bacteraemia, improve clinical outcome, diminish the likelihood of renal involvement during the acute phase of infection, and reduce the risk of renal scarring. In children with febrile UTI and no previous normal US examination, US of the urinary tract within 24 h is advised to exclude obstructive uropathy, depending on the clinical situation. (Raimund Stein et al 2015)

#### **2-1-1-6-1 Asymptomatic bacteriuria:**

In ABU without leucocyturia, antibiotic treatment should be avoided unless UTI causes problems or an operative procedure is planned. In a screening study from Sweden, 2.5% of the boys and 0.9% of the girls  $<1$  yr of age had ABU verified by SPA. Among those infants, one girl and one boy developed symptoms of pyelonephritis close to the time of detection; the others remained asymptomatic. The median persistence of bacteriuria was 2 mo in girls and 1.5 mo in boys. Therefore screening for and treatment of ABU should be discouraged, irrespective of the method of urine sampling.

### **2-1-1-6-2 Cystitis in children:**

>3 mo of age There are conflicting data concerning the duration of antibiotic therapy in this scenario, although there seems to be an advantage in treating these children for >1–2 d [63–65]. Therefore, in patients with uncomplicated cystitis, oral treatment should be given for at least 3–4 d. 6.3. Febrile children: administration route When choosing between oral and parenteral therapy, these factors should be considered: patient age; clinical suspicion of urosepsis; severity of illness; refusal of fluids, food, and/or oral medication; vomiting; diarrhoea; noncompliance; and complicated febrile UTI (eg, upper tract dilatation). As a result of the increased incidence of urosepsis and severe pyelonephritis in newborns and infants <2 mo of age, parenteral antibiotic therapy is recommended. Electrolyte disorders with life-threatening hyponatraemia and hyperkalaemia based on pseudohypoaldosteronism can occur in such cases. Combination treatment with ampicillin and an aminoglycoside (eg, tobramycin or gentamicin) or a third-generation cephalosporin achieves excellent therapeutic results. A daily single dose of aminoglycosides is safer and equally effective as twice daily. The prevalence of antibiotic resistance in uropathogenic *E. coli* differs markedly among countries, with high resistance in Iran and Vietnam. There are upcoming reports of UTIs caused by extended-spectrum  $\beta$ -lactamase (ESBL)-producing Enterobacteriaceae in children. In one study from Turkey, 49% of the children <1 yr of age and 38% of those >1 yr of age had ESBL-producing bacteria. Within these groups 83% were resistant to trimethoprim/sulfamethoxazole, 18% to nitrofurantoin, 47% to quinolones, and 40% to aminoglycosides. Fortunately, the outcome appears to be the same as for children with non-ESBL-producing bacteria, despite the fact that initial intravenous empirical antibiotic therapy was inappropriate in one study. The choice of agent is also based on local antimicrobial sensitivity patterns and should be adjusted later according to sensitivity testing of the isolated uropathogen. Not all available antibiotics are approved by national health authorities for use in paediatric populations, especially in infants.

### **2-1-1-6-4 Duration of therapy in febrile urinary tract infection:**

The duration of parenteral application is still controversial. The consensus of the guideline panellists, as well as the AAP recommendations, is that parenteral antibiotic

therapy should be continued until the child isafebrile, after which oral antibiotics should be given for 7–14 d .If ambulatory (outpatient) therapy is chosen in lateinfancy, adequate surveillance, medical supervision, and, if necessary, adjustment of therapy must be guaranteed. Inthe initial phase of therapy, close contact with the family isadvised .In complicated UTI with uropathogens other than E coli,parenteral treatment with broad-spectrum antibiotics ispreferred . Temporary urinary diversion may berequired in obstructive uropathy, depending on clinicalstatus and/or response to antibiotic therapy.(Raimund Stein et.al 2015)

### **2-1-1-6-5 Prophylaxis:**

Some prospective randomised studies have challenged the efficacy of antibacterial prophylaxis . However, a subgroup of patients, missed by the large randomised studies, benefits from prophylaxis . The Swedish reflux study clearly demonstrated that chemoprophylaxis is effective in preventing new renal scars in infant girls with reflux III and IV. No patients in the prophylaxis group developed new renal scars, whereas 8 of 43 girls in the surveillance group and 5 of 42 in the endoscopically treated group had new renal scars at DMSA scanning after 2 yr. None of the 75 boys developed a new renal scar . A recent study compared children with infantile vesicoureteral reflux (VUR) with recurrent UTI (33 male, 11 female; mean age: 3.2 mo) and without recurrent UTI (40 male, 7 female; mean age: 4.8 mo) . They demonstrated that during the first year of life, the earlier the first UTI occurs, the higher the chance of recurrence. Higher grades of reflux, bilateral VUR, and the first infection not caused by E coli significantly increase the risk of recurrent UTIs . Clearly, there is a benefit for girls with dilating reflux, and long-term antibacterial prophylaxis should be considered in those cases of high susceptibility to UTI and risk of acquired renal damage. The recently published Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR) trial including 607 children (280 with a reflux I or II and 322 with a reflux III or IV) demonstrated that antimicrobial prophylaxis with trimethoprim/sulfamethoxazole reduced the risk of recurrence by 50%. In particular, children with a febrile index infection, bladder and bowel dysfunction (BBD), or dilating reflux benefitted from prophylaxis. The number of new renal scars was not different in this study . The indication for using cephalosporins for chemoprophylaxis should be reconsidered in regions with a high incidence of ESBL-

producing bacteria in children. Cranberry juice is increasingly used to prevent UTI. In one randomised Finnish trial, cranberry juice did not significantly reduce the number of children who experienced recurrence of UTI, but it was effective in reducing the actual number of recurrences and related antimicrobial use. In another study of only 40 children, cranberry juice with high concentrations of proanthocyanidin (37%) reduced the average incidence of UTI over a 12-mo period to 0.4 patient/year with 1.15 in the placebo group. Compliance with prophylaxis is important. In some studies, between 17% and 69% of the patients were compliant. Compliance depends greatly on parent and patient education. In boys with phimosis, early treatment should be discussed (local corticosteroid or surgery). (Raimund Stein et al 2015)

#### **2-1-1-6 Monitoring of urinary tract infection:**

With successful treatment, urine usually becomes sterile after 24 h, and leucocyturia normally disappears within 3–4 d. Normalisation of body temperature can be expected within 24–48 h after the start of therapy in 90% of cases. In patients with prolonged fever and failing recovery, treatment-resistant uropathogens or the presence of congenital uropathy or acute urinary obstruction should be considered. Immediate US examination is necessary, if not performed initially as recommended. Procalcitonin (among other laboratory inflammatory parameters such as C-reactive protein and leukocyte count) can be used as a reliable serum marker for early prediction of renal parenchymal inflammation with a first febrile UTI. In patients with febrile UTI, serum electrolytes and blood cell counts should be obtained. (Raimund Stein et al 2015).

##### **2-1-1-6-1 Patients at risk:**

Patients at risk are those with antenatally diagnosed uropathy, photopaenia on DMSA scanning after UTI, abnormal US examination (eg, upper urinary tract dilatation, small duplex kidney [or even small/dysplastic kidney], thick bladder wall, postvoid residual urine [if possible, US should always be performed with a full and empty bladder]), ureterocele, posterior urethral valves, urogenital abnormalities, intestinal connections to the perineum, previous UTI, dysfunctional voiding, enlarged bladder, poor

urine flow, constipation, abdominal mass, spinal anomaly, family history of VUR, and those with poor family compliance. If no other cause is found, additional imaging is recommended for those with recurrent fever, poor growth, failure to thrive, or high blood pressure. If the parents refuse further imaging (voiding cystourethrography [VCUG] or DMSA scanning), they must be informed that there is at least a 30% chance of reflux and that renal scarring can develop. (Raimund Stein et al 2015)

### **2-1-1-7 Imaging:**

#### **2-1-1-7-1 Ultrasound:**

Renal and bladder US is advised in all children with febrile UTI to exclude dilatation or anomalies of the upper and lower urinary tract if no improvement is seen within 24 h because some conditions are life threatening. It can be delayed in those with a previous normal US examination, depending on the clinical situation. Abnormal results are found in approximately 15% of cases, and 1–2% have abnormalities that require prompt action (eg, additional evaluation, referral, diversion, or surgery) (KB, Roberts 2011). In other studies, renal US has revealed abnormalities in up to 37% of cases, whereas VCUG showed VUR in 27% of cases (JB, Sastre et al 2007). Dilating VUR (with [intermittent] dilatation of the renal pelvis and calices) was missed by US in 24–33% of cases; in two published series, 14 of 23 patients with normal US had recurrent pyelonephritis (I, Preda et al 2010), with another study finding the figure to be approximately two of three patients <2 yr of age who presented with febrile UTI. Postvoid residual urine should be measured in toilet-trained children to exclude voiding abnormalities. If pelvic US shows filling of the rectum >30 mm, constipation must be considered (R, Burgers et al 2013- AJ, Klijnet et al 2004). US alone misses up to 33% of patients at risk; therefore, additional imaging is recommended (DMSA/VCUG).

#### **2-1-1-7-2 Renal scintigraphy:**

In some children and infants, sedation is required to achieve good quality scanning. A radiation dose of approximately 1 mSv should be taken into account when considering



multiple DMSA scans during initial and follow-up imaging . Changes in DMSA clearance during acute UTI indicate pyelonephritis or parenchymal damage, and they correlate well with the presence of dilating reflux and the risk of further breakthrough infections and future renal scarring .DMSA scanning can be used as a first-line diagnostic procedure based on observations that dilating VUR occurs in most children with an abnormal DMSA scan . To exclude reflux early and avoid recurrent UTI, DMSA scanning should be performed within 1–2 mo of the UTI episode. However, these findings are different in newborns. After the first symptomatic community-acquired UTI, most renal units with VUR grade III had normal early DMSA scanning .(Raimund Stein et.al 2015)

### **2-1-1-7-3 Voiding cystourethrography:**

VCUG is still the gold standard for the exclusion or confirmation of VUR. The radiation dose can be reduced (eight times lower) by using grid-controlled variable-rate pulsed fluoroscopy rather than continuous fluoroscopy . The radiation dose in children 10 yr of age is approximately 0.1–0.55 mSv. Using the techniques available for radiation protection, it is possible routinely to reduce the radiation dose below the lowest reference level valid for newborns . Due to the risk of renal scarring, VCUG or DMSA scanning is recommended after the first episode of febrile UTI, depending on sex, age, and clinical presentation . Although exclusion of reflux requires investigations that are invasive and unpleasant, as well as costly and time consuming, there is some evidence that not using VCUG and/or DMSA scanning fails to diagnose VUR in patients who are at risk for further renal scarring. Two approaches are recommended for the diagnosis of VUR: the bottom-up method (VCUG and, if positive, a DMSA scan) or the top-down method (DMSA scan and, if positive, VCUG) . In one study, the percentage of permanent renal scarring was higher in those with reflux (37%) than in those without reflux (12%), even if the delay between the onset of symptoms and treatment was shorter for those with reflux (4.3 ± 1.8 d) than for those without reflux (4.9 ± 2.4 d) . The timing of VCUG does not influence the presence or severity of VUR . Performance of early VCUG in patients with proven sterile urine does not cause any significant morbidity . VCUG should be performed after UTI has been treated. To date, no randomised study has demonstrated that

it is safe to perform VCUG during ongoing UTI and that the results of VCUG change the treatment.

#### **2-1-1-8 Bladder and bowel dysfunction:**

BBD is a risk factor for which every child with UTI should be screened at presentation. Correction of lower urinary tract dysfunction is important to decrease the rate of UTI recurrence. If there are signs of BBD during infection-free intervals, further diagnosis and effective treatment are strongly recommended. Treatment of constipation leads to a decrease in UTI recurrence. Exclusion of BBD is therefore strongly recommended in any child with febrile and/or recurrent UTI, and, if present, treatment of BBD is necessary.

#### **2-1-2 Anger Gamma Camera:**

The basic principle of operation of the Anger type gamma camera has remained essentially unchanged since its inception in the late 1950's.

It is the instrument of choice for imaging both static and dynamic radioisotope distribution in vivo. It has been perfected over the years and has been particularly adapted for imaging the 140keV gamma rays emitted by technetium 99m. The combination of this generator-produced isotope and the Anger camera has provided the nuclear medicine physician with a powerful tool, which has contributed to the continued growth of the field of nuclear medicine (Othman S. 1999). It consists of a large detector in front of which the patient is positioned. The console contains timers and counters to determine the length of the exposure, pulse height analyzers to reject scattered radiation and a display from which hard-copy images can be recorded on photographic film or on print out paper. These images are composed of several thousand small spots, each spot represents the image of the one gamma-ray scintillation.

The basic gamma camera comprises six functional main parts:

- Collimator
- Scintillation crystal
- Light guide
- Photomultiplier tubes

- Positioning electronics
- Display

### **2-1-2-1 Collimators:**

The collimator is a device, which projects an image of radioisotope distribution into the scintillation crystal by absorbing all gamma rays, which do not travel in the desired direction.

The collimators used in nuclear medicine are made of lead and have holes in them, which allow, as we just said, only those photons traveling in predetermined directions to pass through and enter the crystal.

There are several types of collimators, which differ in the number, angle and arrangement of their holes and these will result in images with varying levels of spatial resolution and sensitivity.

The choice of collimator will depend on the radionuclide in use and the type of study being undertaken.

There are many types of collimators:

1-According to shape:

- \* Pinhole collimators
- \* Parallel multihole collimator
- \* Converging/Diverging collimator

2-According to function:

- \* High sensitivity collimator
- \* High resolution collimator

### **2-1-2-2 Scintillation crystal:**

The scintillation material used in all current Anger gamma camera is NaI (Tl). Gamma camera devices, which use high purity germanium detectors, have also been developed. Large field of view Anger Cameras typically employs a NaI (Tl) crystal of 400mm diameter and 13mm thick.

Some recent cameras have incorporated thinner crystals (e.g 6mm) to improve intrinsic resolution for low energy gamma ray emitters.

Sodium iodide has two main advantages:

Firstly, it has high attenuation coefficient due to its high atomic number, and secondly, it has a light output.

#### **2-1-2-3 Light guide:**

The light guide acts as an optical coupler between the exit window of the crystal, and the photomultiplier tubes. It is made from a transparent plastic, Silicone grease or oil is used as optical coupling material between the exit window and the light guide and the light guide and tubes.

Spatial resolution may be improved by using a thin light guide.

#### **2-1-2-4 Photomultiplier tubes:**

Early gamma cameras used 7 to 19 tubes. During recent years, there has been a tendency to use a larger number (e.g 61 or 75) of small diameter tubes to improve spatial resolution, although this often leads to non-uniformity problems.

Photomultiplier tubes are devices which convert light flashes into electrical pulses (light energy into electrical energy).

The gain of a tube is highly dependent on the applied voltage and high stability of this voltage is therefore mandatory.

#### **2-1-2-5 Positioning electronics:**

The function of the positioning electronics is to provide accurate signals describing the position and energy of the light scintillation from the incident gamma rays.

The positions signals are determined by  $X_+$ ,  $X_-$  signals,  $y_+$ , and  $y_-$  by theoretical division of the photomultiplier tube array into horizontal and vertical divisions respectively.

In separate circuit, the output of all photomultiplier tubes are combined to form a Z signal.

The Z signal is proportional in amplitude to the total amounts of light produced by a scintillation event in the crystal and is used for pulse-height analysis.

The  $X_+$ ,  $X_-$ ,  $y_+$  and  $y_-$  signals are then combined to obtain x and y position signals.

#### **2-1-2-6 Display:**

Having obtained x and y signal what remains is displaying this as an image. The Z signal is sent to the pulse height analyzer (PHA). If the Z signal falls within the (PHA) window set for the radionuclide in use, the (PHA) enables the  $X/Z$  and  $Y/Z$  signals to record the event on cathode-ray oscilloscope.

The  $X/Z$  and  $Y/Z$  signals may also be digitized by analogue to digital converters (ADC'S) for storage and later processing on a computer directly interfaced to one or more scintillation cameras.

## **2-2 previous studies:**

**Stockland et.al. (1996)** determined whether age, C-reactive protein(CRP), body temperature, or results of voiding cystourethrography at diagnosis of first-time symptomatic urinary tract infection could predict the risk of renal damage as evaluated by dimercaptosuccinic acid (DMSA) scintigraphy performed 1 year after the infection. This study included 157 children (median age, 0.4 year, range, 5 days to 5.8 years) with first-time symptomatic urinary tract infection, in children 1 year of age or older, a body temperature of 38.5 ° C or higher was necessary for inclusion. CRP and body temperature were measured at the time of infection, and voiding cystourethrography was performed shortly thereafter. DMSA scintigraphy was performed 1 year later in all children. During a 2-year period all children from birth to age 6 years who were treated at the Children's Hospital because of culture-verified acute first-time symptomatic UTI underwent DMSA scintigraphy in association with the infection and after 1 year. A body temperature of 38.5 ° C or higher was required for inclusion of children aged more than 1 year, whereas younger children were included irrespective of body temperature. Children with urinary tract obstruction were excluded. One hundred seventy-five consecutive children were included and had the initial DMSA scintigraphy performed. DMSA scintigraphy was performed a median of 1.1 years (range, 0.5 to 2.5 years) after the index UTI. The examinations were performed on a General Electric AT gamma camera with a general-purpose collimator. Approximately 4 hours after intravenous injection of 0.5 MBq  $^{99m}\text{Tc}$ -labeled DMSA per kilogram of body weight (minimum of 10 MBq), a posterior view with 250,000 counts was acquired. The results of DMSA scintigraphy 1 year after the index UTI were abnormal in 59 (38%), equivocal in 33 (21%) and normal in 65 (41%) of

the children. Bilateral abnormalities were found in 6 (10%) of the 59 children; 20 (34%) of the 59 children showed an abnormal split renal function. There was no significant influence of age on the frequency of abnormal results on DMSA scintigraphy. There was a positive correlation between temperature and abnormal DMSA scintiscan ( $p = 0.001$ ). A temperature of  $38.5^{\circ}\text{C}$  or higher was found in 92% (sensitivity) of those with an abnormal DMSA scintiscan, whereas the specificity was 20%. The positive and negative predictive values were 41% and 80%, respectively. There was a positive Correlation between grade of reflux and abnormal DMSA scintiscan ( $p < 0.001$ ). Reflux was found in 47% (sensitivity) of the children with abnormal DMSA scintigraphy findings, whereas the specificity was 82%. The positive and negative predictive values were 62% and 72%, respectively.

**Nakamura et.al. (2009)** investigated factors affecting the breakthrough urinary tract infection rate during prophylactic antibiotic treatment in children with primary vesicoureteral reflux. Medical charts were retrospectively reviewed in children with primary vesicoureteral reflux diagnosed at age 12 months or less who received prophylactic antibiotics and underwent  $^{99\text{m}}\text{Tc}$ -dimercapto-succinic acid scan. Parameters assessed for their relation to breakthrough urinary tract infection were gender, presenting symptoms, age at presentation, prophylactic antibiotic type, reflux grade at presentation and scan findings. The study enrolled 52 boys (90%) and 6 girls (10%). Mean age at presentation was 3.7 months (range 0 to 10), mean age at p-Abx discontinuation was 17.2 months (range 3 to 33) and mean followup was 42.5 months (range 3 to 126). Of the patients 30 (52%) were 3 months old or younger and 28 (48%) were older than 3 months. Presenting symptoms were febrile UTI in 46 children (79%) and abnormal ultrasound during prenatal screening without an overt febrile UTI episode in 12 (21%). Bilateral and unilateral VUR was detected in 32 and 26 children, respectively. At presentation VUR was grade 1 to 5 in 1 (2%), 8 (14%), 9 (16%), 26 (45%) and 14 cases (24%), respectively. Cephem p-Abx was given in 46 children (79%), while trimethoprim-sulfamethoxazole, and penicillin and penem were also given in 4 (7%) and 8 (14%), respectively, at physician discretion. DMSA scan was abnormal in 36 children (62%) and normal in 22 (38%). During followup BUTI developed in 12 boys (21%) younger than 1 year. There was no significant difference in the BUTI incidence based

ongender ( $p = 0.328$ ), age at presentation (3 months or less vs greater than 3 months  $p = 0.336$ ), presenting symptoms (febrile UTI vs ultrasound abnormality  $p = 0.999$ ), p-Abx type (cephem vs others  $p = 0.427$ ) and VUR grade at presentation (1–3 Vs 4–5  $p = 0.082$ ). Only abnormal DMSA scan showed a significant difference. Of 36 children with abnormal DMSA scan 11 (31%) had BUTI, while BUTI developed in only 1 of 22 (5%) with normal DMSA scan ( $p = 0.021$ ). The log rank test revealed that the BUTI-free rate was significantly lower in children with abnormal DMSA scan ( $p = 0.033$ ). Interestingly all BUTIs developed within 6 months after the first presentation. Nine of 12 children with BUTI underwent surgical correction for VUR and the remaining 3 were still on p-Abx. Of the 56 patients 23 underwent repeat DMSA scan, of whom new scars developed in 2 and the previous scar became obscure in 1. Seven of 12 children with BUTI underwent repeat DMSA scan, which showed a new scar in 1.

**W.H. Cerwinka et.al (2013)** compared the accuracy of dimercaptosuccinic acid (DMSA) renal scan to magnetic resonance urography (MRU) in the identification of renal parenchyma defects (RPD). From October 2007 to April 2010, 30 children were prospectively enrolled, of whom 25 completed the study. Only patients with voiding cystourethrography (VCUG)-proven VUR (grades IIeV) and at least one episode of APN were included. Children with prior anti-reflux procedure or prior urologic reconstructive surgery, voiding dysfunction, or anomalous renal configuration were excluded. All patients underwent DMSA scan and MRU on the same day, and were kept sedated for both studies. Sedation was provided by a dedicated sedation team. The MRU study was performed in the time interval between injection with the DMSA dose and acquisition of the static renal scintigraphy images. Thirty children were enrolled in the study; 25 underwent both DMSA scan and MRU. There were five boys and 20 girls whose most recent APN was diagnosed at a median age of 9 months (range, 0.25e143 months). Most frequently, one episode (range, 1e4) of APN had occurred with a median maximum temperature of  $39.4 \text{ }^{\circ}\text{C}$  (range,  $38.5\text{e}41.7 \text{ }^{\circ}\text{C}$ ). Imaging studies were obtained, on average, 6 months (range, 2e40 months) after diagnosis of APN. VUR was seen unilaterally in five and bilaterally in 20 children with VUR grade I in four, grade II in



eight, grade III in 16, grade IV in 11, and grade V in six renal units. Age, gender, family history, onset of VUR on VCUG, VUR laterality, temperature, and number of APNs were not associated with severity of renal parenchymal injury. VUR grade ( $p < 0.02$ ) and elapsed time from APN to imaging studies ( $p < 0.04$ ) correlated positively with the extent of RPDs. The ultimate consensus diagnosis was 18 affected kidneys in 15 children. RPDs were bilateral in three children. There were 32 kidneys without defects. There were five kidneys classified with mild RPDs, six with moderate RPDs, and seven with severe RPDs. Overall, there was little difference in the detection of defects using either DMSA scan or MRU. The main difference occurred in distinguishing mild and moderate. Agreement of DRF determined by DMSA scan or MRU, both volumetric (vDRF) and Patlak (pDRF) was significant ( $p < 0.0001$ ). The concordance correlation coefficient (95% confidence interval) for DMSA scan with MRU vDRF was 0.81 (0.63, 0.98), for DMSA scan with MRU pDRF 0.86 (0.72, 1.00), and for MRU vDRF with MRU pDRF 0.87 (0.73, 1.00). side-by-side analysis indicated MRU to be more accurate in identifying RPDs than DMSA scan.

**Richard D. et.al (2010)** discussed the role of Sonography in the Evaluation of Pediatric Urinary Tract Infection. Urinary tract infection (UTI) is a common pediatric malady, and a frequent source of morbidity in the pediatric population. The gold standard for the diagnosis of UTI is growth of pathogenic bacteria in urine culture. Many complex factors play a role in the pathogenesis of UTI in children. When bacterial virulence factors, such as adherence and motility factors, outweigh host resistance factors, UTI is favored to occur. The symptoms of UTI in children can be quite varied, depending on whether the infection is confined to the urethra, bladder, or upper urinary tract. The purpose of investigating the child's urinary tract after infection is (Biggi, Alberto et.al 2001) to discover a possible cause for the infection to prevent recurrence and lessen morbidity; (RR Bailey 1981) to determine whether the kidneys are normal, involved, or at risk for scarring; (Bethesda 1997) to determine whether vesicoureteral reflux (VUR) exists. (J.B. Bingham, and M.N. MAISEY 1978) to identify urinary tract calculi, which may perpetuate or result from repeated UTI; and .to identify urine outflow obstruction. US evaluation of the urinary tract in the pediatric patient with UTI should include evaluation of the kidneys;

ureters (if visible); and urinary bladder. The bladder should be reasonably well-distended, and examined in transverse and sagittal planes. In the transverse plane, images should be obtained from the bladder dome to the bladder outlet. In the sagittal plane, images should include the bladder outlet, the bilateral distal ureters, and ureteral insertion sites. Color Doppler US can be useful in identifying the latter when ureteral jets are seen. Large bladder diverticula can also result in dysfunctional voiding because of one's inability to completely or effectively empty his or her bladder. In the acute setting, bladder wall thickening may be caused by cystitis, which may be of bacterial or viral origin. The gray-scale images show irregular bladder wall thickening; color flow Doppler US shows hyperemia of the bladder wall.<sup>20</sup> Bladder wall thickening in cystitis caused by The highest frequency transducer that penetrates the area should be used. For infants and toddlers, a curved 8- to 13-MHz transducer, for young children, a curved array 4- to 9-MHz transducer, and for adolescents, a 2- to 5-MHz curved array transducer can be used. hypertension and end-stage renal disease.<sup>9,10</sup> Although more recent studies question this association, the high prevalence of and frequent morbidity associated with pediatric UTIs have perpetuated the need for continued examination of the role of imaging in its diagnosis and management.

**P. Rossier et.al. (2000)** evaluated the diagnostic value of Energy Doppler Ultrasound (EDUS) in acute pyelonephritis (APN) compared to renal DMSA scan. This study included 26 children with a clinical diagnosis of probable APN who underwent grey scale US, energy Doppler US and DMSA study within 24 hours. The diagnostic criteria of hypoperfusion on EDUS, 28 other children with renal pathology other than APN served as control of US and EDUS. 16 neoplastic lesions and 1 angiomyolipoma (size range 1-10 cm) were included in the first group: 11 lesions showed multiple vascular signals with malignant features. Whereas in 5 lesions the signals were scanty. Non peculiar pattern for angiomyolipoma was detected. Arterial vessels showed maximum velocities of 0.26-0.62 m/s with 0.7 to 3.6 PI values. In the second group were included primitive neoplastic lesions (2 clear cell adenocarcinomas, 1 granular cell carcinoma and 1 oncocytic cell carcinoma), 2 metastases, 4 angiomyolipomas, 1 infarct. The only

hypervascular lesions were the 2 clear cell adenocarcinomas. Systolic velocity ranges were 0,40 e 0,78 m/set with 0,5 e 1,4 PI values. In the complex cysts group were included 17 lesions: papillary carcinomas, 7 multiloculate cysts, 3 complicated complex cysts. Only in malignant lesions signals were detected in the internal septa or parietal nodules. Systolic velocity range was 0,3 e 0,7 m/set with 0,8 e 1,4 PI values. 13 children fulfilled the criteria for AON by DMSA. All of them had a focal defect of perfusion on EDUS at the same site. 13 had no defect seen on DMSA. In this group 10 were normal on EDUS, but 3 had an area of hypoperfusion. On the DMSA scan, the same areas showed heterogeneity. None of the 28 children with other renal pathology (other than APN) had a perfusion defect on EDUS. The sensitivity of EDUS in this series is comparable to that of DMSA. We use a EDUS setting which demonstrates the (cortical blush) (renal angiogram) of the parenchyma. AON is seen as an area of hypoperfusion, this is a defect of this cortical blush. EDUS appears to be less specific (77%) than DMSA, unless we take into account the heterogeneity of DMSA scans in the location as the defects of EDUS in the 3 cases mentioned. EDUS has a sensitivity comparable to DMSA scans to diagnose acute pyelonephritis.

**Marcus Weitz et.al (2013)** tested the hypothesis that the relative renal volume assessed by ultrasound provides an equally reliable but less invasive tool for assessment of kidney function as compared to renal scintigraphy in patients with primary vesicoureteral reflux. Renal ultrasound and renal scintigraphy were performed in 85 patients (median age 4.5 years, range 0.25 e 7.7) and repeated in 74 patients after 2 e 13 months (mean 7) of the primary investigation. Renal size was measured by ultrasound, and relative renal volume was calculated for each kidney by using the formula of a prolate ellipsoid. Renal function was estimated for each side (split renal function) by scintigraphy with  $^{99m}\text{Tc}$  MAG3. Mean relative volume assessed by ultrasound was 0.53 (range 0.13 e 0.90) for the right and 0.47 (range 0.10 e 0.87) for the left kidney. Mean split renal function calculated by scintigraphy was 0.52 for the right kidney and 0.48 for the left kidney. There was a statistically significant correlation between the relative renal volume determined by ultrasound and the split renal function determined by scintigraphy for the right and the left kidney ( $r=0.98$ ;  $p < 0.001$ ). The correlation was still significant in the patients'

subgroups with different extent of split renal function and grade of VUR. The mean difference between relative renal volume (ultrasound) and split renal function (scintigraphy) was 2.8% (SD 4.1%). The largest observed difference was 8%. The 95% CI of split function and relative renal volume was 10.8/−5.2%. Follow-up examination was done in 74 out of 85 patients and compared with their previous examination results. Mean relative renal volume of the right kidney estimated by ultrasound was 0.56 compared to prior 0.52. Mean relative renal volume of the left kidney estimated by ultrasound was 0.44 compared to prior 0.48. Mean split renal function of the right kidney estimated by scintigraphy was 0.55 compared to prior 0.52. Mean split renal function of the left kidney estimated by scintigraphy was 0.45 compared to prior 0.48. There was a statistically significant correlation between relative renal volume determined by ultrasound and split renal function determined by scintigraphy ( $r = 0.91$ ;  $p < 0.001$ ). Kidney deterioration greater or equal to 3% calculated by renal scintigraphy was detected in 21 out of 74 (28%) patients. Ultrasound with assessment of relative renal volume may be a useful alternative to renal scintigraphy in patients with pVUR. Benefits of this imaging approach include less exposure to ionizing radiation, and decreased invasive, time consuming and expensive renal scan examinations.

**Svante Swerkersson** et al. (2006) studied the relationship among vesicoureteral reflux, urinary tract infection and permanent renal damage in children. The researcher retrospectively analyzed 303 children younger than 2 years with a first time, nonobstructive, culture verified urinary tract infection. The protocol included ultrasonography and voiding cystourethrography within 3 months after urinary tract infection, and 99mtechnetium dimercaptosuccinic acid scintigraphy after 1 to 2 years. Information about temperature at first UTI was lacking in 2 patients, and data about CRP were lacking in 1. Of 161 boys 118 (73%) had a febrile UTI (temperature 38.5°C or greater), as did 128 of 140 girls (91%). A total of 232 children (77%) had a maximum CRP of 20 mg/l or greater. Median CRP was 49 mg/l (range 0 to 290) in boys and 65 mg/l (0 to 290) in girls, a difference that was significant ( $p = 0.05$ ). Despite a maximum temperature of less than 38.5°C, 21 children had a CRP of 20 mg/l or greater (median 60, range 20 to 148). Of these 21 patients 14 were younger than 1 month, and all were male.

Reflux was found in 22% of the boys (36 of 163) and in 31% of the girls. Dilating VUR (grades III to V) was found significantly more often in boys (22 of 36 with VUR) than in girls (14 of 44 with VUR,  $p \leq 0.01$ ). Only 1 boy had grade V VUR. There was a significant relationship between maximum CRP at first UTI and grade of VUR in boys ( $p \leq 0.05$ ) and girls ( $p \leq 0.01$ ). Also, UTI recurrence with fever ( $\geq 38.5^\circ\text{C}$  or greater) occurred in 36 children (12%) during followup until the second DMSA scan at 1 to 2 years. The risk for new febrile UTIs increased with the presence and severity of VUR ( $p \leq 0.001$ ). At the followup examination 80 of 303 patients (26%) had abnormal DMSA scintigraphy. The rate of abnormality was 19% (43 of 223 patients) in those without demonstrable VUR. There was a significant relationship between DMSA abnormality and the presence and severity of VUR ( $p \leq 0.001$ ). The relative risk of renal abnormality with 95% confidence limits in relation to VUR grade is shown in (grade I, 1.20 [0.43 to 3.35]; grade II, 2.17 [1.33 to 3.56]; grade III, 2.50 [1.55 to 4.01] and grades IV to V, 4.61 [3.23 to 6.57]). There was a significantly increased risk in males and females with VUR grade II and higher. The maximum temperature at first UTI correlated with renal abnormalities on followup DMSA scan ( $p \leq 0.05$ ). There was also a significant relationship between the maximum CRP at first UTI and renal abnormalities on followup DMSA scan ( $p \leq 0.001$ ). Children with recurrent UTI had permanent renal damage significantly more often than those without recurrent UTI ( $p \leq 0.01$ ). Age and gender were not significantly related to the presence of renal damage.

### **Chapter three**

#### **Materials and methods**

The researcher followed the methodology of experimental studies over specific sample of (62) children patients suffering from (UTI). The sample were small even though Sudan was one of the first countries in Africa to use the radioisotopes in treatment and diagnosis of many diseases, and the gamma camera entered the department of RICK in 1985. In spite of all that, the studies found that, the referring of children patients with UTI to assess the defects of upper urinary tract inflammation as other routine investigation is very rare (0.02).

Sample size is usually taken by:  $n = \frac{t^2 pq}{e^2}$

Where:

n = sample size

t = confidence level

d = precision desired

p = probability of having the TC99mDMSA investigations (0.02)

q = probability of not having the TC99mDMSA investigation (0.98)

$$\therefore n = \frac{(1.96)^2 \times 0.02 \times 0.98}{(0.05)^2} = 60 \text{ patients}$$

### **3-1 Source of data collection:**

The data were collected from children referred to the nuclear medicine department in RICK after a documented UTI, defined by a positive urine culture and health-facility-based children with infected urinary tract.

### **3-2 Inclusion criteria:**

Children (age below 15 years) referred for a radionuclide renal investigations by a pediatric physician or pediatric surgeon form.

### **3-3 Methods of data collection:**

Primary data were collected from patient's records, with precoded interview and a static renal scan with TC99mDMSA.

### **3-4 Instruments of data collection:**

Mediso Gamma camera-SEMENS, Digital, Model: Digital Nuclei, software: Acquisition console, Processing: DIAG.

### **3-5 Cortical Scintigraphy in Urinary Tract Infections:**

Since the mid of 1980 up to now, a series of studies have demonstrated the superiority of renal cortical imaging in detecting both acute pyelonephritis and renal scarring compared with both IVU and ultrasonography. Cortical scintigraphy overall detected approximately twice as many defects as US and approximately four times as many defect as IVU(Dizdarevic,Sabina1999-2001)

Cortical scintigraphy also should be performed as a follow-up study in order to determine whether the kidney has healed or scarred. If scarring develops, the patient will need long-term management to prevent recurring renal injury and subsequent renal failure as well as to detect and treat hypertension, which may develop as a result of scarring(DF,Eggli andM.Tulchinsky 1993)Either TC99mDMSA (dimercaptosuccinic acid) or TC99m glucoheptonate can be used for cortical scintigraphy. TC99mDMSA is now recognized as the reference method to detect focal areas of renal parenchyma damage. This applies to acute pyelonephritis, renal scars regardless of the cause, Renovascular disease, the poorly functioning kidney and the complex duplex kidney(Dizdarevic, Sabina MD 1999-2001)

Approximately 40-50% of an injected dose is present in the cortex two hours after injection. The dose of radiopharmaceutical is calculated based on body weight, with a minimum dose necessary for adequate imaging. Because TC99mDMSA is a fixed tubular agent, no dynamic excretory images can be obtained. Glucoheptonate is partially concentrated and excreted in the urine and partially bound to the renal tubule. Between 10% and 20% of glucoheptonate dose is present in the cortex two hours after injection. Extraction and drainage of the radiopharmaceutical can be obtained. Stasis in a hydronephrotic or dilated renal pelvis will interfere with cortical imaging. DMSA has an advantage over glucoheptonate in that it provides lower bladder and gonad exposure. TC99mDMSA scintigraphy is emerging as a method of choice, because it combines high specificity sensitivity with convenience, repeatability, and acceptable radiation dose(JM,James andHJ.Testa1994)Although TC99mDMSA has been available and used for over ten years, there is, no general agreement on when to apply the TC99mDMSA scans in UTI, i.e in the acute phase, in the follow-up or both.(R.Sixt 1996)

Acute pyelonephritis has been shown to be necessary etiologic factor development of subsequent renal scarring, and the mechanism of renal injury in pyelonephritis has been extensively studied in the experimental mode. The rate of resolution of defects due to pyelonephritis is age dependent, occurring more slowly in infants and smaller children and more rapidly in teenagers. With TC99mDMSA scintigraphy, the true incidence of scarring with pyelonephritis can now be studied (Dizdarevic,Sabina 1999-2001)Six months is appropriate routine follow-up time. Studies to detect renal scarring should probably not be performed earlier than 3 months after acute infection. However, a study to evaluate anewacute febrile illness can be perfored at any time.(Dizdarevic,Sabina 1999-2001)

Scarring also demonstrates a spectrum of appearances. The hallmark of chronic pyelonephritis or renal scarring is volume loss, either focal or global, in the affected kidney. Volume loss accompanies focal cortical defects or obvious cortical thinning. The scars may be large or small, single or multiple.(Dizdarevic,Sabina 1999-2001)The role cortical scintigraphy in covert bacteriuria, in patients with only lower tract infection clinically, and in siblings of patients with VUR remains to be more fully evaluated.(Dizdarevic,Sabina 1999-2001)The TC99mDMSA renal scan avoids some of the problems of IVU. It does not require preparation of the patient and is not affected by bowel gas, it avoids risk inherent in the use of contrast medium, it gives better visualization of the renal parenchyma than IVU, the radiation dose is significantly less than with IVU.(RR.Bailey 1981)

### **3-5-1 Ideal characteristics of a Radiopharmaceutical:**

1-Half-life should be similar to the length of the test.

2-The radionuclide should emit gamma-rays and there should be no charged particle emission.



- 3-The energy of gamma-rays should be between 50 and 300 keV.
- 4-The radionuclide should be chemically suitable for incorporating into a pharmaceutical without altering its biological behavior.
- 5-The radionuclide should be readily available at the hospital site.
- 6-The pharmaceutical should localize only in the area of interest.
- 7-The pharmaceutical should be eliminated from the body with a half-life similar to the duration of the examination.
- 8- The radiopharmaceutical should be simple to prepare(PF, Sharp et.al 1989)

### **3-5-2 Mechanism of accumulation:**

The cortical uptake of TC99mDMSA depends on renal blood flow and proximal tubular cell integrity. Renal handling of TC99mDMSA is not completely understood. DMSA is fixed in the proximal tubular cells and in the upper part of the loop of Henle.

TC99mDMSA may reach these cells via the peritubular route or by tubular reabsorption, which follows glomerular filtration. TC99mDMSA is almost completely bound to plasma proteins, which prevents it from being filtered by the glomeruli.(J.B. Bingham, and M.N., MAISEY, 1978).In the isolated and artificially perfused rat kidney, it was shown that TC99mDMSA is removed from the circulation through the renal peritubular capillary route (P Goldraich, NoemiaandH.Goldraich,Isidoro1995)

### **3-5-3 Patient preparations:**

No special preparation is necessary for the exam. The child may eat and drink normally on the day of the scan.

The child is encouraged to drink plenty of fluid on the day of the scan. This helps to get kidneys in peak working order and helps to flush the isotope through promptly.

The patient is asked to micturate immediately before the scan.

### **3-5-4 Patient reassurances:**

Preparation for a high-quality nuclear medicine examination must include the staff, the child patients and the parents. Adequate awareness and handling of the child and parent are required by the staff in the department, including the appointment staff, receptionists, nurses and technicians. The first contact between the nuclear medicine department, the child patient and the parent may well set the basis of the relationship between parent and the staff.

Preparation of the child begins when the parent and child make the appointment, at which time the attitude of the receptionist or appointment clerk must be positive and encouraging(LK,Harding1994)

Preparation of the child also is important. This will vary according to the child's maturity. Most children, especially young ones, have fantasies about what may happen when they have "that test". A prospective study undertaken on inpatients undergoing a TC99mDMSA scan showed that all the children had fears about what was going to happen to them and that some children had been told by other inpatients exaggerated untruths.

The parent offers the best form of comfort and security for the child. For this reason, we try to explain the entire procedure to the parent and emphasize that the attitude of the parent will be reflected by the child. At times, the parent needs a great deal of help so that he or she can face the proposed examination positively and be a support to his or her child. The time invested in ensuring that the parent has a positive attitude toward the examination, and that the parent knows the importance of his or her role in supporting the child, is fully compensated when the examination is successfully completed. We suggest that the parent stays with the child throughout every part of the examination and keeps in touch with the child. Some parents are captivated by equipment, the staff should recognize this and both satisfy the parent's curiosity but also remind the parent that he or she should help and support the child.(Gordon Isky1998)

### **3-5-5 Pediatric dosages:**

It is important to remember that rapidly growing tissue are generally extremely sensitive to ionizing radiation and that certain organs, such as the growing bone, take up radionuclides more avidly than those of adults. The radioactive dose is distributed in a much smaller volume than in adults. Giving rise to a higher absorbed dose.

Most investigations, which are done on adults, can also be used for children, providing the doses are adjusted. The metabolism, biodistribution and excretion of drugs are different in children from those in adults. Dose should preferably be calculated according to body surface area or body mass (not according to age).

Tables are available for dose adjustments and estimation of radiation dose.

Administered radiopharmaceutical activity schedules (or dosage schedules) have two, usually conflicting, objectives: to ensure that sufficient radiopharmaceutical is given to yield scintigraphic images of diagnostic quality under the prevailing study conditions, while within these constraints, minimizing the radiation burden (T. SMITH. et al 1996). The administered activity may not be too low, since the study will then no longer provide useful information.

Special care should be taken to check the following for each study requested for a child:

- Is the indication correct?
- Can the scintigraphic study be replaced by any other method, which would cause less radiation exposure, e.g. ultrasound.

### **3-5-6 Methods of the study:**

Scintigraphy was performed with intravenous injection of <sup>99m</sup>Tc-DMSA labeled with <sup>99m</sup>technetium. The schedule for various ages was based on body surface area (maximal adult dose 110 MBq minimal dose 20 MBq) [7]. After injection (2-3h), three views (one posterior and two posterior oblique) were obtained with a small-view gamma camera connected to a computer, using a low-energy high-resolution collimator and pixel dimension of 1.3-1.8 mm. All magnified images were acquired for up to 10 min in each projection, mainly using dynamic acquisition (20s/frame).

The recognizable findings of acute pyelonephritis on TC99mDMSA renal scan included either one or more areas of focal decreased cortical uptake or diffuse areas of diminished cortical uptake of TC99mDMSA with no evidence of cortical loss, the normal reniform outline being preserved. The involvement of each kidney was visually graded as mild (less than 25% of the kidney), moderate (25%-50% of the kidney), or severe (more than 50% of the kidney) (A, Piepsz et.al 1996)

### **3-5-7 Imaging interpretations:**

Good-quality renal static images on a TC99mDMSA scan must show cortical uptake with a decreased concentration in the areas overlying the collecting system. The renal outlines must be very well defined, in order to avoid the possibility of missing small scars.

Normal kidneys have similar sizes. Cortical uptake is homogeneous with three minor areas of decreased uptake that correspond to the pelvicalceal system. No TC99mDMSA activity is seen over the bladder or other viscera. Flattening of the superolateral border of the upper pole of the left kidney due to splenic impression may occur.

### **3-5-8 Normal characteristics of renal scan:**

The normal TC99mDMSA study demonstrates uniform distribution of radiopharmaceutical throughout the cortex. The papillary pyramids, and renal collecting systems do not accumulate TC99mDMSA and are seen as centrally located photopenic defects covered by a rim of cortex. These defects are particularly well seen on posterior oblique views.

### **3-5-9 Abnormal renal scan:**

There are three recognizable patterns of pyelonephritis:

- A Solitary focal defect, involving a portion of one kidney, the defect has mass effect with no evidence of volume loss,
- The multiple focal defects involving either one or both kidneys.
- The diffuse involvement of an entire kidney.

### **3-5-10 Dynamic study:**

It is a dynamic renal scan (arenogram, a MAG-3, a DTPA scan) is investigation gives information about the blood flow to the kidney and how well each kidney is functioning for production of urine output.

If substances, which pass into the urine, are labeled with a radionuclide and injected intravenously, their passage through the kidney can be observed with a gamma camera.

The two agents of choice are TC99mDTPA (diethylenetriaminepentacetic acid) and TC99mMAG-3 (mercaptoacetyltriglycine), TC99mDTPA is filtered by the glomeruli and not absorbed or secreted by the tubules, where as MAG-3 is absorbed or secreted by the tubules,. Where MAG-3 is both filtered by the glomeruli and secreted by the tubules.(Donald R. et.al2001) The main indications for dynamic study are:

1. Measurement of relative renal function in each kidney, this helps the surgeon to decide whether there is nephrectomy or more conservative surgery.
2. Investigation of urinary tract obstruction, particularly, pelvic ureteric junction obstruction.
3. Investigation of renal transplants.
4. Urinary tract infection
5. Renovascular problem
6. Evaluation in renal failure

Particularly important is the fact that the studies are cost effective, relatively non-operator dependent, and non-invasive with minimal discomfort and known risk factor.

### **3-5-11 Positioning & images:**

The gamma camera is positioned posteriorly over the kidneys and a rapid injection of the radiopharmaceutical is given.

Early images show the major blood vessels and both kidneys. Subsequently, activity is seen in the renal parenchyma and by 5 minutes the collecting systems should be visible. Serial images over 20 min show progressive excretion and clearance of activity from the

kidneys. Quantitative assessment with a computer enables a renogram curve to be produced and the relative function of each kidney calculated. (Armstrong, Peteret.al 1998)

# Chapter four

## Result

This chapter consists of result that obtained from children patients in Nuclear medicine department of RICK and the following tables demonstrate the data collected from patients. The results were analyzed using Statistical Professional for Social Science (SPSS) program version 10.00. In order to be able to compare between observed and expected group of frequencies, we must be able to state what frequencies would be expected. The null hypothesis states the proportion of objects

falling in each of the categories in the presume population. That is, from the null hypothesis we may deduce what are the expected frequencies. The chi-square technique tests whether the observed frequencies are sufficiently close to the expected ones to be likely to have occurred under null hypothesis ( $H_0$ ), and if any cell contents a number less than 5% it's automatically recommended Fisher Exact Test.

The null hypothesis may be tested by:

$$X^2 = \sum_{i=1}^k \frac{(O_i - E_i)^2}{E_i} \quad \text{-----} (1)$$

Purposive sample will be used for selection with specific criteria: Fulfill the criteria been previously investigated for renal infection analytical , descriptive & case study.

### 4-1 Variables of data collection:

- Socio – demography background about the patient (Gender, age, the first onset.....).
- Health related information. ( History of the disease in the family,.....)
- Diagnosis (Positive – negative)
- Kidney (Rt./ Lt./both)
  - Site of the infection inside the kidney

In summary (62) children with proved UTI referred to the radiation & Isotope Center of Khartoum (RICK) will be involved in  $^{99m}\text{Tc}$ -DMSA scintigraphy using gamma camera with dose calculated according to the child weight. The imaging will be reported by nuclear medicine physician. A clinical sheet will be filled for each patient's age, sex, residences, complains, lab investigations, etc.

$^{99m}\text{Tc}$ -DMSA sheet will be filled for each patient, involving kidney, Right or left, multiple or single, first or follow up ....etc.

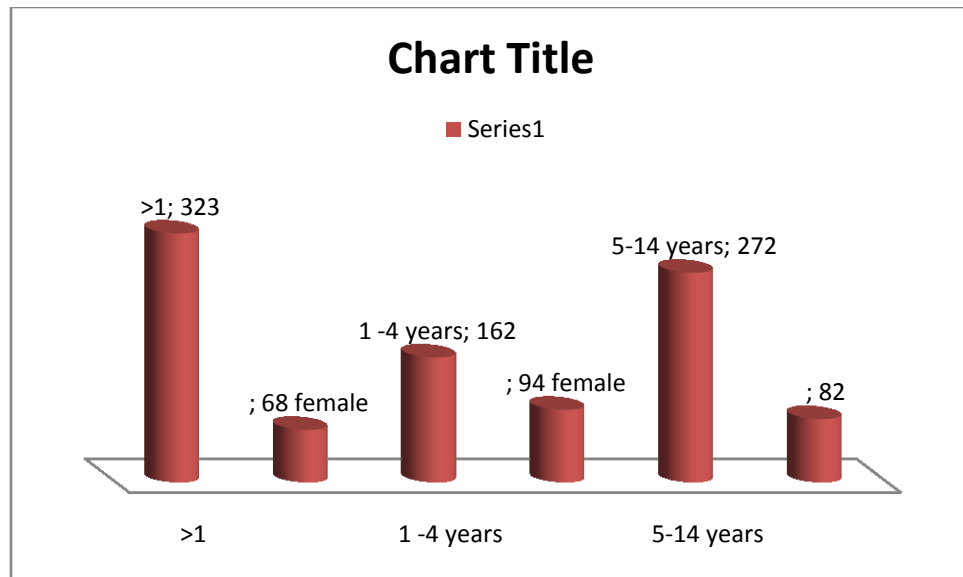
The data collected will be analyzed using computer system.

There are number of different sampling distributions for chi-square, one for each value of df. The size of df reflects the number of observations that are free to vary after certain restrictions have been placed on the data. These restrictions are not arbitrary, but raters are inherent in the organization of the data.

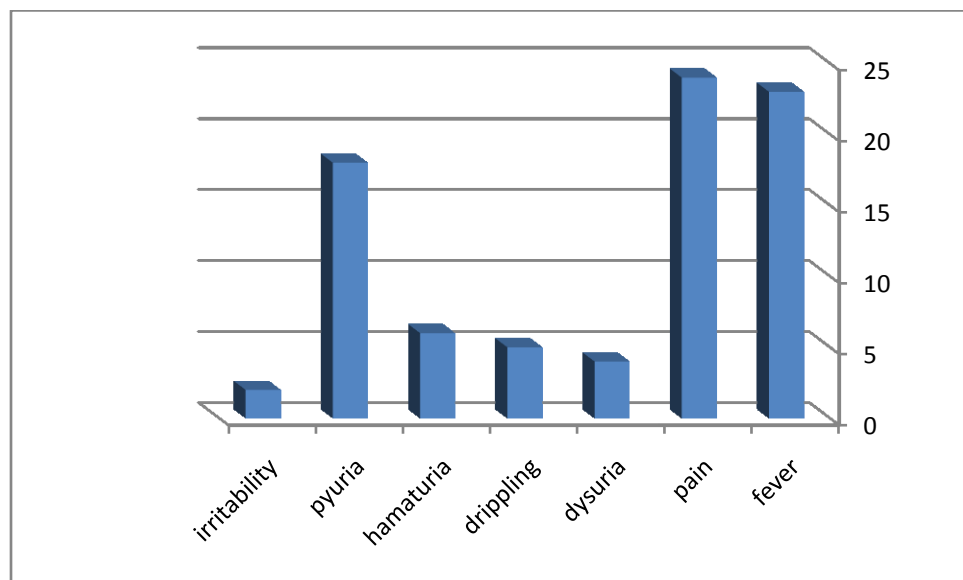
We calculate the value of  $X^2$  by formula (1). The significance of this obtained value of  $X^2$  may be determined by reference to appendix (C ). If the probability associated with the occurrences under  $H_0$  of the obtained  $X^2$  for  $df = k-1$  is equal to or less than the previously determined value of  $\alpha$  (the critical region), then  $H_0$  may be rejected. If not,  $H_0$  will be accepted.

For small expected frequencies i.e when  $df = 1$ , for example, each expected frequency should be at least 5. When  $df > 1$ , the  $x^2$  test for the one-sample case should not be used when more than 20% of the expected frequencies are smaller than 5 or when any expected frequency is smaller than 1. Expected frequencies can sometimes be increased by combining adjacent categories. For more details of  $X^2$  one sample test the reader can see, Sdney Siegel "Nonparametric statistics for the behavioral sciences".

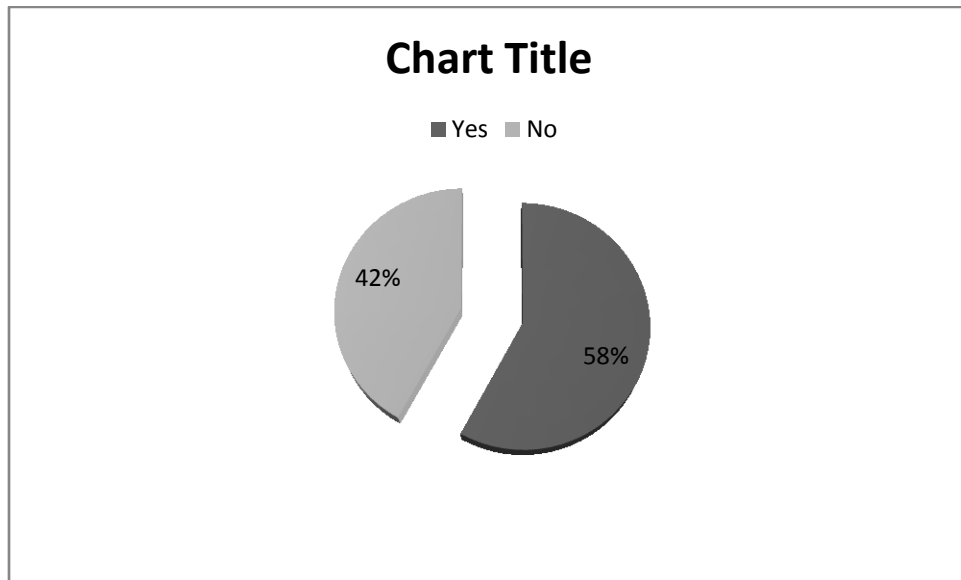




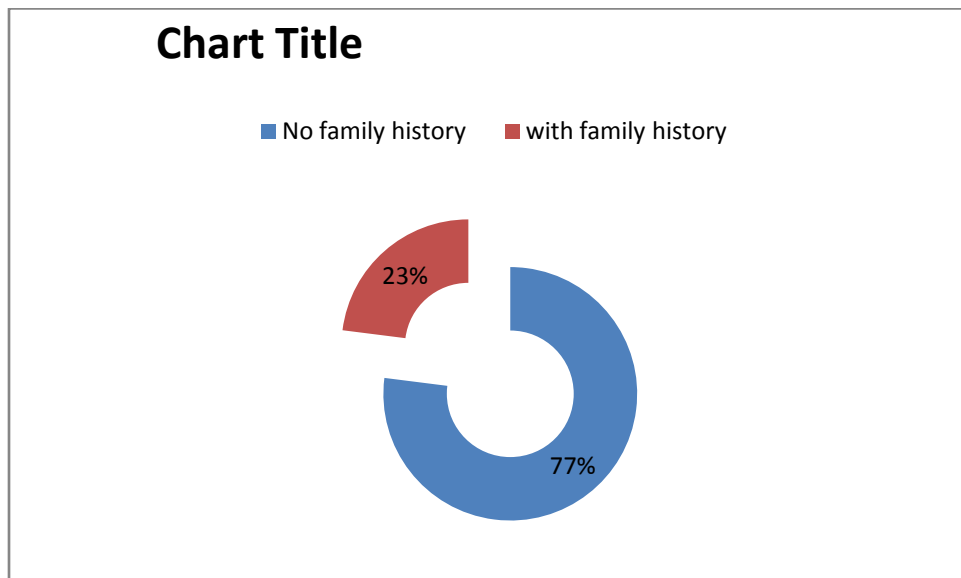
**Figure 4-1: Relative distribution of UTI according to sex and age in Sudanese children patients with UTI during 2000 – 2002.**



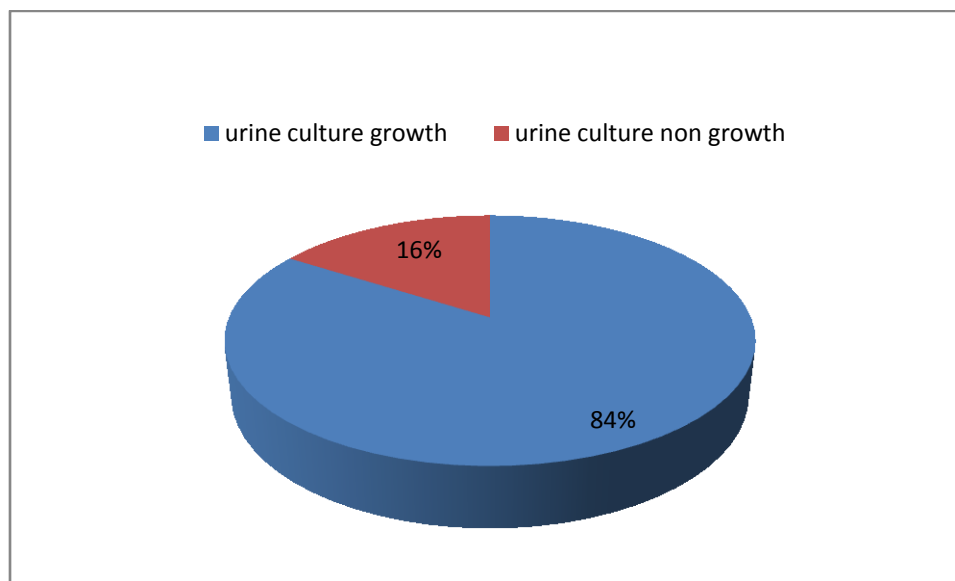
**Figure 4-2: Symptoms and compliance of UTI in Sudanese children patients with UTI that were investigated in RICK during 2001 – 2003.**



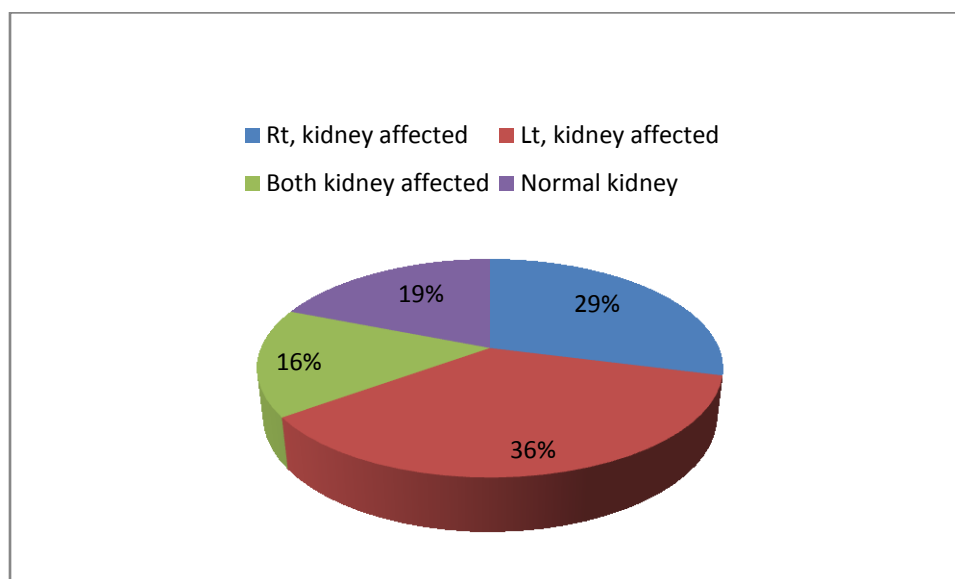
**Figure 4-3: Patients history second attack of Sudanese children patients with UTI that were investigated in RICK during 2001 – 2003.**



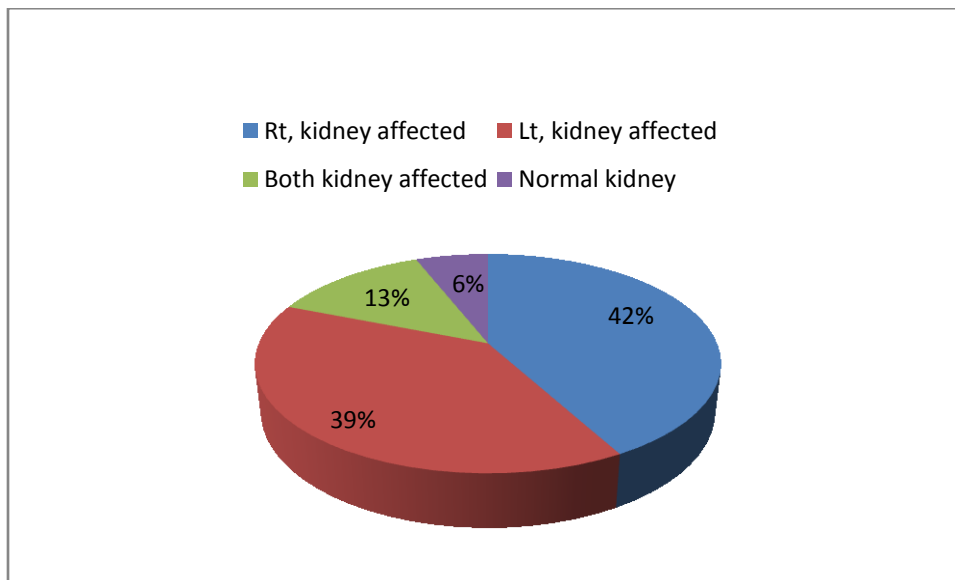
**Figure 4-4: The patient family history of Sudanese children patients with UTI that were investigated in RICK during 2001 – 2003.**



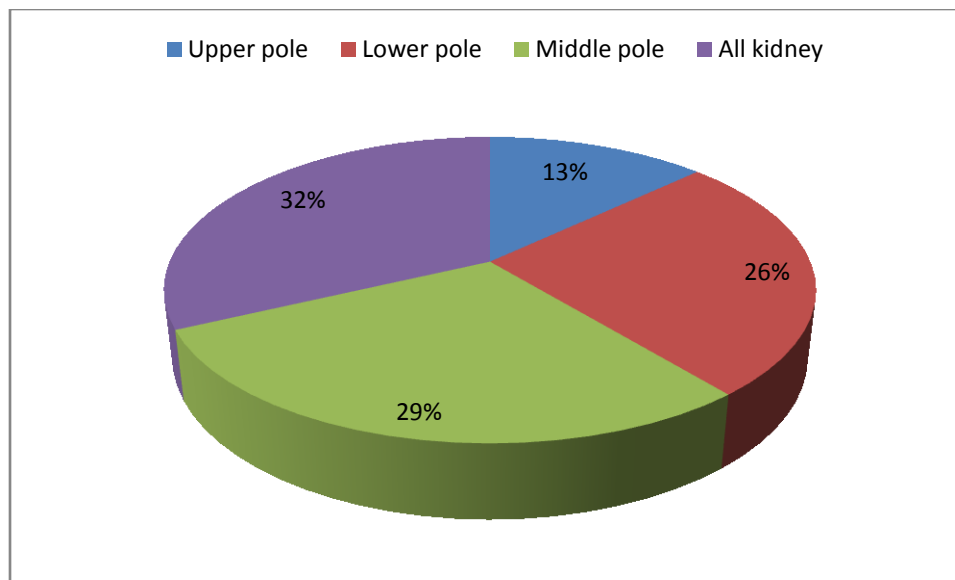
**Figure 4-5: Urine culture of Sudanese children patients with UTI that were investigated in RICK during 2001 – 2003.**



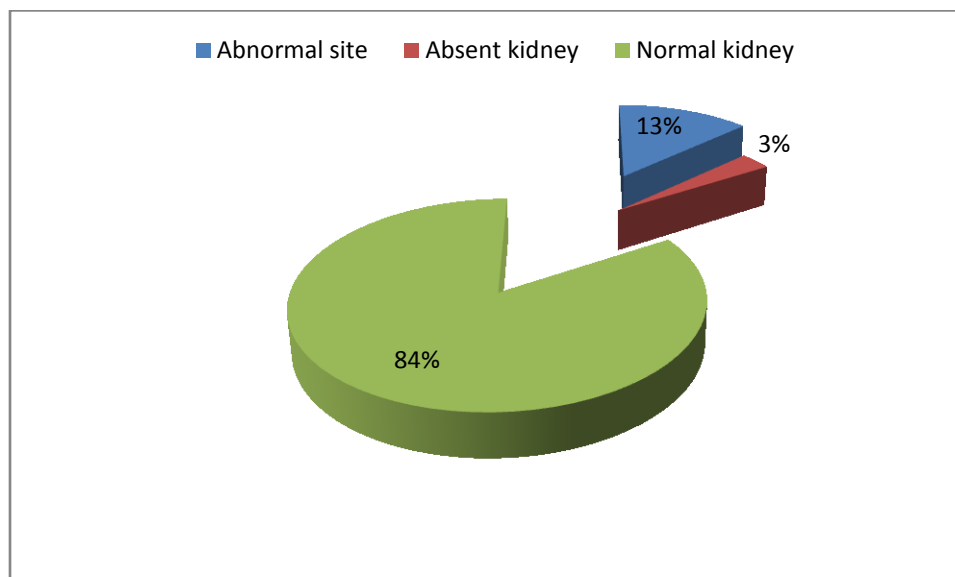
**Figure 4-6: Affected kidneys by ultrasound of Sudanese children patients with UTI that were investigated in RICK during 2001 – 2003.**



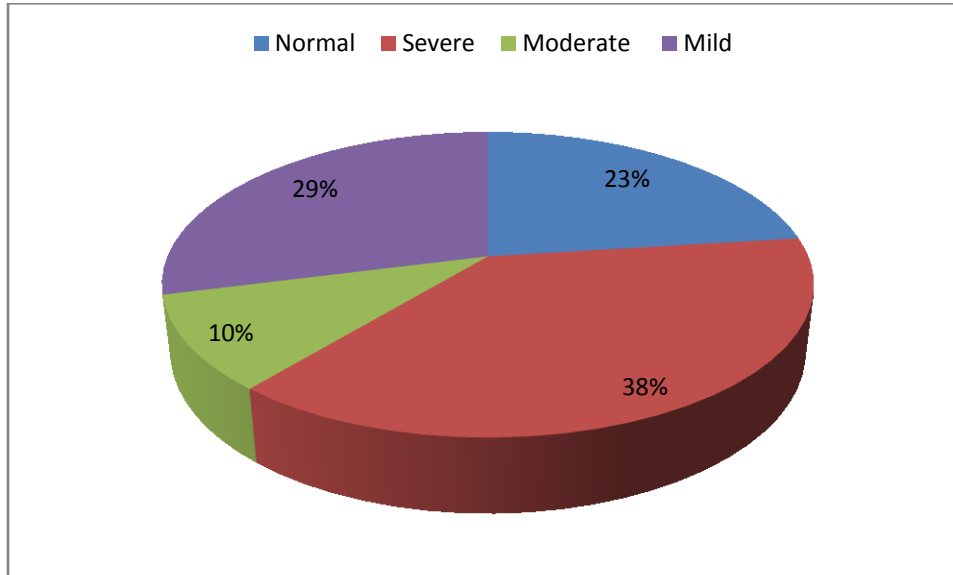
**Figure 4-7: Affected kidneys in  $^{99m}\text{Tc}$ -DMSA of Sudanese children patients with UTI that were investigated in RICK during 2001 – 2003.**



**Figure 4-8: Affected site of kidneys of Sudanese children patients with UTI that were investigated in RICK by  $^{99m}\text{Tc}$ -DMSA during 2001 – 2003.**



**Figure 4-9: Morphology of kidneys of Sudanese children patients with UTI that were investigated in RICK by  $^{99m}\text{Tc}$ -DMSA during 2001 – 2003.**



**Figure 4-10: Obstructed kidneys of Sudanese children patients with UTI that were investigated in RICK by  $^{99m}\text{Tc}$ -DMSA during 2001 – 2003.**

**Table 4-1: shows the  $\chi^2$  test between affected kidney according to  $^{99m}\text{Tc}$ -DMSA and affected kidney by Ultrasound.**

	Rt. Kidney DMSA	Lt. Kidney DMSA	Both. Kidney DMSA	Normal DMSA
Rt. Kidney U\S	7	1	1	0
Lt. Kidney U\S	0	9	1	1
Both Kidney U\S	2	2	1	0
Normal U\S	4	0	1	1

**Table 4-2: shows the relative function of the Rt. Kidney studied by  $^{99m}\text{Tc}$ -DTPA study of Sudanese children patients with UTI during 2001 – 2003**

	Frequency	Percent	Valid Percent	Cumulative Percent
<b>Good</b>	<b>12</b>	<b>38.7</b>	<b>38.7</b>	<b>38.7</b>
<b>Poor</b>	<b>15</b>	<b>48.4</b>	<b>48.4</b>	<b>87.1</b>
<b>Non</b>	<b>4</b>	<b>12.9</b>	<b>12.9</b>	<b>100</b>
<b>Total</b>	<b>31</b>	<b>100</b>	<b>100</b>	

**Table 4-3: shows the relative function of the Lt. Kidney studied by  $^{99m}\text{Tc}$ -DTPA study of Sudanese children patients with UTI during 2001 - 2003**

	Frequency	Percent	Valid Percent	Cumulative Percent
<b>Good</b>	<b>15</b>	<b>48.4</b>	<b>48.4</b>	<b>48.4</b>
<b>Poor</b>	<b>9</b>	<b>29</b>	<b>29</b>	<b>77.4</b>
<b>Non</b>	<b>7</b>	<b>22.6</b>	<b>22.6</b>	<b>100</b>
<b>Total</b>	<b>31</b>	<b>100</b>	<b>100</b>	

## **Chapter five**

### **Discussion, conclusion and recommendation**

#### **5-1 Discussion:**

The optimum regime to investigate children with urinary tract infection (UTI) remains uncertainly. The researcher studied sixty two patients with (UTI) confirmed by the following Investigations: clinical examination, laboratory tests as red blood cells count (RBC), pus cell, and bacteria growth (urine culture) and other examinations, in terms of intravenous urography (IVU), Ultrasonography (US) and  $^{99m}\text{TC}$ -DMSA scan.

In this study, the researcher tried to assess if  $^{99m}\text{TC}$ -DMSA static renal scan performed after an acute infection in a group of patients chosen according to certain risk's criteria, would allow the selection of those who showed the risk of progressive renal damage. This research aimed at evaluating the variability of  $^{99m}\text{TC}$ -DMSA scintigraphy versus technical methods, of Ultrasonography US for the diagnosis of acute parenchymal renal infections among children. The  $^{99m}\text{TC}$ -DMSA renal scan was taken as the gold standard method for determining acute parenchymal renal infections in the upper urinary tract. All patients had the following investigations:

- Urine analysis & urine culture
- US investigation
- DMSA investigation

A clinical sheet had been filled for each patients containing age, gender, residence, complain, laboratory investigation, ...etc.

The following results demonstrate the data collected from the patients:

From the results obtained in figure (4-1) the researcher divides the patients into three groups as:

Group (I) less than one year

Group (II) from 1-4 years and

Group (III) from 5-14 years

According to this, the age of patients presented with UTI, ranged between less than one year up to 15 years, and the mean age was 1.61 years. The age of 68% of the sample patients ranged between 5-14 years. This means that UTI is a common problem in the third group of children. This could be due to the ability of children in this age to express



their feelings, while other younger couldn't do that and their parent may confused the symptom with other diseases.

In addition, according to the gender distribution there is 37% as male and 63% as female , as illustrated in figure (4:2) Because the female urethra is shorter than the male's, and this, together with antibacterial action of some secretions of the male's prostate gland, probably account for why women are more likely than men to develop UTI, such result indicates that, the disease is predominant among females rather than males, as stated by Bethesda and lithicum(3)

In this study, the researcher studied the following aspects:

- I) Symptoms and patient's complains. In which the study found that (77%) of patients were with abdominal pain, (74%) with fever, (58%) pyuria, (19%) hematuria, (16%) dripping (13%) with dysuria, and (7%) with irritability, as shown in figure (4-2). The common problems of UTI in the sample group of the study is abdominal pain and fever, because these are usually the obvious symptoms to the parents.
- II) Past history of previous attack: in which the study found that, 58% of the patients had recurrent urinary tract infections and 42% with the first time of infections, as illustrated in figure (4-3) . The high yield of renal abnormalities by <sup>99m</sup>TC-DMSA scanning emphasizes the importance of testing all cases of UTI, including patients with a first – time infections with this modality. Documentation of the pattern of abnormalities may help in planning for subsequent management of UTI in these patients.
- III) Family history disease, out of which the analysis revealed that, 77% of patients had no family history of the disease and 23% of patients had family history as shown in figure (4-4) . In addition, chi-square test was applied to see whether there was a relation between the studied groups, as p value was 0.264, which revealed that there was no relation between patients with family history and patients without UTI experience.
- IV) Laboratory test, as urine culture, which revealed that 84% of patients had a bacterial growth in their lower urinary tract and 16% of patients, showed

negative result in their lower urinary tract. That means most of the patients were with UTI experience, as showed in figure (4-5), and from patient's laboratory data. The study found that, 90% of patients were with abnormal pus cells and 55% were with abnormal RBCs as shown in figure (4:8). This showed that most of the sample groups confirmed UTI by the positive urine culture test.

Depending on the results of US obtained from the figure (4-6), the study showed that 36% of patients with affected left kidneys, 29% of patients with affected right kidneys, 19% of patients had normal kidneys and 16% of patients with bilateral renal problems.

The p-value of Chi-Square was 0.018, which means that there was a difference between the two investigations. i.e  $^{99m}\text{TC}$ -DMSA is more effective in detection of inflammatory disease of renal parenchyma. This result goes with the same result mentioned by Verboven M, Ingels M(40)

From the observed data of the 62 patients that had been investigated by US, then  $^{99m}\text{TC}$ -DMSA, the study revealed that:

There were 12 patients of normal results of US investigations, and when they were investigated by  $^{99m}\text{TC}$ -DMSA, the result were that 8 patients had infections in their right kidneys, 2 patient in both kidneys, and 2 patient had normal kidneys as seen in table (4:1) . An US examination alone should not be relied on in the child with an acute urinary tract infection. Prediction of this result goes with same result mentioned by Fowlerk.(JR,Mackenzieet.al 1994)and (IG,Verberet.al 1988)In conclusion, the TC $^{99m}$ DMSA study as mentioned by Ditchfield MR, Nadel HR(9) is the most reliable test to investigate the UTI in children.

The distribution of the site of kidneys affected by acute parenchymal renal infections revealed by using  $^{99m}\text{TC}$ -DMSA renal scan, illustrated that, (32%) of the patients were affected at all kidneys, followed by the middle pole (29%), the lower pole (26%), and the affected site of the upper pole of the kidneys (13%), as showed in figure (4-7). This means that acute UTI affected most kidneys areas, followed by middle , lower and upper.

In addition, the cortical scintigraphy with  $^{99m}\text{TC}$ -DMSA could illustrate the morphology of the kidneys, from the 62 patients the study found that, 13% of patients were with abnormal kidneys sites, 3% of patients were with absent kidneys, 84% patients were with normal kidneys sites as shown in figure (4-8).

By using the dynamic renal scan with  $^{99m}\text{TC}$ -DTPA to assess the functioning and obstructed kidney, the study found that, the percentages of obstructed kidneys in the patients were: 29% of patients had mild obstructed kidneys, 9.7% had moderate obstructed kidneys, 38.7% had severe obstructed kidneys and 22.6% with normal kidneys as shown in figure (4-8). According to the relative functioning of the right kidneys, the study found that 39% of the patient had good functioning of the kidneys, 48% of the patients had poor functioning and 13% had non-functioning kidneys as shown in table (4-2 and 4-3). As for the relative functioning in the left kidneys the study found that, 48% of the patients had good functioning of the kidney, 29% of the patients had poor functioning and 23% had non – functioning kidneys as shown in table (4-3).  $^{99m}\text{TC}$ -DTPA scintigraphy supports the investigation of the relative function of the kidneys to demonstrate more information about the problem of the kidney.

## **5-2Conclusion:**

UTI is a common condition in children and may lead to renal parenchymal infection with a risk of later hypertension and renal insufficiency.

From the mid-1980 to present, a series of studies have demonstrated the advantage of renal cortical imaging in detecting both acute pyelonephritis and acute parenchymal renal infections compared with US. Cortical scintigraphy overall detected approximately twice as many defects as US. In spite of the fact that it has not yet, taken a major place in the imaging technique.

When a physician recommends a pediatric nuclear medicine examination, there should be little hesitation in studying the child.

There is an excellent safety record with regard to long-term outcome in children . Radiation doses are low and present little risk to the child. The risks of not studying a child by nuclear medicine examination are much greater than radiation risk.

This study shows many advantages of nuclear medicine in diagnosing the acute parenchymal renal infections, as a possibility of estimating the severity of the disease. In addition , possibility of evaluating children patient's risk of developing renal damage, beside that the nuclear medicine studies are helpful in the assessment and follow-up of the child with UTI looking particularly for acute parenchymal renal infections in the child suspected of having renal damage, in addition that this method is not costly for patients.

The renal cortical scintigraphy with  $^{99m}\text{TC}$ -DMSA is presently the method of choice to detect renal parenchyma disease.

### **5-3 Recommendation:**

Pediatric nuclear medicine offers many diagnostic opportunities to solve clinical problems. In order to perform the problem of acute UTI, there are several recommendations, which may be deduced from this study:

- 1- Conduction of early treatment of acute UTI, because it leads to early cure, while untreated urinary infection ncan lead to serious kidney damage.
- 2- Acute UTI in a young child may be a sign of an abnormality in the urinary tract that could lead to repeated problems, therefore the researcher recommends that a doctor should be seen if there is any suspicion that a child has a UTI.
- 3- The researcher recommends, early<sup>99m</sup>TC-DMSA scanning performed around the time of infection as a good technique for localization of the level of infection in the urinary tract.
- 4- Wherever available, <sup>99m</sup>TC-DMSA scan should be considered as apart of the first line investigations in any patient presenting with UTI.
- 5- This investigation should be used in the routine evaluation of children with urinary tract infection.
- 6- <sup>99m</sup>TC-DMSA scan should be added to initial work-up of children with UTI.
- 7- Availability of modern machines as SPECT set, to meet the modern techniques in nuclear medicine technology.
- 8- Establishment of additional nuclear medicine department in Sudan, especially pediatric ones.
- 9- More light should be focused a bout the importance of Nuclear medicine in defecting many pathological abnormalities, which cannot otherwise be properly detected by other diagnostic modalities.

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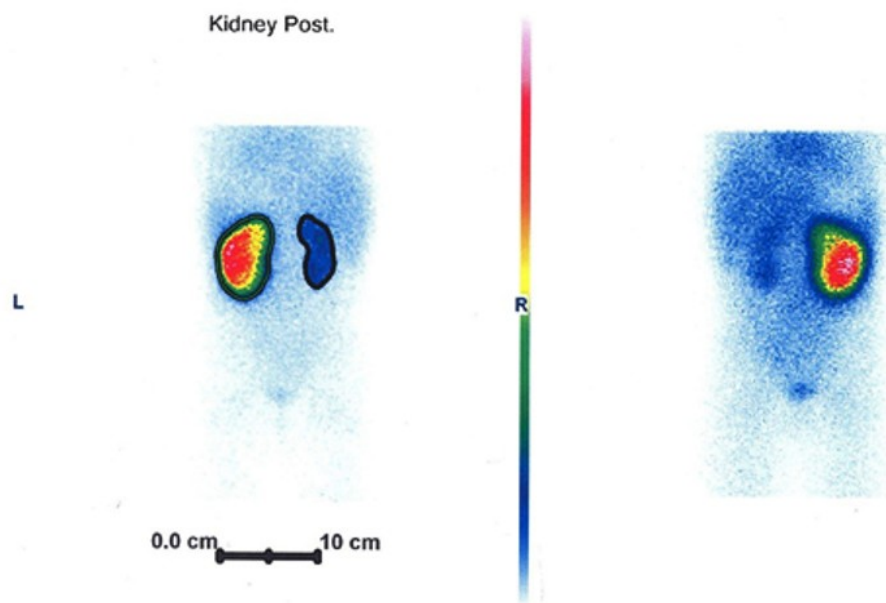
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## **APPENDECIES:**



Ratio based on geom. mean

Left kidney: 89.3 %

Right kidney: 10.7 %

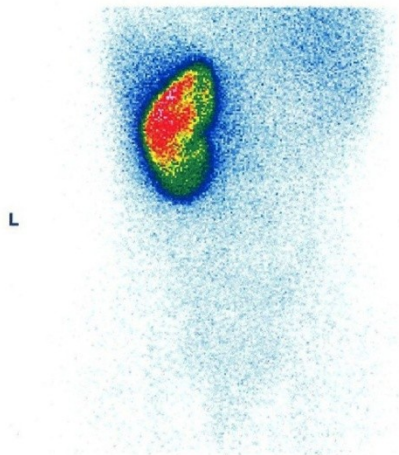
**Opinion:**

Lt. Kidney with hydronephrosis. Rt. Kidney with features of acute pyelonephritis



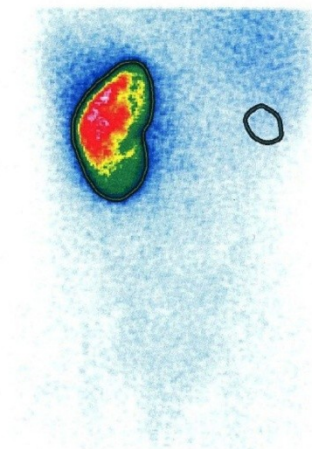
Procedure Name: StaticKidney

DMSA POST\_H2[1]



0.0 cm 10 cm

DMSA POST\_H2[1] (Filter: Smooth)



0.0 cm 10 cm

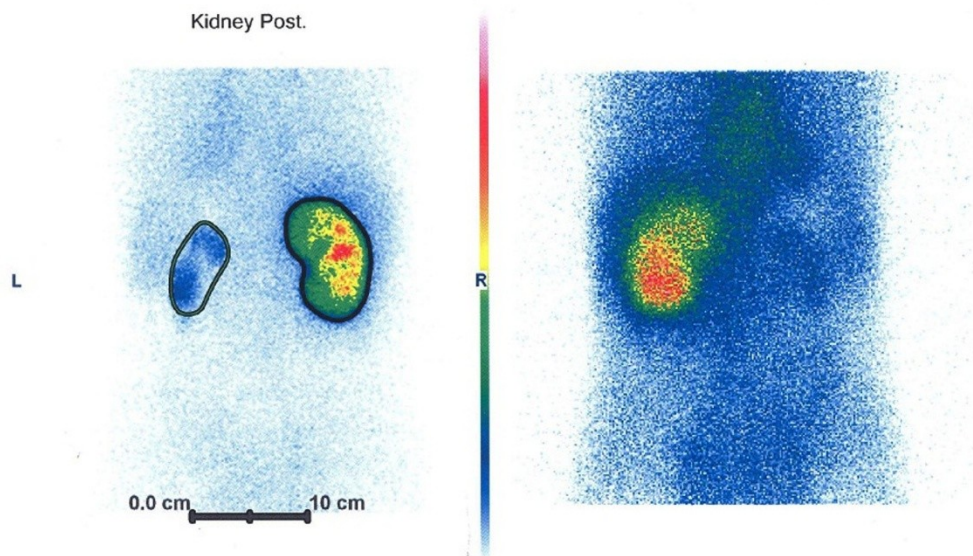
Ratio from posterior view  
Left kidney: 99.1 %

Opinion:

Lt. Kidney with hydronephrosis.

Rt. Kidney is not showed in this study

UTI of Lt. kidney is suggested



Ratio based on geom. mean  
Left kidney: 10.7 %  
Right kidney: 89.3 %

**Opinion:**

Rt. Kidney with acute hydronephrosis. Lt.  
Kidney with features of chronic pyelonephritis.  
chronic UTI in the Lt. kidney is suggested.

