AN AUDIT OF PELVI-URETERIC JUNCTION OBSTRUCTION AT RED CROSS CHILDREN’S HOSPITAL: A SIX YEAR REVIEW

2009

By

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SUBMITTED TO THE UNIVERSITY OF CAPE TOWN
In fulfilment of the requirements for the degree

MPhil
FACULTY OF HEALTH SCIENCES
UNIVERSITY OF CAPE TOWN

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I Isaac Ejembi Ocheke (Dr), hereby declare that the work on which this dissertation is based is my original work (except where acknowledgement indicates otherwise) and that neither the whole work nor part of it has been, or is to be submitted for another degree in this or any other university.

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CERTIFICATION

We, the undersigned jointly certify that the study reported in this dissertation is the
original work carried out by the candidate, Isaac Ejembi Ocheke under our supervision
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DEDICATION

This work is dedicated to all the sick children of ward E2 who with their problems, have made my knowledge and understanding of Paediatric nephrology much better and clearer.
ACKNOWLEDGEMENT

It has been an amazing and eventful two years that has just passed by. With a thankful heart full of appreciation, my hands are lifted up to God for this wonderful period of my life history.

My boss and mentor, Prof M McCulloch’s human touch to every aspect of relationship over this period of my training was inspiring. She taught me that every human being need to be treated with love, respect and shown the highest degree of concern. I am deeply grateful to her.

I sincerely appreciate the invaluable knowledge and experience I have gleaned from these people, without whose help and assistance I would have been incomplete in my training: Drs Gajjar, Sinclair, Nourse, Savage and all the retired but not tired professors and older colleagues in the renal unit.

Dr Sampson Antwi, a colleague and companion over these two years, has been wonderful and very helpful in all the trying, challenging and difficult moments.

All the staff of ward E2, for their friendship, tolerance and hard work and putting patient’s interest above everything else, I am deeply grateful to you.

All the wonderful doctors I worked with in the renal unit and ward E2 in general, thank you very much for your love, concern and friendship over these two years. To Nicole and her colleagues, for her amiable, exceptional personality and wonderful administrative skills, I am deeply thankful.

Finally, to my dear wife and our children whose esteemed companionship, love and friendship I deeply cherish but missed for this period I have been away, thank you for the sacrifice you have made for me.
ABSTRACT

Pelvi-ureteric junction obstruction is an important cause of congenital renal and urinary tract abnormality. It is the commonest cause of antenatally detected hydrenephrosis. The increasing use of antenatal ultrasound as a screening tool for congenital abnormalities in the developing foetus has resulted in a more frequent rate of detection of foetal hydrenephrosis with the likely consequence of significant anxiety among parents. This is because most of these infants with antenatally detected hydrenephrosis will be subjected to frequent radiological and other investigations and there will also be concern about outcome. Knowing what postnatal investigations are necessary for any child with this condition and when to do it becomes a priority. This is because it is known that a significant percentage of children with antero-posterior (AP) diameter of 12mm or less experienced complete and spontaneous resolution of the hydrenephrosis in early life.

This study is a retrospective folder review of one hundred children with PUJ obstruction managed at Red Cross Children’s Hospital over a six-year period from Jan 2002 to Dec 2007. There were 133 kidneys identified with PUJ obstruction. In seventy percent of cases the obstruction resolved spontaneously. In the remaining 30% the obstruction persisted by the first year of life. Only one child in this review was diagnosed postnatally with PUJ obstruction, the rest had their condition identified by antenatal ultrasonography. Nineteen (19) children with persistence and/or worsening hydrenephrosis with decreasing MAG3 relative uptake received surgical treatment; two out of the 19 had repeat pyeloplasty because of worsening hydrenephrosis and decreasing MAG3 differential renal uptake, another two had nephrectomy because of increasing hydrenephrosis and deteriorating of function by repeat MAG3. The commonest surgical procedure was dismembered pyeloplasty.

The left kidney is affected more frequently than the right. PUJ obstruction is commoner in males than in females with a ratio of 4:1. Urinary tract infection was proven in 8.3% of all the cases reviewed and was most likely in those who would require surgical intervention. Klebsiella pneumoniae was the most common organism implicated.
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ABBREVIATIONS

PUJ            Pelviureteric junction
GFR            Glomerular filtration rate
MAG3          Mercapto acetyl triglycine
IVP              Intravenous pyelography
US              Ultrasound
CT            Computerised tomography
MRI            Magnetic resonance imaging
UTI            Urinary tract infection
AP            Antero – posterior
ESRD         End stage renal disease
ESRF         End stage renal failure
ICD 10    International classification of disease 10
Mm              Millimetre
PUV             Posterior urethral valves
VUR             Vesico ureteric reflux
VUJ             Vesico-ureteric junction
SFU             Society of foetal urology
MCDK         Multicystic dysplastic kidney
RBF             Renal blood flow
PGP      Protein gene product
CKD            Chronic kidney disease
VACTERL     Vertebral/vascular, anal, cardiac, tracheo-oesophageal/oesophageal, radial/renal.
β2M            Beta 2 micro globulin
TGFβ            Transforming growth factor beta
PDGF           Platelet derived growth factor
NAG N           acetyl- β- glucosaminidase
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CHAPTER ONE

INTRODUCTION

1.0. General overview of pelvi-ureteric junction (PUJ) obstruction

With the advent of ultrasound and its widespread use for antenatal foetal evaluation, antenatal hydronephrosis is being diagnosed more commonly and a clear strategy for postnatal follow up is required. Pelvi-ureteric junction (PUJ) obstruction is the most common cause of antenatally detected paediatric hydronephrosis.¹ According to Koff,² hydronephrosis is not a pathological process but a compensatory physiological mechanism by which the renal pelvis protects the kidneys from high pressures and renal damage. However, antenatal hydronephrosis is being diagnosed more frequently in a substantial number of pregnancies for which a clear guideline and strategy for postnatal follow up is required.

In the era before the advent of ultrasonography, diagnosis of PUJ obstruction was made most commonly in childhood when symptoms related to this condition manifested.³ The most common presenting symptom was abdominal pain, reported in about 50% of patients, followed by urinary tract infection (UTI) and haematuria in that order. Other symptoms included abdominal masses and gastrointestinal discomfort. In only 25% of patients³ were diagnosis made within the first year of life, the bulk of the diagnosis was made in older children.

As antenatal ultrasound screening becomes more popular and readily accessible to most pregnant women, foetal hydronephrosis due to pelvi-ureteric junction obstruction will be more frequently diagnosed. There is no doubt that such screening program will induce both parental and physician’s anxiety. This will raise questions as to what an optimal and acceptable management should be. A systematic review and meta-analysis of antenatal hydronephrosis demonstrated that spontaneous resolution occurred in most cases when the antenatal pelvic anterior-posterior (AP) diameter in the third trimester was less than 12mm but was less frequent when dilatation was greater than 12mm.⁴ In another prospective study of the natural history
of antenatal hydronephrosis, Ransley et al\textsuperscript{5} reported that, pyeloplasty was necessary in only 25\% of cases detected antenatally. He also noted that normal function in affected kidneys, (that is differential renal function by renogram scan of more than 40\%), did not exclude subsequent need for pyeloplasty as some children that were followed up conservatively, later developed impairment in kidney function.

Choosing an optimal therapeutic option in a child with antenatally diagnosed hydronephrosis secondary to PUJ may therefore be difficult due to the high variability in function, degree of obstruction, extent of renal damage and potential for regeneration of the growing kidneys. Thus, the choice between whether to manage patients conservatively while monitoring them closely for any evidence of deterioration of renal function or to operate early, before any loss of function remains contestable.\textsuperscript{6,7,8,9} Some people have observed that the need for surgery in infants with PUJ obstruction can be successfully predicted by specific patterns of polypeptides in urine.\textsuperscript{10} Again, this also is not completely accepted as it is mainly an experimental tool. The most predictive clinical parameter identified to date is the degree of renal pelvic dilatation, (AP) diameter. Dhillon et al\textsuperscript{11} have shown that with increasing AP diameter there is a progressive risk of decrease in relative renal function or development of symptoms. The risk, they noted is minimal if the AP diameter is less than 20mm but almost 100\% if it is greater than 50mm. However, this relationship is time dependent and the risk of deterioration will increase at lesser degrees of dilatation with increasing time.

Generally, it has been observed that the outcome of hydronephrosis due to PUJ obstruction depends on the severity of disease, which is characterised by bilateral ureteral involvement, severity of obstruction, duration of disease before intervention and other co-morbidities.\textsuperscript{12} The goal of evaluation and management therefore is to identify all infants with significant renal or urinary tract abnormalities, preserve renal function as much as possible and relieve obstruction. Importantly also, there has been increasing calls to reduce or limit unnecessary investigations and minimise parental distress in infants with clinically insignificant impairment of function or those who may eventually have normal kidneys and urinary tracts.\textsuperscript{5,13,14} The issue of cost of multiple investigations also becomes important; highlighting the need for appropriate
investigations which give the best advantage to the patient yet observing best practice guidelines especially in resource poor health facilities in developing countries.

The issue of complications deserves mentioning. This could arise from the disease process or as a result of treatment. Severe PUJ obstruction with associated massive hydronephrosis, severe or recurrent bacterial infection of the urinary tract, delayed surgical treatment and complications that may accompany surgical correction may further compromise residual renal function.

Furthermore, any contribution to current information on PUJ obstruction from a developing country will be invaluable, as it will highlight challenges and constraints faced in this setting. It would also provide some guidelines for physicians practising in developing countries on how to manage a child with PUJ obstruction, stimulate awareness among clinicians and contribute to the body of knowledge on this condition, as most PUJ obstruction literature currently comes from the developed countries.

1.1 Relevance of the study to the practice of paediatric nephrology

The contribution to overall incidence of chronic kidney disease (CKD) by congenital renal tract abnormalities is being recognised as a significant factor. In developed countries where accurate statistics are available, it is estimated that renal tract malformations are the most common cause of chronic kidney disease in children which also contribute significantly to end stage renal failure (ESRF) in the paediatric population.\textsuperscript{15} The true picture of CKD and ESRF in Africa and most developing countries is largely unknown for obvious reasons, however, congenital abnormalities are one of the common causes of CKD in South Africa.\textsuperscript{16}

When detected early the morbidity associated with some of the congenital urinary tract abnormalities can be decreased significantly by a structured management approach. Such may include regular follow up, urine analysis and microscopy for detection of UTI, ultrasound evaluation and blood pressure monitoring. On the other hand, where the kidney function has been severely compromised due to longstanding
obstruction, conscientious long-term follow up may retard further deterioration of renal function.

In the severe form of the disease, delay or failure to identify early and treat can have dire consequences on the immature kidney and the affected child in general, both in early and later life. Such complications include the development of CKD and progression to end stage renal disease with the attending problems. Most information on PUJ obstruction in the literature is from the developed countries where comprehensive management programs have been put in place for this condition. However, in Africa and other developing countries, there are very few reports on this condition. Scarce resources of both materials and specialised personnel remain challenging facts. Therefore knowledge of the incidence, modes of presentation, natural history of disease, management and long term outcome is important to develop an approach that is suitable for our setting.

Red Cross Children’s Hospital is the leading children’s hospital in Africa. The department of paediatric nephrology has a well-outlined program for the management of children diagnosed with PUJ obstruction. This study is therefore an audit of patients managed in the renal unit over the past six years to assess the applicability and relevance of the current management protocol and possibly suggest new ways and approach to managing children presenting with this condition in the future.

1.2 Research questions

All but one patient diagnosed and managed for PUJ obstruction in this study were referred to Red Cross from maternity units of Groote Schuur and Mowbray Maternity hospitals. These hospitals are also affiliated to the University of Cape Town. The only child whose diagnosis was confirmed following investigations for UTI was referred from another hospital.
This study aims to address the following questions:

i. How many children were diagnosed with PUJ obstruction within the period?
ii. What other modes of presentation exist apart from antenatal ultrasound detection of hydronephrosis?
iii. What is the distribution of the disease (bilateral, left and right sided involvement)?
iv. What is the gender variation?
v. Was there complete resolution, persisting or deteriorating PUJ obstruction?
vi. What is the incidence of UTI in this population?
vii. Were there other co-morbidity/ies?
viii. What percentage of children needed surgical correction?
ix. What is the degree of improvement in function following surgery, using MAG3 renogram?
x. Was there any correlation between surgery and later serum creatinine (at 12 months)?

1.3. Study objectives
The study objectives include the following:
i. Describe patient characteristics
ii. Describe the pattern of PUJ in the study group with regard to severity of disease
iii. Audit the course of disease over a twelve-month follow up period, describing disease progression (spontaneous resolution, unchanged and progressive deterioration)
iv. Identify how many children did not have preceding antenatal ultrasound
v. Audit the age at which surgical intervention is offered
vi. Identify presence and frequencies of UTI
vii. Describe other co morbidities
vii. Determine outcome with regards to serum creatinine and post surgery MAG3.
1.4. Outline of the dissertation

The presentation of this study will be in accordance with the Faculty guideline and will comprise of six chapters. Chapter 1 gives a general but brief introduction of the subject matter, PUJ obstruction. It also highlights the relevance of this study to the paediatric nephrologist practising in a developing country and finally a brief description of the study objectives. Chapter 2 is a literature review on PUJ obstruction from relevant journal articles and texts of paediatric nephrology. Chapter 3 describes the study methodology. Chapter 4 presents the study findings under results while chapter 5 discusses these findings and relates them to those presented in literature. Chapter 6 is the conclusion drawn from the study and also include recommendations and limitations of the study. It contains as well, all the references and appendixes to materials presented in the study. The Vancouver referencing method will be used for all the references in this study.
CHAPTER TWO

LITERATURE REVIEW

2.0 EPIDEMIOLOGY

Pelvi-ureteric junction (PUJ) obstruction is the commonest cause of antenatal hydronephrosis.\textsuperscript{1} The incidence of foetal hydronephrosis caused by PUJ obstruction in routine antenatal ultrasound screening ranges from 1:500 to 1:1500 live births.\textsuperscript{1,17,18} Among 3,856 foetuses who had ultrasound assessment in the last trimester in New Zealand, hydronephrosis was seen in 298 or 7.7%. Among this population of children with antenatal hydronephrosis, only 0.4% had persistence of hydronephrosis attributable to PUJ obstruction\textsuperscript{19} suggesting that antenatal hydronephrosis might generally be described as a transient phenomenon.

Pelvi-ureteric junction obstruction generally occurs as a sporadic anomaly, though familial inheritance has been reported with a pattern suggesting autosomal dominant inheritance with incomplete penetrance.\textsuperscript{19} The incidence is increased in the presence of other urinary tract anomalies such as multicystic dysplastic kidney disease (MCDK) and the VACTERL spectrum.\textsuperscript{20} Boys are affected more frequently than girls with the male to female ratio of 2:1 while the lesion occurs more commonly on the left than on the right side and in 10 to 40\% of cases are bilateral.\textsuperscript{21}

The natural history of PUJ obstruction varies considerably. Whereas in some kidneys, the obstruction resolves spontaneously, in others it becomes increasingly severe giving rise to progressive functional deterioration. A meta-analysis of 25 articles showed improvement in 98\% of patients, with grades 1-2 hydronephrosis strongly suggesting that mild degree of hydronephrosis is a relatively benign, self-limiting condition with resolution or improvement across all studies. In a substantial proportion however, the obstruction remains stable with no impact on renal function over many years.\textsuperscript{22}
In a series of children who were initially managed conservatively at Great Ormond Street Hospital, 17% came to pyeloplasty because of deteriorating function, 27% showed evidence of resolving obstruction while 56% remained stable with persisting obstruction but no functional deterioration.\textsuperscript{11} It was further shown that progressive obstruction and dilatation can occur in a previously normal or mildly dilated kidney. It is therefore not definitely possible to make a precise prediction of the outcome in any individual.

2.1. EMBRYOGENESIS AND PATHOGENESIS

The embryogenesis of PUJ occurs during the fifth week of gestation and the initial solid cord like ureteric bud, an outgrowth of the mesonephric or Wolffian duct becomes canalised about the sixth week of gestation. Beginning from the midsection canalisation proceed to the PUJ and the vesico-ureteric junction (VUJ) with the PUJ being the last to canalise.\textsuperscript{23,24,25} Inadequate canalisation of this area is thought to be the main embryological explanation for PUJ obstruction. Failure of canalisation on the other hand is attributable to a host of intrinsic abnormalities which include the following: improper innervation with diminished synaptic vesicles, low protein gene product (PGP) and S-100 protein (a nerve supporting cell marker), aberrant pyeloureteric smooth muscles which typically exhibits hypertrophy and perifascicular fibrosis and synaptophysin, (a synapse vesical marker), these are all found to be decreased in the resected specimens of PUJ.\textsuperscript{25,26,27,28,29,30}

The importance of inadequate innervation as a cause of PUJ obstruction was highlighted in the study by Harish et al.\textsuperscript{31} Their study showed that the length of the visibly constricted segment ranged between 2-15mm (mean 5.37mm) while the abnormally innervated segment was much longer than the mean in 24 of the 30 cases; it was the same length with the abnormally innervated portion in 5 PUJ specimens analysed. They concluded that the maximum difference in length between the visible constriction and the lower limit of defective innervation was 8mm, a finding that has significant implication when considering surgical resection of the stenotic segment as a therapeutic option.
PUJ obstruction can also be caused by extrinsic compression secondary to bands, kinks and aberrant renal vessels. In about 40% of cases, an aberrant accessory lower pole segment vessel is found and observed to compress the ureter causing mechanical obstruction. The anterior surface of the renal pelvis is associated with a lower pole vessel in 65% of cases while the posterior surface is in contact with a vessel in 6% of the kidneys examined. A characteristic feature of such extrinsic obstruction is that it presents late in childhood with intermittent abdominal or flank pain. Furthermore, it is important to note that not all antenatally recognisable hydronephrosis is due to PUJ obstruction. Other causes include vesico-ureteric junction obstruction, congenital megaureter, ureterocoele, ectopic ureter and most importantly physiologic hydronephrosis. The latter is based on the concept of pressure and volume dependent flow, thus at low urinary flow rates, no obstruction exists; however, as the flow rate increases, the urinary bolus is not completely conducted, causing the renal pelvis to distend. This mechanism of hydronephrosis is the pressure dependent flow pattern. On the other hand, when extrinsic compression exists which might be transient and mild, urine flow is only impeded after a definite volume of urine is collected in the renal pelvis causing dilatation and results in the concept of volume dependent flow hydronephrosis. The significance of these two mechanisms is that they are transient and disappear on postpartum ultrasound.

2.2. PATHOPHYSIOLOGY
The drainage of urine from the pelvis to the ureter is determined by factors such as urine volume and flow, degree of PUJ obstruction, functional capacity of glomerulus and collecting system and the compliance of renal pelvis all of which define the pelvic pressure. At first, the renal pelvis dilates in response to increased pelvic pressure, with ureteral muscles showing evidence of hypertrophy. Experimental animal models of complete ureteral obstruction demonstrates changes that suggest that the upward transmission of ureteral pressure affects tubular pressure, tubular function, renal blood flow (RBF) and glomerular filtration rate (GFR). Significant and prolonged obstruction invariably results in tubular dilatation, glomerulosclerosis, inflammation and fibrosis.
2.3. EFFECTS OF OBSTRUCTION ON RENAL DEVELOPMENT

The developing kidney is highly susceptible to injury from impaired urine flow as a result of obstruction. \(^{39}\) Temporary complete unilateral ureteral obstruction in experimental animal models demonstrated evidence of reduction in growth of the obstructed kidney which is directly related to the duration and severity of obstruction. \(^{40,41}\) The clinical implication of this finding is that even temporary but severe obstruction is capable of causing permanent impairment in growth potential of the affected kidney. Furthermore, since renal growth is a major determinant of long-term renal function, bilateral, severe obstruction or unilateral obstruction even acutely may be a significant risk factor for chronic kidney disease.

Chronic unilateral ureteric obstruction also causes delays in maturation of all components of the nephron (glomerulus to collecting duct), the microvasculature and renal interstitium. \(^{41}\) Obstruction in the developing kidney causes major haemodynamic changes with profound renal vasoconstriction mediated by the renin-angiotensin system. \(^{42,43,44,45}\) The activation of the renin-angiotensin system is a major factor for observed kidney damage in partial or unilateral ureteric obstruction. Such obstruction can mimic renal artery stenosis and because of its intense vasoconstrictor action, the resulting angiotensin II leads to decreased glomerular filtration rate. Angiotensin II also profoundly affects the expression of growth factors in the developing kidney that ultimately are responsible for changes in the renal histology. One important example of such a growth factor which is up regulated significantly is transforming growth factor β1 (TGF-β1), \(^{44,46}\) and the degree of up regulation correlates directly with fibrosis and collagen deposition in obstructed kidneys.

2.4. CONSEQUENCE ON TUBULOINTERSTITIAL TISSUE

The hallmark of chronic severe obstructive uropathy are the development of tubular atrophy and interstitial fibrosis, both changes contributing significantly to impairment in renal growth. Tubular atrophy results from progressive destruction of tubular epithelial cells by apoptosis or programmed cell death. \(^{47,48}\) Chronic unilateral ureteral
obstruction in experimental animal models showed that stimuli for tubular apoptosis include mechanical stretch of epithelial cells in dilated tubules and altered gene expression.\textsuperscript{36,48,49,50} This finding may also be the reason for tubular atrophy in children with prolonged ureteral obstruction due to PUJ obstruction, manifesting in loss of urine concentrating ability and polyuria in some patients.

Renal interstitial changes are also a prominent feature in chronic unilateral ureteric obstruction. This is characterised by infiltration of macrophages and fibroblasts, which release cytokines such as TGF-$\beta_1$. Activated macrophages and their products can also induce both tubular apoptosis and progressive interstitial fibrosis.\textsuperscript{51} These interacting processes are dynamic and once activated by the persistence of significant urinary tract obstruction may progress unhindered if obstruction is not relieved or even after surgical correction. Once the process has progressed to tubular atrophy and extensive interstitial fibrosis, the impairment of renal growth becomes irreversible.

2.5. NEPHRON LOSS AND TUBULAR FUNCTION

It has been observed that temporary but complete unilateral ureteral obstruction during nephrogenesis or during nephron maturation in infancy can permanently reduce the number of nephrons in the obstructed kidney.\textsuperscript{52} Loss of renal mass as a result of this process leads to compensatory growth of the contralateral kidney and can occur even after short periods of ureteral obstruction.\textsuperscript{49,52} Contralateral renal growth has been used as an indirect indicator of ipsilateral obstructive injury in newborn.\textsuperscript{52}

One of the consequences of tubular atrophy as highlighted earlier, is the impairment of tubular function with significant clinical implication. In such kidney, there is down regulation of tubular sodium transporters and aquaporins and distortion of medullary architecture, leading to limited renal concentrating capacity.\textsuperscript{53,54} These factors contribute to the phenomenon of post obstructive diuresis that often follows the relief of severe obstruction especially in bilateral urinary tract obstruction. The other factors responsible for this phenomenon include immaturity of affected kidney and retention of osmotic compounds prior to relief of obstruction. The clinical implications of this
are reduced renal sodium handling resulting in negative sodium balance, abnormal
distal tubular potassium and hydrogen secretion due to type IV renal tubular acidosis.
These changes can impact negatively on growth of affected children.\textsuperscript{55} Tapia and
Gonzalez noted that 72\% of the children with unilateral PUJ obstruction had heights
that were below the 50\textsuperscript{th} percentile for height preoperatively in those younger than
one year.\textsuperscript{8} The distribution of heights in the group that had pyeloplasty normalised
with significant increase in overall percentile rank for height in all ages. They
concluded that unilateral PUJ obstruction systemically affects body growth and that
the effect of pyeloplasty goes beyond the direct relief to the affected kidney and also
noting that the benefits of surgical correction may be of greater impact when
performed in infancy.

It is therefore clear, considering these facts that pelvi-ureteric junction obstruction
does not merely cause urinary outflow restriction with accompanying renal
parenchymal damage that is simply and completely amenable to surgical correction
alone. There are fundamental cellular, molecular, histological and functional changes
associated with PUJ obstruction as well, which may not completely resolve with
surgical relief but persist even if such obstruction is temporary, partial or complete in
the foetal ureter. It is likely that multiple genes and a host of other environmental
factors may be involved. Appropriate surveillance measures are therefore necessary
in order to identify risk factors for the development of such abnormalities. Where
possible, preventive measures should be initiated and where indicated, prompt
surgical correction is indispensable.

2.6. CLINICAL FEATURES
The mode of presentation of pelvi-ureteric junction obstruction varies depending on
the age of the child and the severity of obstruction. These features could be identified
during the antenatal period, immediate postnatal and in later childhood. In the
developed countries where antenatal ultrasound screening is done routinely, most
cases of PUJ obstruction would have been diagnosed during the postnatal evaluation
of antenatal hydronephrosis. In the absence of routine antenatal screening as is the case in many developing countries the diagnosis may be delayed until a complication develops.

2.6.1 Features of antenatal PUJ obstruction
During the foetal life, the presence of hydronephrosis may be the earliest features of PUJ obstruction and can be detected readily on antenatal ultrasound examination as early as the 12th to 14th week of gestation. Severe bilateral obstruction may result in maternal oligohydramnios due to inadequate urine output with the possibility of such child presenting with respiratory difficulty at birth due to pulmonary hypoplasia.

2.6.2 Features in infants and older children
A child with a markedly dilated renal pelvis in-utero that has severely compromised lung development resulting in lung hypoplasia may present with respiratory distress in the immediate postnatal period. In the absence of antenatal ultrasound acute respiratory distress may be first clue to the underlying kidney disease. Older children may present with a palpable abdominal mass caused by the enlarged kidney due to the obstruction. Other presentations may include flank or abdominal pain that may worsen during brisk diuresis as may follow excessive ingestion of fluid. These symptoms may be accompanied by nausea and vomiting, leading to an evaluation of the gastrointestinal tract. Children may also present incidentally with renal injury after experiencing minor trauma, haematuria or hypertension. In children with significant disease and associated impairment of renal function, they may present with features of renal failure, malnutrition and stunting.

Isolated pre auricular tags and pits detected in the newborn may indicate an increased risk of urinary tract anomalies. In one study, urinary tract abnormalities were identified by ultrasound examination in 6 out of 70 consecutive newborns with pre auricular tags. PUJ obstruction may also be associated with other genitourinary anomalies such as horse shoe kidney and MCDK.
There is a slight increase in prevalence of PUJ obstruction in children with Down syndrome compared to general population.\textsuperscript{63, 64, 65} It may be an incidental finding in a child for instance, who is being investigated for other urinary abnormality like urinary tract infection.

Generally however, widespread use of antenatal ultrasonography in many health institutions has contributed immensely to the detection of foetal hydronephrosis and postnatal pick up rate of PUJ obstruction. Importantly not all antenatal foetal hydronephrosis is due to PUJ obstruction. In settings where antenatal ultrasound service is poor, children with PUJ obstruction may present later in life.

\textbf{2.7.0. DIAGNOSIS}

This involves a combination of investigations carried out on the child with antenatal ultrasound hydronephrosis suggestive of PUJ obstruction and includes the following.

\textbf{2.7.1. Antenatal Ultrasound.}

During foetal life, the presence of hydronephrosis can be detected readily on antenatal ultrasound examination as early as the 12\textsuperscript{th} to 14\textsuperscript{th} week of gestation.\textsuperscript{55,56} As mentioned earlier, even though PUJ obstruction is the commonest causes of antenatal hydronephrosis, other causes should also be considered as well. The Society of Foetal Urology (SFU) has developed useful criteria for the diagnosis and grading of antenatal hydronephrosis based on the degree of pelvic dilatation, number of calyces affected and the presence and severity of parenchymal atrophy. There are four grades as presented below: \textsuperscript{66}

- Grade 0 -- Normal examination with no dilatation of renal pelvis
- Grade I -- Mild dilatation of the renal pelvis only
- Grade II-- Moderate dilatation of the renal pelvis including a few calyces
- Grade III -- Dilatation of the renal pelvis with visualisation of all the calyces, which are uniformly dilated, and normal renal parenchyma
Grade IV – Similar appearance of the renal pelvis and calyces as Grade III plus thinning of the renal parenchyma. These are shown in the figure 2:1 below.

**Society of Fetal Urology grading system for hydronephrosis**

Fig 2.1: Ultrasound pictures of the various grades of hydronephrosis. (Source: Ref 66)

Grade 0: no dilation (not shown). Grade 1: renal pelvis is only visualized. Grade 2: renal pelvis as well as a few, but not all, calyces is visualized. Grade 3: virtually all calyces are visualized. Grade 4: similar to Grade 3 but, when compared to the normal contralateral kidney, there is parenchymal thinning.

Using this guideline, foetus with abnormal AP diameter can be identified and assessed subsequently in the early postnatal period for confirmation of PUJ obstruction.

### 2.7.2. Post natal Ultrasound.

Postnatal ultrasound assessment of children identified antenatally with hydronephrosis and presumptive diagnosis of PUJ obstruction is the starting point in diagnostic evaluation. It is recommended that ultrasonographic evaluation take place on the second or third day postpartum or this may be done at a later stage. Before this date, ultrasound scan may give a false negative result because of neonatal dehydration and physiologic oliguria. In neonates with bilateral and severe hydronephrosis however, earlier ultrasound evaluation is necessary. The importance
of such earlier review is to rule out the possibility of lower tract obstruction such as posterior urethral valves. Such evaluation should focus on the kidney, assessing for cortical thinning and perinephric collection, calyceal and pelvic dilatation and evidence of bladder abnormalities.

In one study, looking at neonates with unilateral hydronephrosis presumed to be due to PUJ obstruction, approximately 20% of such hydronephrosis disappeared on postnatal ultrasonography.\textsuperscript{3} In another review, postnatal ultrasonography assessment showed that 11% was due to PUJ obstruction, 48% was transient, 15% was due to physiologic cause and the rest were due to other causes.\textsuperscript{67} The clinical relevance of these findings emphasise the need for detailed and serial postnatal re-evaluation of all children with antenatal hydronephrosis in order to identify those with clinically significant PUJ obstruction. This will help to identify children who may need further evaluation from those who do not and to initiate treatment while discontinuing further investigations in those with normal kidney and urinary tract.

2.7.3. Micturating Cysto Urethrogram (MCUG).

In boys, a micturating cysto urethrogram (MCUG) is performed especially in severe or bilateral PUJ obstruction, to exclude posterior urethral valves (PUV), and vesico ureteric reflux (VUR) in both sexes. This procedure is done in males less than three years of age, or who are not yet potty trained by inserting a urinary catheter into the bladder and then instilling contrast material. Indirect MAG3 is however recommended in older males and females as this approach is less traumatic. Fluoroscopic monitoring is performed while the bladder is filling and during micturition.\textsuperscript{67}

2.7.4. Diuretic Renogram.

Diuretic renography is usually performed to assess total and relative kidney function and also to ascertain the degree of obstruction where ultrasonography strongly suggests presence of PUJ obstruction.\textsuperscript{68} It measures the drainage time from the renal pelvis and assesses total and relative kidney function. This procedure also requires
the insertion of urinary catheter into the bladder to relieve any pressure that can be transmitted to the ureters and kidneys. Intravenous access for hydration and administration of the radioisotope and diuretic is needed. The preferred radioisotope is technetium-99-mercaptoacetyltriglycine (MAG3). This compound is taken up by the renal cortex, filtered across the glomerular basement membrane to the renal tubules and excreted into the renal pelvis and urinary tract. The study consists of two phases: the initial and the second phase.

In the initial phase, radioisotope is injected intravenously and renal parenchymal cortical uptake is measured during the first two to three minutes. The relative contribution of each kidney to overall renal function also known as split or differential renal function is assessed quantitatively. The differential renal function is considered significantly affected when it is less than 40%, indicating impaired function. It has been shown that initial renal function by diuretic renogram on the obstructed side of less than 35% has a 100% sensitivity and positive predictive value for a poorly preserved renal outcome and a more significant alteration in renal histology.

In the second phase at peak renal uptake, intravenous furosemide is administered and the excretion of isotope from the kidney is measured. This is referred to as the ‘washout curve’ and it demonstrates the extent of obstruction if present. In the normal kidney, the administration of furosemide results in a prompt washout. In a dilated system, if washout occurs rapidly (less than 15 minutes) after diuretic administration, then it is not obstructed. If the washout is however, delayed beyond 20 minutes, the pattern is consistent with obstruction. This interpretation must be accepted with caution so as not to pursue surgical relief immediately as one study showed that, 24 of 39 children whose diuretic renography indicated unilateral ureteric obstruction had normal renal function after a prolonged follow up.

2.7.5. Intravenous Pyelogram (IVP)

In the past an intravenous pyelography (IVP) was the standard investigation to confirm PUJ obstruction. It has been replaced by radioisotope imaging due to the
adverse effects associated with its use, including large dose of ionizing radiation, nephrotoxicity associated with the contrast media and increased incidence of anaphylactic reaction.\textsuperscript{74}

\subsection*{2.7.6. Computerised Tomography and Magnetic Resonance Imaging (CT/MRI).}
Computed tomography scan (CT) and magnetic resonance imaging (MRI) are useful diagnostic tools providing excellent images, but are much more expensive and not used routinely.\textsuperscript{3}

\subsection*{2.7.7. Newer Biochemical Tests.}
There are other novel laboratory tests that may detect the presence of clinically significant PUJ obstruction, although their use currently is experimental. These include urinary levels of beta 2- microglubulin (β2M), N- acetyl- β- glucosaminadase (NAG), Epidural growth factor (EGF), platelet-derived growth factor (PDGF) and transforming growth factor β (TGFβ).\textsuperscript{75,76,77} These compounds are expressed in the urine when there is evidence of tubular injury as in obstructive state. In an experimental model, the urinary concentration of NAG in rats with partial ureteral obstruction increases in the first two weeks of obstruction and decreases with the relief of obstruction. Similarly, in a clinical study, NAG level in urine at the time of pyeloplasty was seven times higher than those in the bladder urine from normal control patients. The enzyme levels in the bladder of patients however, suggested normalisation of NAG excretion six weeks after surgery.\textsuperscript{76,77} These laboratory tools might be useful in both diagnosis and subsequent follow up of children after pyeloplasty to monitor their urinary levels as guide to complete relief of ureteric obstruction. The advantages of this approach are that it is non-invasive as it involves only a urinary specimen for analysis.

\section*{2.8. MANAGEMENT}
The goals of treatment in patients with PUJ obstruction are the preservation of renal function and the prevention of symptoms. Relief of the obstruction usually, by surgical means restores normal urine passage through the junction into the upper ureter.78, 79, 80

The postnatal management of the infant with PUJ obstruction may include regular follow up with serial renal ultrasound examinations in those with mild hydronephrosis, as many of these patients will experience progressive spontaneous resolution of their obstruction.80 In a meta analysis involving 1678 infants with antenatal hydronephrosis suggestive of PUJ obstruction, it was shown that the likelihood of significant kidney and urinary tract disease increases with the severity of hydronephrosis.81 In this study, only 12% of infants with mild hydronephrosis, (AP diameter of 9mm or less) demonstrated impairment of renal function as compared to 45% with moderate hydronephrosis (AP diameter of 9 to 15mm) and 88% with severe hydronephrosis (AP diameter greater than 15mm) respectively in the third trimester.

There is however considerable controversy with regards to the acceptable treatment modality namely, early surgical correction as compared with long term conservative observation in infants with moderate to severe obstruction. Houben et al82 noted in their study that pyeloplasty in infants was a low risk procedure and supported early surgical correction of PUJ obstruction. In another study, individual renal function improved significantly in children younger than one year with preoperative differential function less than 45% but not in older children.8 Vaughan and Gillenwater83 in an animal study noted that the duration of obstruction is very important in predicting recovery of renal function, with only partial recovery to be expected when the obstruction is present for more than two weeks. Furthermore, Mayor et al84 demonstrated there was an advantage in early correction, noting that if obstruction was relieved between one and two years of age, renal function improved much less than in children operated on at a younger age. He thus concluded that continued deterioration of renal function was expected when surgery was delayed. Chiou et al71 also showed that tubular function correlated with post pyeloplasty renogram. Increased fractional excretion of sodium chloride and initial diuretic
renogram of 35% or less was predictive of poor renal outcome even after surgical correction of obstruction. In contrast, Ransley et al\textsuperscript{5} proposed that there is no indication for immediate pyeloplasty in infants with prenatally diagnosed hydronephrosis especially in those who demonstrate good function postnatally. They did not however state whether this observation was true for all categories or degrees of hydronephrosis due to PUJ obstruction since severe obstruction (grades 3 and 4) is known to be associated with poor renal outcome even after pyeloplasty. In a retrospective review comparing renal histology at pyeloplasty with pre operative diuretic renogram, Elder et al\textsuperscript{85} showed that there was a 25% disparity between pre-operative renal function and renal biopsy finding even among patients whose differential renogram was 40% or less. This finding demonstrates that a normal renogram in children with PUJ obstruction does not exclude significant underlying abnormal renal histology. This may also explain why complete recovery of renal function can not be predicted solely based on the pre operative renogram.

From the foregoing discussion, early surgical correction of PUJ obstruction in infants who have renal function of 40% or less on MAG3 renogram is preferable to delay of surgery. Unfortunately however, abnormal renal histology cannot be predicted merely by pre-operative renogram. The existence of such histology may explain why progressive functional deterioration is observed in some children.

2.8.1. MEDICAL AND CONSERVATIVE MANAGEMENT

There is an increased incidence of urinary tract infections in children with PUJ obstruction than in the general paediatric population.\textsuperscript{86, 87} Use of prophylactic antibiotics may be considered. Alternatively, vigilance and early treatment of urinary tract infections is warranted. For children who have unilateral, mild to moderate hydronephrosis secondary to PUJ obstruction and those infants with significant hydronephrosis or increasing AP pelvic diameter, well structured regular ultrasound surveillance, accompanied by interval diuretic renogram is advisable. This is necessary because between 15% to 33% in this category show progressive ipsilateral deterioration in renal function, ultimately needing pyeloplasty.\textsuperscript{5,88}
Even though UTI is much commoner in children with this condition, the use of antimicrobial prophylaxis remains debatable in view of the risk of development of resistant organisms and whether it is beneficial in reducing the risk of renal damage.

2.8.2. SURGICAL MANAGEMENT

Foley\(^89\) in 1936 described the result of twenty pyeloplasties using a ‘YV’ approach that was accepted as the operative modality for a long time. However, Anderson and Hynes published their experience with an operation that included complete transection of the upper ureter, subsequent spatulation of the ureter and trimming of the redundant pelvis.\(^90\) This highly successful technique has become the criterion for standard surgical repair used today, has a high success rate with few complications in most cases and resolution of the obstruction in 90 to 95% of cases, including neonates.\(^91\)

Laparoscopic dismembered pyeloplasty is also reported to yield results that are comparable with those of open pyeloplasty with success rate as high as 96-98% with the benefits of endoscopic approach which include less postoperative pain, short hospitalization and reduced postoperative recovery time. This approach however, requires technical skills, involves lengthy operation time and it is costly.\(^2\) Ultrasound examination is repeated approximately four to six weeks postoperatively. This is useful to assess the degree of resolution following surgery by measuring AP diameter of the pelvis. Further evaluation includes post-pyeloplasty MAG3 to assess renal function and establish whether hydronephrosis has subsided.

Temporary drainage surgical procedures such as nephrostomy or ureterostomy may be carried out occasionally in neonates with severe hydronephrosis to allow urine drainage and decompress the affected kidney.

Complications following surgery may manifest in the form of bleeding, urine leak, delayed opening of the anastomosis and failure of resolution or worsening of hydronephrosis with the possibility of needing repeat pyeloplasty.\(^92, 93\)
The benefits of early pyeloplasty in children with very strong indications for surgery have been highlighted. These include improvement in somatic growth and renal function when surgery is done in the first year of life. It is therefore important to identify without delay children who satisfy the criteria for early pyeloplasty and offering such therapy to prevent or reduce the risk of permanent renal function impairment or chronic kidney disease.
CHAPTER THREE

METHODOLOGY

3.0. STUDY DESIGN
This is a retrospective folder review of a cohort of children diagnosed with hydronephrosis secondary to PUJ obstruction managed at the Red Cross Children’s Hospital. They included children referred postnatally from Groote Schuur and Mowbray Maternity Hospitals with antenatally detected hydronephrosis and those identified following evaluation for other kidney diseases as UTI at Red Cross Childrens’ Hospital. The review covered a six-year period between January 2002 and December 2007.

3.1. Inclusion criterion
All neonates with postnatal AP diameter of the renal pelvis 5mm or greater, captured by the Hospital database within the study period were included in the study.

3.2. Exclusion criteria
- Children with other renal conditions (PUV, MCDK, Single kidney, Duplex systems and VUR).
- Those with PUJ obstruction diagnosed prior to January 2002 but managed within the study period.

3.3. Identification of study population
PUJ obstruction is deemed present in any child if the postnatal ultrasound measurement of the antero-posterior diameter of the pelvis is 5mm or more. In this study, mild hydronephrosis is AP pelvis diameter of 5-10mm; 10-15mm is moderate while AP pelvis diameter of greater than 15mm is severe.

The postnatal ultrasound examination was done in these infants after the first forty-eight hours of birth. Neonates with bilateral hydronephrosis however had repeat
ultrasound evaluation on the first day of life followed by a micturating urethrocystogram (MCUG) in males within a few days to rule out posterior urethral valves. The first MAG3 nuclear study was routinely done six weeks postnatally in those with significant hydronephrosis or increasing AP pelvic diameter though in some children, delay occurred due to logistic problems.

3.4. STUDY AREA
Red Cross Children’s Hospital is a highly specialised children’s teaching hospital arm of the University of Cape Town, situated in Cape Town. The hospital caters for children with specialised medical need from the entire Western Cape, Northern Cape, and a significant proportion of children from Eastern Cape. Referrals are also received from other provinces in South Africa and few from neighbouring southern African countries.
The hospital has two hundred and ninety bed spaces. The renal unit is a highly organised subspecialty, offering state-of-the-art renal services to children with diverse renal conditions who are referred for specialised care.
3.4. ETHICAL CLEARANCE

The Research Ethic Committee of the Faculty of Medical Sciences, University of Cape Town gave approval (REC REF: 060/2009) for the study, appendix (ii). Approval to retrieve hospital files was granted by the CEO of Red Cross Childrens’ Hospital. Proof of approval included in the appendix.(iii)

3.5. DATA COLLECTION

The folder numbers of the children were first identified using the ICD 10 coding and all the folders that conformed to the diagnosis of PUJ obstruction were consecutively retrieved from the record department. Information collated from these folders is as outlined in the data collecting proforma, appendix (i). Confidentiality was strictly
maintained by recording only the hospital numbers of the patients. Data collected from each study subject was handled by the researcher only. This includes entry into computer and statistical analysis.

3.6. DATA PROCESSING AND ANALYSIS

Data obtained was entered into statistical software, Epi Info 2007 (version 3.4.3) and analysed using simple statistics. Results are presented in tables and graphs where necessary.

Mean, median, standard deviation and other parameters of central tendency or dispersion will be generated as necessary and P value of less than 0.05 at 95 percent confidence interval will be considered significant.
CHAPTER FOUR

RESULTS

4.0. CHARACTERISTICS OF THE PATIENTS

One hundred and thirty one (131) patients with an ICD 10 coding for PUJ obstruction were identified. Of these, 100 folders were eventually analysed. Of the 31 folders not included, twelve had their diagnosis made prior to 2002, 11 of the folders could not be traced and 8 had other kidney conditions that excluded them from the study.

4.1. Sex and postnatal age at first ultrasound

There were 80 males and 20 females, giving the male: female ratio of 4:1. The mean age at first postnatal ultrasound was $2.96 \pm 3.8$ weeks (range, 1 day to 26 weeks). Eighty four percent of the study population had their postnatal ultrasound within the first week of life.

4.2. Distribution of PUJ obstruction

The left kidney is affected in forty percent (40%), bilateral involvement in 32% and the right kidney affected in 28%. This pattern is represented in the figure below.
Fig 4.1: Distribution of PUJ obstruction.
4.3. The course of disease

There were 132 kidneys (left side 40, right side 28 and bilateral 32) identified with significant hydronephrosis on antenatal ultrasound. During the postnatal ultrasound scan, one additional PUJ obstruction was identified giving to a total of 133 renal units. By the sixth month of follow up, only 86 kidney units still had significant evidence of obstruction. This gives a 35.3% rate of spontaneous resolution of obstruction within that period. In the next 6 months of follow up, a further 65.1% of the remaining kidneys had experienced further resolution of obstruction. This pattern of regression of disease is presented in fig iv.

Fig 4.2: The pattern of regression of PUJ obstruction.
4.4. Mean AP diameter of the pelvis in relation to age categories

The mean AP diameter in relation to antenatal and postnatal ultrasound measurement and the sixth and twelfth month follow up measurements are represented in the table 4.1.

<table>
<thead>
<tr>
<th>Age category</th>
<th>Number of dilated pelvises</th>
<th>Mean AP diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antenatal</td>
<td>132</td>
<td>13.17 ± 11.2</td>
</tr>
<tr>
<td>Postnatal</td>
<td>133</td>
<td>10.9 ± 7.1</td>
</tr>
<tr>
<td>6 months</td>
<td>86</td>
<td>10.57 ± 7.6</td>
</tr>
<tr>
<td>12 months</td>
<td>30</td>
<td>12.53 ± 9.7</td>
</tr>
</tbody>
</table>

Table 4.1: Number of dilated pelvises at various age categories and mean AP diameter.
4.5. Distribution of grades of hydronephrosis at three age groups

Majority of the patients identified with hydronephrosis in the antenatal period (81.1%) had mild to moderate grades. There was evidence of progressive decrease in AP pelvis diameter on subsequent follow up in most of the children as shown in table 4.2.

<table>
<thead>
<tr>
<th>Age at ultrasound</th>
<th>Grading of AP pelvis</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antenatal</td>
<td>Mild</td>
<td>59 (44.7)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>48 (36.4)</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>25 (18.9)</td>
</tr>
<tr>
<td>At 6mths</td>
<td>Mild</td>
<td>49 (57%)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>19 (22.1)</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>18 (20.9)</td>
</tr>
<tr>
<td>At 12 mths</td>
<td>Mild</td>
<td>17 (56.7)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>7 (23.3)</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>6 (20)</td>
</tr>
</tbody>
</table>

Table 4.2: Kidney units and grades of AP diameter at three age categories
4.6. Number of children that had other radiologic investigations

MAG3 was the commonest radiologic investigations carried out on the children with PUJ obstruction in this study as shown in the figure below.

![RADIOLOGIC INVESTIGATIONS](image)

Figure 4.3. Number of children that had other radiologic investigations
4.7. Preceding antenatal ultrasound screening
Except for a single patient who presented with UTI in early infancy and whose condition was diagnosed on subsequent investigations, the presence of hydronephrosis in all the other patients was discovered by antenatal ultrasound screening.

4.8. Age at surgery
Nineteen children (14.3%) had surgical intervention. The mean age of surgical or other intervention was 10.83 ± 12.67 months (range 1 day to 48 months) of whom 11 (61%) were operated in the first six months of life. Among the children who had surgery in the first six months, majority (5 out of 11) had pyeloplasty at two months. Thirty nine percent had surgery beyond the first six months of life: 2 at fourteen months while one patient each had surgery at 18, 19, 21, 30 and 48 months respectively. One patient had percutaneous nephrostomy on the first day of life because of massive hydronephrosis causing respiratory embarrassment.

Figure 4.4: Age at surgery and number of patients
4.9. Type of surgical procedure

The commonest surgical procedure was pyeloplasty as shown in the figure 4.5. Two patients required a repeat pyeloplasty because there was declining relative function on repeat MAG3 renogram and progressive increase of the AP diameter above preoperative value. Two children had total unilateral nephrectomy.

Figure 4.5: Types of surgical intervention for PUJ obstruction in 19 children.
4.0.1. Outcome of surgical management

Nineteen children with unilateral PUJ obstruction had surgical correction of the obstruction mainly because of deteriorating renal function (declining differential function on MAG3 renogram). Other reasons included recurrent UTI, associated pain and increasing AP pelvis by ultrasound. The treatment outcome based on preoperative and post-operative findings are shown in table 4.3. Two children had worsening function following the initial surgery necessitating nephrectomy. Their pre-operative MAG3 were 20% and 31% while the post operative MAG3 decreased subsequently to 8% and 15% respectively. The mean MAG3 when analysed separately without these two showed marginal improvement of function, 38.2% and 40% pre and post operatively. However, analysis of all the children together with those who had surgery is shown in the table below.

<table>
<thead>
<tr>
<th></th>
<th>Preoperative Mean (Range)</th>
<th>Postoperative Mean (Range)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAG3 (%)</td>
<td>37.1 (20-50)</td>
<td>31.4 (8-58)</td>
<td>0.256 (N.S)</td>
</tr>
<tr>
<td>AP diameter (mm)</td>
<td>26.6 (11-65)</td>
<td>22.5 (8-47)</td>
<td>0.546 (N.S)</td>
</tr>
<tr>
<td>Serum creatinine pre and at 1 year post-surgery (µmol/l)</td>
<td>58.6 (48-76)</td>
<td>40.17 (25-65)</td>
<td>0.0263 (S)</td>
</tr>
</tbody>
</table>

Table 4.3: showing the pattern of response to surgical correction.

(MAG3 %) – Relative kidney function of the affected kidney of the overall renal function as measured by MAG3.
(N.S= Not significant, S = Significant)
4.0.2. Prevalence of UTI

Urinary tract infection was identified in eleven children (11%). One patient each had three and two episodes of UTI respectively with the same organism (E. coli) before surgery. Five of the eleven children (45%) with UTI went on to have surgical correction for the obstruction. Klebsiella pneumoniae was the commonest organism cultured from the urine. This finding is presented in the figure below.

Fig 4.6: Prevalence of organisms cultured from urine in children with UTI
4.0.3 Other co morbidities

There were few children with other co morbid conditions. These include:

- Down syndrome, (2 cases)
- Severe mental retardation with delayed motor development (1 case)
- Microcephally with associated mental retardation (1 case)
- Attention deficit and hyperactive disorder in one (1 case)
- Severe gastro esophageal reflux disease with gastrostomy tube (1 case)
CHAPTER FIVE

DISCUSSION

5.0. Introduction
As antenatal ultrasound service becomes widespread, it is expected that there may be increase in the number of genitourinary tract abnormalities that will be identified. Pelvi-ureteric junction obstruction is considered a common congenital urinary tract abnormality and by far the commonest cause of antenatally detected hydronephrosis. It has been reported that a large proportion of postnatally confirmed PUJ obstructions when followed up over time improves or completely resolves and thus would not need any specific therapy. However, a significant proportion persists and may show evidence of deterioration of function in the affected kidney. Although exact guidelines for the timing of follow up and therapy are still being debated, physicians are thus left with the challenge of obtaining the best renal outcomes for their patients. This challenge becomes more obvious in resource poor societies, where health care provision is constrained by scarcity of both human and material resources. There are few implications of this in a setting like ours:

- How long should patients be followed up to identify those whose obstruction will resolve?
- Will there be satisfactory compliance by parents with follow up schedules?
- When should surgical intervention be contemplated?

There is an increasing number of children with chronic kidney disease world wide from congenital renal abnormalities with a significant proportion progressing to end stage renal failure (ESRF) who would as of necessity require renal replacement therapy. This increase may be real or due to greater awareness and improved methods of diagnosis. Accurate data on chronic kidney disease in children in Africa is lacking, but it may be appropriate to assume that a significant proportion of CKD children reside in this region. The economic cost of renal replacement therapy is enormous and clearly can not be borne by most poor countries in Africa, and one of
the solutions therefore is early identification of problems and initiation of measures that will slow or arrest the progression of chronic kidney disease.

5.1. Sex and age at first ultrasound
Most studies demonstrate male preponderance in the incidence of PUJ obstruction. The male female ratio of 4:1 in this study is moderately higher than most reports. It may be difficult to fully explain the reason for this. In their study, Sheu JC et al\textsuperscript{92} reported a male female ratio of 4.7:1 in a cohort of 102 children who had pyeloplasty for PUJ obstruction. This report however, was only in the population that had surgical intervention and did not include the overall population of children with PUJ obstruction. It may be suggested that male sex is associated with a more severe form of PUJ obstruction, thus explaining their need for surgery as compared with their female counterparts. This is because impaired renal function to a large extent depends on the severity of obstruction and AP pelvis diameter. Majority of patients had their first postnatal ultrasound at age 1 week or more. This finding is in keeping with established guidelines. It has been recommended that the first postnatal ultrasound in children who have antenatal detection of hydronephrosis with presumptive diagnosis of PUJ obstruction should be done on the second or third day\textsuperscript{93} except in severe disease, (bilateral hydronephrosis). If the ultrasound scan is done too early (first forty eight hours) significant PUJ obstruction may be missed because of the physiological dehydration that is present in the neonate in the first few postnatal days.

5.2 Side most affected by PUJ obstruction
The findings of this study are comparable with most reports on the pattern of distribution of PUJ obstruction. Left sided involvement predominates in this study as in most reports though in a lesser proportion compared with values reported, while bilateral affectation occurring in 32% is slightly higher.\textsuperscript{3,20} It is not clear why the left side is affected most of the time by this condition or the significance of preferential left sided involvement. It may be speculated that the left ureter is more vulnerable to ischaemic damage because it is longer than the right ureter. The left renal artery has a
longer and more tortuous tract compared to the right renal, which may influence blood supply to the left ureter.

5.3. The pattern of progression of PUJ obstruction

Spontaneous resolution of obstruction, persistence or deteriorating disease (declining relative function of affected kidney on MAG3 renogram) is an important guide as to how frequent imaging studies should be carried out and when decision to intervene surgically should be made. Within the first six months of follow up, 36.3% of the obstructed kidneys have resolved spontaneously. By the next six months (at one year of follow up), only thirty children of the initial cohort of hundred children were still being followed up. In other words, 70% of the PUJ obstructions resolved or normalized (some following surgery) with stable renal function at 12 months allowing discharge of this group from further follow up. This figure is similar to the findings of Ransley et al\textsuperscript{5} and Josephson et al\textsuperscript{13} who found respectively, the incidence of resolution or stable renal function to be 77% and 65.5% even in children with initial poor drainage and wide AP diameter. It has been noticed that the degree of resolution depends to a large extent on the severity of obstruction and size of AP diameter, with the larger postnatal AP diameter being likely to persist.

5.4 Preceding antenatal ultrasound screening

It is significant to note that only one patient of all the children did not have his condition identified prenatally. The importance of a structured investigation in a child with urinary tract infection was highlighted here as it was during such investigations for UTI that the PUJ obstruction was identified. This is different from what is observed in the developed countries where all foetuses have the advantage of prenatal ultrasound screening and such anomaly would have been detected. Even though, only one child was identified in this category, it is possible there may be other children in the larger population whose mother never had antenatal ultrasound screening or whose condition was not identified despite prenatal ultrasound. Patients in such category are at increased risk of development of chronic kidney disease at early age either as a direct consequence of progressive renal damage from primary
problem or from complications such as UTI. Furthermore, this high rate of prenatal detection of hydronephrosis due to PUJ obstruction may not be reflective of routine antenatal screening in our setting as in most developed countries. This is because only high-risk pregnancies are usually referred to the tertiary health facilities such as Groote Schuur where such a screening exercise exists.

5.5. Age at surgery
The importance of early surgical correction of obstruction done within first year in children with MAG3 renogram of 40% or less has been emphasised because of the beneficial effect on subsequent improvement of renal function. In the present study, surgery was performed within the first six months (most by 2 months) of life in just over sixty percent in children who had the indications. This included a decrease in MAG3 renogram of 10 percent or more on repeat study, initial MAG3 of less than 40 percent and large AP diameter greater than 20mm. The mean age at the time of surgery of 10.83 months is commendable but contrasts with the 2.5 years reported by Tapia and Gonzalez\(^8\) and the 21.7 months by Sheu\(^9\) respectively. In the remaining children, pyeloplasty was performed at varying period of time up to forty-eight months of life.

The renal outcome following pyeloplasty and the age at which it was performed is very important. Tapia and coworker noted that the function of the obstructed kidney improved significantly if the pyeloplasty was done before the patient was one year old. They also reported that pre-operative relative function on MAG3 renogram of less than 45% was associated with poorer outcome. In this study, main indications for surgery included decreasing function on MAG3, recurrence of UTI and evidence of worsening obstruction. The benefit of early surgery was highlighted by Palmer et al\(^9\) in a randomized study. They followed up 32 infants with significant hydronephrosis (SFU grade 3) due to PUJ obstruction randomized into two equal groups, one for pyeloplasty and the other for observation using ultrasound and tempered renography at regular intervals. At the end of the study period, they concluded that infant pyeloplasty significantly improved subsequent grade of hydronephrosis and drainage pattern at 6 months and 1 year postoperatively. Renal function stabilization was
similar in the two groups; however, 25% of the patients in the observation group required surgery ultimately for worsening hydronephrosis and reducing differential function. Mayor et al\textsuperscript{84} also found there is an advantage in early correction noting that renal function improved much better in children operated less than one year of age. However, not all children in this study who had early surgical correction experienced improvement in renal function indicating there may be other factors at play that need further evaluation.

5.6. Type of surgery
Outcome from Anderson-Hynes dismembered pyeloplasty is considered the best of all the other procedures for correction of PUJ obstruction. Seventy five percent of the patients in the study had this form of surgery. Other less common procedures such as percutaneous nephrostomy and endoscopic dilatation were also performed in some children. Pyeloplasty was the common surgical procedure used by other groups as well.\textsuperscript{8,82,92} A temporary decompressive procedure like percutaneous nephrostomy may be beneficial in a patient with a severely dilated obstructed system associated with infection. On the other hand it may introduce infection in a sterile obstructed system in which case primary pyeloplasty is preferred. Two children who had this surgical intervention in the present study had recurrent episodes of urinary tract infections with associated progressive deterioration of their renal function when compared with initial MAG3 renogram.

5.7. Outcome of management of PUJ obstruction
The rate of resolution of PUJ obstruction within the first twelve months and surgical intervention of 70% and 20% respectively in this study is similar to reports from other studies. In this audit, the two most important determinants for pyeloplasty were deteriorating MAG3 renogram findings and increase of AP pelvic diameter. Factors that are associated with outcomes have been noted to include pre-operative differential renal function and degree of ureteral obstruction. Percutaneous nephrostomy preceding pyeloplasty was identified to negatively impact on outcome
as subsequent follow up MAG3 renogram demonstrated progressive decline following such procedure in this study. The pre-operative serum creatinine was obtained in the early neonatal period and this mainly reflected the maternal serum creatinine because of transplacental transfer. Subsequent serum creatinine level remained normal at 12 months in all the children in the study even in those who had surgical intervention as had unilateral disease.

5.8. Co-morbidities

The existence of PUJ obstruction in association with other conditions has been described, particularly with Down syndrome. As noted in the result, two children with PUJ obstruction also had trisomy 21 disorder. There were other children with isolated co-morbidities that may not have any specific or defined association with PUJ obstruction. The existence of such co morbidities may simply be sporadic incidence.

5.9. Complications

Urinary tract infection was identified as the commonest complication in this study. The overall rate of UTI was 8.3%. This figure is much lower than most reports. Lee et al\textsuperscript{95} reported a rate of 36% in infants followed up who were not treated with prophylactic antibiotics. However, when the incidence of UTI was stratified based on the grades of hydronephrosis, it was noticed that UTI was more frequent in infants with grade three and four, occurring in over 70% of the patients. In the present study, it is evident that a significant proportion of children who would ultimately need surgical intervention are likely to develop UTI as noted in 26.3% of those with documented urinary infection. One may suggests from this finding that higher grades of hydronephrosis may be related to significant obstruction and consequent urine stasis, which will thus encourage infection. Although the number of children with UTI is small, it is interesting to note \textit{Klebsiella pneumoniae} was the commonest organism identified, this against the backdrop that
80-85% of UTI in children with normal urinary tract is caused by *Escherichia coli*. Similar finding has also been noted in other studies\(^{96,97,98}\) where they reported *Klebsiella, Proteus* and coagulase negative *Staphylococci* as the commonest organisms isolated in obstructive uropathy. Other complications include urinary ascites in two patients and severe respiratory distress in one who had massive hydrenephrosis causing lung compression.
CHAPTER SIX

6.0. CONCLUSIONS

Pelviureteric junction obstruction is an important and common cause of prenatal hydronephrosis. Where universal antenatal screening is available, early detection of foetuses with the condition is possible. However, in populations with limited access to antenatal sonography, children with significant obstruction may present later in life with variable clinical features and careful assessment is necessary in order to identify such group.

One of the greatest challenges of antenatal diagnosis of hydronephrosis secondary to PUJ obstruction may be the significant anxiety caused to both parents and physicians involved with such a child. This stems from the uncertainty with regard to prenatal and postnatal management: how should the parents be counseled and what should be the best approach to management? A clear guideline for diagnosis and postnatal management is important for institutions and populations. Such standardized protocol for postnatal management of antenatal hydronephrosis and outcome measures of such management is important. This will be helpful in order that parental anxiety and unnecessary radiologic investigations are avoided so that only children with strong indications for further management are given such.

From the present study, a significant number of children with pelvi-ureteric junction obstruction were identified during the period under review. It is important to note that only high risk pregnancies are referred to Groote Schuur Hospital from where most of the study population was recruited. Therefore, a more generalized comment about prevalence may not be representative of the general population. It is significant to note that all but one child had the presence hydronephrosis due to PUJ obstruction identified through antenatal ultrasound evaluation. This finding underscores the importance of provision of universal antenatal ultrasound screening for all pregnant women and the benefits that can arise from such.

Pelvi-ureteric junction obstruction is observed to be much commoner in males. This finding is similar to other reports. The reason for the male preference is not clear but
may be related to differences in genetic make up or hormonal expression. The left kidney is also more frequently affected than the right as has been reported by other studies.

The rate of spontaneous resolution observed in this study is similar to other reports. Such resolution is most obvious in mild to moderate AP pelvic dilatation on postnatal sonography and occur within the first year of life.

In children that required surgery, dismembered pyeloplasty was the commonest surgical procedure with greater proportion having the surgery in the first six months of life. Outcome of surgery was satisfactory in majority of the children though there were few complications.

The overall prevalence of urinary tract infections is lower than in most studies. The presence of UTI is more likely in children with severe disease. The commonest organism isolated from the urine is Klebsiella pneumoniae.

Renal outcome following surgery generally is good. On the whole, the mean postoperative MAG3 and AP pelvic diameter was not statistically different from the preoperative values. However, there was significant improvement in postoperative MAG3 as well as AP pelvis diameters of individual kidneys.

Children who had percutaneous nephrostomy preceding pyeloplasty seem to do very poorly in terms of renal outcome. At the Red Cross renal unit, nephrostomy is usually performed in children who have very poor to borderline renal function on MAG3 or those with severe infections. There is a poor renal outcome in this group of patients. However, the fact that only two children were observed in this category may make any firm conclusion difficult.

The pre and post-operative serum creatinine differs significantly. It is important to note however, that some of these values were obtained within the neonatal period when serum creatinine was a reflection of the maternal renal function. Furthermore, this information has no significant clinical value in children with unilateral obstruction as compensatory function usually takes place in the contralateral kidney. Secondly, a single serum creatinine is influenced by other factors and to make it more relevant, a GFR estimation and a trend in GFR would have been a better assessment.
of renal function. This was not possible as most of the children in this study do not have data for the estimation of this parameter.

6.1. RECOMMENDATIONS

The following recommendations can be made based on the findings of this study:

There is need for further collaboration between the departments of Foetal medicine, Radiology, Paediatric nephrology and urology to produce a clear guideline for the management of antenatal hydronephrosis and PUJ obstruction including diagnosis, follow up and surgical therapy.

Children who have very large hydronephrosis from PUJ obstruction and thus significant risk of UTI should be regularly monitored for UTI and promptly treated with appropriate antibiotics when infection is present or otherwise placed on appropriate prophylactic antimicrobials as the case may be. This however may be based on institutional decision.

A stronger emphasis on universal accessibility to antenatal ultrasound screening should be made, such that not only high-risk pregnancies that attend the tertiary facilities enjoy this benefit.

A prospective study detailing the prevalence of PUJ obstruction, its natural history, management and outcome will be a valuable tool to clarify this condition in this population. Such information will not only serve the interest of South Africa but may
also be a useful guideline and tool for management of PUJ obstruction in the African continent.

6.2. LIMITATIONS

This is a retrospective study and as such, it is limited by the information available on any particular patient. For example, serum creatinine and electrolytes were not routinely done for every child except in very limited number of children (those being prepared for surgery or with severe infections). Disease progression was monitored by regular ultrasound assessment of the affected kidney and MAG3 in some. Secondly, those folders that were not traced during the audit could not be included in the study.
REFERENCES


22. Marks SD. How have the past 5 years of research changed clinical practice in paediatric nephrology? Arch Dis Child 2007; 92:357-361


# Appendix 1

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Other investigations.

DMSA findings: …………………………………………………………………

GFR: …………………………………………………………………………

Laboratory findings

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**OUTCOME , LONGTERM**

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03 February 2009

RECOMMENDED 06/2/09

Dr LB Ochegba
Paediatric Nephrology
Red Cross Children’s Hospital

Dear Dr Ochegba

PROJECT TITLE: AN AUDIT OF PELVIURETERAL JUNCTION OBSTRUCTION AT RED CROSS CHILDREN’S HOSPITAL: A FIVE YEAR REVIEW

Thank you for submitting your study to the Research Ethics Committee for review.

It is a pleasure to inform you that the Ethics Committee has formally approved the above mentioned study.

Approval is granted for one year until 03 February 2010. Please submit an annual progress report if your study continues beyond the approved period. Alternatively, please submit a brief summary of your findings so that we can share our results.

Please ensure that the ongoing ethical member of the study remains the responsibility of the principal investigator.

Please quote the REC REF in all your correspondence.

Yours sincerely,


Appendix 2
DEPARTMENT OF HEALTH

Appendix 3

Dear Dr. Otsuka,

RESEARCH: AN AUDIT OF PELVI-URETERAL JUNCTION OBSTRUCTION—A FIVE-YEAR REVIEW

It is gratifying to comment the above mentioned study at Red Cross War Memorial Children's Hospital.

Yours faithfully,

Dr. T. Blake
Senior Medical Superintendent