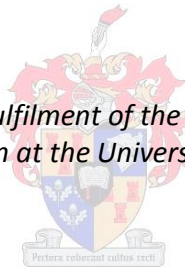


Assessing the renal handling of a dietary protein load in patients managed for Nephroblastoma

by
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*Thesis presented in partial fulfilment of the requirements for the degree
Master of Nutrition at the University of Stellenbosch*



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DECLARATION

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ABSTRACT

Introduction and purpose

The aim of the study was to determine the renal handling of a once-off bolus dietary protein load in patients treated for nephroblastoma. Patients who have been managed for nephroblastoma always have suboptimal amounts of kidney tissue as a result of their medical management which includes nephrectomies, chemotherapy and or radiotherapy. Little data are available indicating the extent of renal impairment expected in such patients as a result of their disease and management. The study was to determine whether the use of regular screening tests such as serum urea, creatinine and urine microalbumin, in conjunction with a dietary protein load could help detect early progressive deterioration of kidney function in nephroblastoma patients.

Methodology

The study was a quantitative non-randomised intervention study in which patients served as their own control before and after a protein load.

Thirty-four participants were included in the study. Each participant was provided with a supplemental protein drink providing 2 g/kg body weight of protein. Serum creatinine, urea and urine microalbumin were assessed at baseline and four hours after the intervention. These pre- and post intervention biochemical values were then analysed together with descriptive data relating to the participants, such as age, stage of nephroblastoma, aspects of medical management and the period of time since they had been treated for nephroblastoma, and statistical relationships were assessed. Data were collected from May 2010 to November 2010.

Results

Descriptive statistics indicated that the mean [\pm Standard deviation (SD)] age of the population was 92 (\pm 55) months, the mean age at diagnosis was 41 (\pm 27) months and the mean age from the diagnosis to the time of the study was 51 (\pm 53) months. There was a statistically significant increase ($p = 0.00$) in serum urea post intervention; however, no significant difference was noted between pre- and post intervention serum creatinine and urine microalbumin values. The stages of nephroblastoma failed to show a statistical correlation with the response to the dietary protein bolus load in terms of the difference in pre- and post intervention biochemical data. No statistical correlation was found between post-pubescence and response to the protein load. Similarly, no statistical correlation could be demonstrated for a longer period between the diagnosis and the time of this study, on the one hand, and the prevalence of high values in the biochemical data, on the other.

Conclusion

The study was unable to demonstrate statistically that participants managed for nephroblastoma had poor renal handling of a once-off dietary protein load in terms of the objectives specified. The study had limitations including a small population with even smaller subgroups of participants, therefore results of the study need to be interpreted in context to the size of the population.

OPSOMMING

Doel

Die doel van die studie was om die renale hantering van 'n eenmalige bolus dieetproteïenlading by pasiënte wat vir nefroblastoom behandel word, te bepaal. Pasiënte wat vir nefroblastoom behandel word, het altyd 'n suboptimale hoeveelheid nierweefsel as gevolg van hulle mediese behandeling wat nefrektomies, chemoterapie en / of radioterapie insluit. Min data is beskikbaar omtrent die omvang van die nierbelemmering wat in sulke pasiënte verwag word as gevolg van hulle siekte en behandeling. Die studie is uitgevoer om te bepaal of die gebruik van gereelde siftingstoetse soos serum-ureum, kreatinien en mikroalbuminurie, in samewerking met 'n dieetproteïenlading, kan help om vroeë progressiewe agteruitgang van nierfunksie in nefroblastoom pasiënte, op te spoor.

Metodologie

Die studie was 'n kwantitatiewe nie-ewekansige intervensie studie waar pasiënte as hul eie kontrole gedien het voor en na 'n proteïenlading. Altesaam 34 deelnemers is by die studie betrek. Elke deelnemer het 'n proteïenaanvullingsdrankie ontvang wat 2 gram proteïen per kilogram liggaamsgewig voorsien het. Serumkreatinien, serum-ureum en mikro-albuminurie is op die basislyn sowel as vier uur na die intervensie gemeet. Hierdie biochemiese waardes voor en na die intervensie is daarna saam met beskrywende data van die deelnemers – soos ouderdom, stadium van nefroblastoom, aspekte van mediese behandeling en tydsverloop sedert behandeling vir nefroblastoom – ontleed. Statistiese verwantskappe is vervolgens beoordeel. Data is vanaf Mei 2010 tot November 2010 ingesamel.

Resultate

Beskrywende statistieke het op 'n gemiddelde [\pm Standaard afwyking (SA)] populasie-ouderdom van 92 (\pm 55) maande, 'n gemiddelde diagnose-ouderdom van 41(\pm 27) maande en 'n gemiddelde ouderdom van 51(\pm 53) maande vanaf diagnose tot en met die studie gedui. Ná die intervensie is 'n statisties beduidende toename ($p = 0.00$) in serum-ureum opgemerk, hoewel daar geen beduidende verskil in serumkreatinien en mikro-albuminurie waardes, voor en na behandeling, was nie. Biochemiese data voor en na die intervensie het geen statistiese verwantskap tussen die stadium van nefroblastoom en die reaksie op die dieetproteïenlading getoon nie. Boonop is geen statistiese verwantskap opgemerk tussen post-pubesensie en die reaksie op die proteïenlading, of tussen 'n langer tydsverloop tussen die diagnose en die studie en die voorkoms van hoë waardes in die biochemiese data nie.

Gevolgtrekking

Wat die studie-doelwitte betref, kon die navorsing nie statisties bewys dat deelnemers wat vir nefroblastoom behandel word, swak renale hantering van 'n eenmalige dieetproteïenlading toon nie. Die beperkinge van die studie sluit 'n klein populasie met selfs kleiner subgroepe in; die resultate van die studie moet derhalwe in die konteks van die grootte van die populasie, geïnterpreteer word.

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Thank you to the Stellenbosch University (SU) Centre for Statistical Consultation and in particular Professor Nelfor the help and support with the statistical analysis of my data, and thank you to the Language Centre (SU) for assisting with the translation of my abstract and the editing of my thesis.

Finally a massive thank-you to my husband, who has been my rock throughout my master's degree. Your support and belief in me has carried me through these years.

Thank you.

CONTRIBUTIONS BY PRINCIPAL INVESTIGATOR AND FELLOW INVESTIGATORS

The principal investigator contributed to the study by means of the following:

- Developed the study protocol.
- Applied for ethics approval and kept the study updated with the Health Research Ethics Committee.
- Designed and developed all data collection sheets and informed consent forms.
- Collected all data required for the study.
- Submitted all data required for analysis.
- Collated all data in the form of this thesis.

The principal investigator was assisted at several points along the way by means of the following:

- Assistance with translating informed consent forms from English to IsiZulu (Language Centre SU).
- Collection of blood samples by the phlebotomist.
- Analysis of blood and urine samples by the laboratory technician.
- Statistical analysis by the Centre for Statistical Consultation (SU).

The supervisor and co-supervisor had input on this research from its protocol inception to the final version.

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LIST OF ACRONYMS AND ABBREVIATIONS

| | |
|-------|--|
| AI | Adequate intake |
| BP | Blood pressure |
| BMI | Body mass index |
| COG | Children's Oncology Group |
| CT | Computed tomography |
| DRI | Dietary reference intake |
| EAR | Estimated average requirements |
| ESRD | End stage renal disease |
| GFR | Glomerular filtration rate |
| HIV | Human immunodeficiency virus |
| HPT | Hypertension |
| IALCH | Inkosi Albert Luthuli Central Hospital |
| KZN | KwaZulu-Natal |
| MAC | Mid-arm circumference |
| NWTS | The National Wilms' Tumour Study |
| OPL | Oral protein load |
| PEM | Protein energy malnutrition |
| RFR | Renal function reserve |
| RNI | Reference nutrient intake |
| RPF | Renal plasma flow |
| SD | Standard deviation |

| | |
|------|---|
| SIOF | The International Society of Pediatric Oncology |
| UAE | Urinary albumin excretion |
| WHO | World Health Organisation |

LIST OF DEFINITIONS¹

| | |
|--------------------------------------|--|
| <i>Anthropometry</i> | The taking of measurements of the human body or its parts. Comparisons can then be made among individuals of different sexes, ages and races to distinguish between normal and abnormal development. |
| <i>Body Mass Index</i> | The weight of a person (in kilograms) divided by the square of the height of that person (in meters): used as an indicator of whether or not a person is over- or underweight |
| <i>Chemotherapy</i> | The prevention or treatment of disease by the use of chemical substances. |
| <i>Creatinine</i> | A product of protein metabolism found in muscle. |
| <i>Glomerular filtration rate</i> | The rate at which substances are filtered from the blood of the glomeruli into the Bowman's capsules of the nephrons. It is calculated by measuring the clearance of specific substances and is an index of renal function. |
| <i>Microalbuminuria</i> | The presence of albumin in the urine at levels that are higher than normal but lower than those detected by standard protein dipsticks. |
| <i>Nephroblastoma (Wilms'tumour)</i> | A malignant tumour arising from the embryonic kidney and occurring in young children usually below the age of three and rarely over the age of eight. |
| <i>Puberty</i> | The time at which the onset of sexual maturity occurs and the reproductive organs become functional. This is manifested by the appearance of secondary sexual characteristics (menstruation and breast development in girls and deepening of the voice in boys). |
| <i>Radiotherapy</i> | The treatment of disease with penetrating radiation, such as X-rays, beta rays or gamma rays, which may be produced by machines or given off by radioactive isotopes. |

Urea

The main breakdown product of protein metabolism. It is the chemical form in which unrequired nitrogen is excreted by the body in the urine. Accumulation of urea in the bloodstream together with other nitrogenous compounds is due to kidney failure and gives rise to uraemia.

CHAPTER 1: INTRODUCTION AND PROBLEM STATEMENT

1.1 INTRODUCTION

The departments of Paediatric Surgery and Dietetics at Inkosi Albert Luthuli Central Hospital (IALCH) are actively involved in the management of all paediatric solid tumours. Patients are diagnosed, treated, followed up and monitored for recurrences, other developing conditions, general health and growth by the Department of Paediatric Surgery, which has a large data set accessible for further studies. This database of patients presents wonderful opportunities for studies on the nephroblastoma population of KwaZulu-Natal (KZN) and outlying areas. The primary researcher was actively involved in the nutritional management of children with solid tumours at IALCH. The opportunity to study this patient population further with a passionate team of doctors inspired the interest in assessing the patients' renal functions in response to a dietary protein load. With the support of both the Paediatric Surgery and Dietetics departments, this study was initiated in 2008 and data gathering was completed by the end of 2010.

1.2 PROBLEM STATEMENT

Patients managed for nephroblastoma undergo unilateral, total or partial nephrectomy, as well as chemotherapy and/or radiotherapy,² all of which reduce the functioning renal cell mass. Patients who have been managed for nephroblastoma always have suboptimal amounts of kidney tissue although it is known that patients with a solitary kidney develop hypertrophy of the remaining kidney in an attempt to compensate for the workload of the kidney that was surgically removed. During periods of rapid growth such as puberty and pregnancy, kidneys are placed under increased pressure physiologically. Currently, little data are available indicating the

extent of renal impairment expected in such patients, especially after periods of increased growth.

It is necessary to determine which patients who have been managed for nephroblastoma are at a high risk of developing renal impairment later in life, especially during times of physiological stress. It was therefore decided to determine whether the use of regular screening tests such as serum urea, creatinine and urine microalbumin could help detect early progressive deterioration of kidney function in nephroblastoma patients.

Establishing that one can use routine biochemical data such as microalbumin as a screening tool for renal impairment in patients with nephroblastoma may enable physicians to identify patients who will require more detailed assessment of kidney function. Renal function of patients managed for nephroblastoma is usually assessed by tools such as the glomerular filtration rate (GFR), renal plasma flow (RPF) and tubular sodium (Na) transport studies.³ Such investigations are valid tools but they are expensive and invasive, making them inappropriate for use as screening tools. The aim of this study was to see whether a simple test such as the effect of a dietary protein load on renal function (investigating the change in patients' serum urea, creatinine and urine microalbumin) could identify subgroups in the nephroblastoma population who were at risk for renal impairment.

1.3 ASSUMPTIONS AND DELIMITATION

Based on the knowledge and experience gained in working with the population of patients who attended IALCH, the following generalisations were made:

- That patients attending the clinic came from middle- to low-income backgrounds with some families depending on government care grants as their only source of income.
- That the majority of patients attending the clinic were ethnic Africans.

CHAPTER 2: REVIEW OF RELATED LITERATURE

2.1 INTRODUCTION

Nephroblastoma, more commonly known as Wilms' tumour, is a common renal solid tumour of childhood.² It was first described by Max Wilms in Germany in 1899.

Initially, surgery was the only means of treatment for these patients, and the overall survival rate was approximately 20%. However, with the introduction of radiotherapy in the 1940s, the survival rate improved to 50%, and finally with the introduction of chemotherapy in the 1960s, the survival rate for patients managed for nephroblastoma increased to > 85% in first world countries.^{3,4} Wilms' tumour is now one of the most successfully treated cancers of childhood.⁵

2.2 TUMOUR ORIGIN

Nephroblastomas are known to arise from embryonic renal tissue, in the renal parenchyma.^{2,4} A Wilms' tumour has a triphasic appearance, presenting with three different cell lines (epithelial cells, blastemal cells and mesenchymal). Some histological variants such as Wilms' tumour with an anaplastic appearance carry a poor prognosis.^{2,6}

Nephroblastomatosis, which is a complex abnormality of nephrogenesis, results in the finding of nephrogenic rests (embryonic renal tissue) within an otherwise normal kidney.^{2,7} These embryonic metanephric tissue remnants may be found in 1% of normal children, 35% of patients presenting with unilateral Wilms' tumour and in all patients presenting with bilateral renal tumours.^{2,4}

Several individual genetic anomalies as well as rare genetic syndromes have been associated with Wilms' tumour. Such syndromes include WAGR syndrome, Denys-Drash syndrome, Beckwith-Wiedemann syndrome and Perlman syndrome.^{2,4}

In the United Kingdom, the Wilms' Tumour Screening Working Group suggests that patients with significant risk factors for Wilms' tumour be referred to a clinical geneticist to attempt to determine or estimate the risk of developing nephroblastoma.²

2.3 INCIDENCE

There has been considerable variation in the reported incidence of nephroblastoma; however, it appears to be more prevalent amongst people of ethnic African origin, both in the developed world and in developing countries.² An article in the *British Journal of Cancer* in 2002 suggested that nephroblastoma had an incidence rate of 1 in 10 000 live births.⁶ However, a 2007 article by G.S. Arul indicated that the annual incidence of Wilms' tumour in the United Kingdom was 0.8 per 100 000 population.²

Wilms' tumour usually presents between the ages of two and seven years, with a median age at presentation of 42 months. Approximately 90% of all patients are under the age of eight years.^{2,4,6}

Of patients presenting with Wilms' tumour, only approximately 4–7% have bilateral tumours. Patients with bilateral tumours are generally diagnosed earlier than patients with unilateral tumours. Furthermore, patients with bilateral tumours are more likely to be associated with developmental delays and abnormalities.^{2,8} A South African study on the clinical presentation of Wilms' tumour reflected the distribution of the population in KZN in 1990. Out of 48 patients, 35 lived in rural areas, compared to 13 from urban areas, and it was indicated that rural patients had larger tumours than urban patients. Thirty-one percent of the patients included in this study had tumours > 10% of their pre-operative body mass.⁹ The male:female ratio was 0.92 for

unilateral tumours and 0.6 for bilateral tumours¹⁰; however, other papers present the ratio as equal.^{2,4} Wilms' tumour has a higher incidence in black populations than white populations, with a threefold higher incidence.^{8,10} Furthermore, children in less developed nations have been seen to present with more advanced disease than children in first world countries.¹⁰

2.4 PRESENTATION

Nephroblastoma is usually diagnosed after parents see and feel a hard abdominal mass in their child.^{2,4} The mass is usually unaccompanied by other symptoms; however, fever is present in approximately 20% of patients and nonspecific abdominal complaints are seen in 10%.⁴ The tumour may be discovered as a result of screening for a predisposing sign, such as varicocele, or because of the side effects of tumour bleeding. These include: anaemia, haematuria, abdominal pain and raised temperature.^{2,4}

2.5 STAGING

Nephroblastoma has been classified by the International Society of Pediatric Oncology (SIOP) and the National Wilms' Tumor Study (NWTs) into five different stages (see Table 2.1).^{4,10}

Table 2.1: Wilms' tumour classification^{2,4,10}

| Stage | Classification |
|------------|---|
| I | Tumour limited to the kidney, completely excised |
| II | Tumour extending outside the kidney, completely excised Invasion beyond the capsule, perirenal/perihilar Invasion of extrarenal vessels Invasion of ureter if completely excised |
| III | Invasion beyond capsule, excision incomplete Invasion to the regional lymph nodes Per-/preoperative tumour rupture Peritoneal metastases |
| IV | Distant haematogenous metastases |
| V | Synchronous or metachronous bilateral renal tumours |

2.6 TREATMENT

There are two approaches to the treatment of nephroblastoma: the Childrens Oncology Group (COG) (having succeeded the NWTS in the United States of America [USA]) and the SIOP approaches. The NWTS focused on primary nephrectomy, followed by chemotherapy with or without radiotherapy, depending on the stage and histology of the tumour.⁴ The SIOP approach, an adaptation of which is used in IALCH in KZN, recommends initial chemotherapy treatment, followed by surgical removal of the tumour. The European SIOP approach is widely used in South Africa as the majority of the tumours presented are extremely large and often already at Stage III or Stage IV. The SIOP approach is beneficial as it decreases the size of the tumour and downstages it, thereby reducing operative risks such as tumour rupture, seeding or nonresectability.^{2,10,11} The SIOP strategy does not influence histology of the tumour despite American concerns that neoadjuvant chemotherapy would obscure anaplastic histology.¹⁰

Chemotherapy drugs used in the SIOP and COG protocols include vincristine, actinomycin-D, adriamycin, apirubicin, ifosfamide, carboplatin and etoposide.⁴ There are many chemotherapy drugs that cause renal damage, including ifosfamide, cisplatin and cyclophosphamide.^{12,13} Ifosfamide is included in the management protocol for Stage IV nephroblastoma at IALCH and is used for patients with remaining metastases after surgery and appropriate treatment. Some of carboplatin's adverse reactions include renal tubular damage and renal insufficiency.¹³ In the mid 1980s, cyclophosphamide, ifosfamide, platinum compounds and etoposide became available. A review of nephroblastoma cases by Dome et al at St Jude Children's Research Hospital was noted in a paper by Spreafico et al who showed that the introduction of cyclophosphamide, ifosfamide, platinum compounds and etoposide led to 50–70% disease-free survival rates for children presenting with recurrent Wilms' tumour.¹⁴

Surgical resection follows pretreatment chemotherapy, which has ensured maximal tumour size reduction, especially in patients with Stage V nephroblastoma. In patients presenting with bilateral tumours, the surgical aim is to resect all malignant tissue whilst leaving enough nephrons to ensure normal renal function; however, in patients with bilateral tumours, bilateral total nephrectomy is sometimes necessary, resulting in the need for dialysis support until future renal transplantation.⁴

Partial nephrectomies are not recommended in patients with unilateral tumours, except in selected cases of small tumours that were detected early through routine screening.^{2,4,10} The use of laparoscopic surgery is also not recommended as it is vital to explore the whole abdomen and remaining kidney. The approach is via a large

abdominal incision whereby the kidney and tumour are widely excised together with the adjacent lymph nodes.¹¹

Radiotherapy is used in 15% of SIOP-protocol-treated cases. It is always used in cases where the tumours were not completely resected, where tumours ruptured, where there was lymph node involvement and where nonresectable metastases occur after chemotherapy, such as in Stage III and Stage IV nephroblastoma.⁴

2.7 ADVERSE EVENTS AFTER NEPHROBLASTOMA MANAGEMENT

Despite the fact that the management of nephroblastoma has a high success rate, treatment-related adverse events may develop during childhood or even later in life. These include orthopaedic presentations, mainly including scoliosis, kyphosis and lower back pain as well as short stature, cardiovascular events, including hypertension, pulmonary events (if chest radiotherapy was part of management), reduction in glomerular filtration rate (GFR), microalbuminuria and second primary malignancies.^{5,15}

Radiotherapy has often been noted as a major risk factor in the development of adverse events. A 2010 study conducted by Van Dijk et al⁵ evaluated the prevalence and severity of adverse events in a cohort of 189 long-term nephroblastoma survivors. Sixty-eight percent had suffered at least one or more adverse events. Twenty-one percent of the survivors had suffered at least five adverse events. Survivors managed with radiotherapy during their treatment were at the highest risk for developing an adverse event compared with the non-irradiated survivors. The study observed that out of the entire patient population, the most frequently encountered adverse events were orthopaedic events, nephrologic changes and

psychosocial events. Thirteen survivors, of whom 11 were female, presented with second tumours. Eight of these second primary tumours were located within the former radiation field or on the border of the radiation field for initial management of nephroblastoma.

Van Dijk further assessed the use of chemotherapy. He documented that the use of anthracyclines or alkylating agents increased the risk of cardiovascular events and that treatment with alkylating agents increased the risk of developing nephrologic adverse events later in life.⁵ Of all adverse events in the study population, there were 43 nephrologic adverse events, including glomerular dysfunction, hypertension and tubular dysfunction in 123 Wilms' tumour survivors. Of these events, hypertension was the most frequent, followed by glomerular dysfunction and then tubular dysfunction. Nonspecified nephrologic adverse events were also noted.⁵ Murat et al recently investigated the blood pressure (BP) profile, cardiac diastolic functions and pulmonary venous flow in 25 unilateral nephroblastoma patients in remission. The findings were that hypertension and prehypertension were frequent complications in nephroblastoma survivors.¹⁵

2.8 RENAL FUNCTION AFTER NEPHRECTOMY

Patients diagnosed with Wilms' tumour will undergo a surgical procedure for removal of the tumour. In patients with unilateral disease, this implies unilateral total nephrectomy. In bilateral disease, the extent of resection is dependent on the tumour size, its position within the kidney and its histology. It is known that patients who have been managed for unilateral Wilms' tumour develop structural and functional changes in the remaining kidney.³

It is noted that patients who have undergone nephrectomy, chemotherapy and in particular radiation therapy to the remaining kidney are at risk of developing impaired renal function.^{3,6} Irradiation may cause radiation nephritis, which causes impairment of renal function.¹⁶ Renal failure – where the need for dialysis and or renal transplantation occurs, is an adverse outcome somewhat unique to Wilms' tumour survivors. This is primarily seen in patients with bilateral syndromic Wilms tumours which include the Denys Drash syndrome and other syndromes involving mental retardation. Non-syndromic Wilms' tumour populations have a smaller risk of less severe degrees of renal dysfunction.¹⁷

In patients managed for nephroblastoma, there are concerns regarding the functional impairment of the remaining kidney; however, data are limited regarding the effects of treatment for Wilms' tumour on remnant renal tissue.⁶

Cozzi et al¹⁸ recently investigated a large cohort of 72 children undergoing treatment for unilateral renal tumour (URT) and their renal function adaptation up to the fifth decade after treatment. Renal function was assessed using estimated glomerular filtration rate (eGFR). The results showed that 78% of patients between the ages of 33 and 51 years had mild to moderate renal functional impairment and that patients between 45 and 54 years presented a mean eGFR significantly lower than the expected physiological renal function of that age group. In addition, a high prevalence of children having undergone nephrectomy for URT experienced mild renal function loss in the second decade of life.¹⁸ A study by Bailey et al⁶ investigated the prevalence and nature of renal toxicity in survivors among children treated for Wilms' tumour. The authors were, however, unable to identify the specific effect of different components of treatment in the development of renal impairment, but they

did document that concern was needed regarding the potential damage to the surviving kidney in patients managed for nephroblastoma.⁶ Twenty to 40 percent of children with unilateral Wilms' tumour treated with nephrectomy present with renal dysfunction (defined as GFR less than the reference range of healthy individuals with two kidneys, i.e. 90 ml/min/1.73 m²).¹⁹ A 2013 review by Green stated that the risk of End Stage Renal Diseases (ESRD) 20 years after diagnosis of unilateral, non-syndromic Wilms rumour was 0.7%, with a greater prevalence of less severe renal dysfunction based on GFR and or the presence of microalbuminuria in 13.8% of survivors who received abdominal irradiation as part of their management, and 11.1% in survivors who did not receive radiotherapy.¹⁷

Hyperfiltration occurs in patients who have a single kidney remaining as a result of a disproportional increase in function over structural changes of the kidney. This may result in permanent renal damage.³ Hyperfiltration is suggested by increased single-kidney GFR as well as proteinuria. Clinical and experimental data have suggested that sustained hyperfiltration in the remnant nephrons results in progressive glomerular damage. This damage increases proportionately to the amount of renal tissue removed and the duration of exposure to hyperfiltration.²⁰ BP is also increased due to the remnant kidney compensating for the loss of function by increasing its workload.^{3,21} A small increase in blood pressure has been associated with unilateral nephrectomy patients using ambulatory blood pressure monitoring.²¹ An increase in a patient's GFR after a dietary protein load is a reflection of the existence of the renal functional reserve (RFR) of the kidney. Hyperfiltration is associated with a loss of RFR, and thus the use of protein stimulation of the GFR has previously been used to identify patients at risk of developing renal damage.³ Studies

assessing renal function after Wilms' tumour management have indicated that tubular function as well as GFR is altered. It is therefore important not only to use GFR as an indication of renal function but also to assess tubular function.³

In patients with Stage V nephroblastoma, treatment is aimed at preservation of renal tissue and function. Children with bilateral nephroblastoma often require removal of more than 50% of their renal mass, placing them at an increased risk for renal failure.²⁰ The inclusion of radiotherapy may contribute further to impaired renal function in such patients.^{16, 17} A study by Saarinen-Pihkala et al described the renal function of three patients managed for bilateral Wilms' tumour in whom kidney-sparing surgery was used after preoperative chemotherapy. No radiotherapy was used in these patients, and the resulting renal function was normal in terms of GFR and serum creatinine and urea, and although these numbers are very small, they suggest that irradiation may be a major contributor to impaired renal function in patients with bilateral tumours.¹⁶

2.9 RECURRENCES OF NEPHROBLASTOMA

Approximately 15% of patients with favourable histology nephroblastoma and 50% of patients with unfavourable histology nephroblastoma experience recurrences or relapses. Most recurrence develops within two years of diagnosis; however, one cannot exclude the risk of relapses occurring later. Relapse in the lungs and pleura account for 50–60% of all relapses, with abdominal relapse representing only 30% and all other sites, including brain and bone, making up 10–15% of all cases.¹⁴

Prognostic indicators have been assessed for both SIOP and COG (previously NWTs) groups. SIOP has identified adverse prognostic factors for relapsed

nephroblastoma. These include initial Stage IV disease, unfavourable histology, time to recurrence of six months or less after diagnosis and recurrences in multiple organs or a previously irradiated field. The NWTs indicates that time to recurrence is a strong predictor of survival, with patients who relapse within five months after nephrectomy assumed to have a worse outcome than those who relapse after six months. This protocol also identifies other adverse factors such as unfavourable histology, advanced tumour stage and relapse outside the lung. The NWTs – 5 concluded that gender was a predictive outcome, with male patients faring worse than female patients, and that patients initially treated with two drugs compared to three drugs had better prognostic outcomes. This places emphasis on initial treatment being a powerful prognostic factor.¹⁴

2.10 NUTRITIONAL STATUS OF PATIENTS MANAGED FOR NEPHROBLASTOMA

The prevalence of malnutrition in children with cancer ranges from 8% to 60%, depending on diagnosis and treatment.²² An association has been described between nutritional status and overall prognosis and outcome of patients managed for cancer. A study by Donalds et al, cited by Ladas et al,²² indicated that there was a direct association between the nutritional status of a patient and the lack of relapse in paediatric patients managed for solid tumours. Children with cancer are vulnerable to malnutrition as they have increased nutrient requirements for age appropriate growth and neurodevelopment, as well as elevated substrate needs due to the disease and its treatment.²³ The prevalence of malnutrition at diagnosis and throughout therapy in all types of childhood cancers and age groups is unknown due to lack of data studied. Factors which can predict the risk for malnutrition include

treatment regimens, age, gender, socioeconomic status, biochemical parameters and baseline nutritional status. A multi-centre study by Zimmermann et al²⁴ found that at least half of the children who had cancer and were managed at their institutions with chemotherapy and or radiotherapy, were malnourished at least once during their treatment. This multi-centre study showed that nutritional status deteriorates rapidly after the initiation of anticancer treatment, and that some patients were malnourished for a large portion of their time being managed. These authors concluded that poor nutritional status is negatively associated with therapy-related toxicities and overall disease outcome.²⁴ The WHO recommendation for nutritional assessment of children and adolescents is a weight for height index. However children with cancer, particularly those with large solid tumours such as nephroblastoma may present with a normal weight despite severe malnutrition, due to the contributing mass of the underlying tumour.²³

In South Africa, malnutrition in patients is common. Factors impacting on the nutritional status of children managed for nephroblastoma and in general include protein energy malnutrition (PEM), human immunodeficiency virus (HIV) status, actual food intake, overall food availability and nutrient provision from food.²⁵

Patients who are malnourished at diagnosis of solid tumours have a poorer survival rate compared with well-nourished patients. This relationship appears to be stronger in patients with localised solid tumours than in patients with advanced metastatic disease.²⁶ A paper by Israels et al²⁷ assessing the clinical guidelines for the management of children with nephroblastoma in a low income setting indicate that patients are often severely and acutely malnourished at presentation. This state of malnutrition is associated with more severe chemotherapy-associated toxicity.²⁷

Patients who present with nephroblastoma are nutritionally managed to provide for growth and development as well as to minimise nutritional depletion due to the side effects of treatment regimens and cancer cachexia.²⁸ Nutritional support prevents loss of lean body mass, which is a vital part of paediatric oncology management.¹² The majority of South African nephroblastoma patients managed are undernourished and present with multiple comorbidities including tuberculosis, HIV, viral infections and other recognised secondary primary disease that can compromise diagnostic and therapeutic plans.⁹

Cancer specific as well as scientifically based recommendations for children with cancer are not yet available. The primary objective for nutritional intervention in children with cancer and therefore nephroblastoma should be the maintenance of body stores, the minimisation of wasting as well as promoting appropriate growth, development and quality of life. Energy requirements may be based on available published paediatric nutritional guidelines and adapted as required.²³ Nutrient requirements for infants, children and adolescents with cancer should be determined with a thorough assessment of each patient's presenting nutritional status, disease state and treatment course. The Dietary Reference Intakes (DRIs) for age and gender can be used to estimate energy and protein requirements for appropriate growth in cancer specific patients. The DRI's for protein are tabulated in table 2.3 below.²⁹ Nutritional requirements for sick children are presented in the table below. This guideline does not differentiate among different disease conditions; it is merely a general guide to oral nutritional requirements in sick children but would include children with cancer.³⁰ The goal of in patients nutritional management is to meet dietary targets based on the requirements set out below.

Table 2.2: Nutritional requirements for sick paediatric patients compared to the EAR* and RNI for age³⁰**

| | Infants 0–1 year | Children > 1 year |
|------------------------------------|--|---|
| Energy for sick patients | High: 130–150 kcal ^{***} /kg ^{****} /day Very high: 150–220 kcal/kg/day | High: 120% EAR for age Very high: 150% EAR for age |
| EAR energy | 95–110 kcal/kg/day | < 90 kcal/kg/day |
| Protein for sick patients | High: 3–4.5 g/kg/day Very high: 6 g/kg/day (0–6 months) increasing to a maximum of 10 g/kg/day up to one year | High: 2 g/kg/day |
| RNI protein | 1.5–2.1 g/kg/day | 1.1 g/kg/day |
| Sodium for sick patients | High: 3.0 mmol/kg/day Very high: 4.5 mmol/kg/day | Not documented |
| RNI sodium | 1.5 mmol/kg/day | 1.7 mmol/kg/day |
| Potassium for sick patients | High: 3.0 mmol/kg/day Very high: 4.5 mmol/kg/day | Not documented |
| RNI potassium | 1.8–3.4 mmol/kg/day | 1.6 mmol/kg/day |

*EAR:estimated average requirement; **RNI:reference nutrient intake

*** kcal (kilocalories)

**** kg (kilogram)

Table 2.3 DRI's and Adequate Intake (AI) values for protein across different age groups²⁹

| Age group | Protein (g/kg/day) |
|---------------|--------------------|
| 0 – 6 months | 1.52 |
| 7 – 12 months | 1.2 |
| 1 – 3 years | 1.05 |
| 4 – 8 years | 0.95 |
| 9 – 13 years | 0.95 |
| 14 – 18 years | 0.85 |

A good nutritional status is beneficial for patients managed for nephroblastoma during treatment and thereafter. The mid-arm circumference (MAC) is a measure of muscle, fat and bone. It is a good measurement to use in assessing malnutrition in children, especially when weight and stature measurements are not reliable, such as in cases where tumour mass influences total body weight. In addition to weight and height values, triceps skin-fold measurements are a good indicator of energy reserves in children.³¹ Nutritional support may enhance therapy, decrease complications and, hopefully, improve survival.³² The long-term consequences of anti-neoplastic therapies has been observed by a cohort done by Bauer et al.²³ This cohort indicated that survivors of children with neuroblastoma, nephroblastoma, Hodgkin's disease and soft tissue sarcomas were more likely to be underweight in the long term. However the degree of long term was not indicated.²³

2.11 DIETARY PROTEIN AND RENAL FUNCTION

Dietary protein intake can modulate renal function, and there is an ongoing concern that habitual consumption of dietary protein in excess of recommended amounts promotes chronic renal disease through increased glomerular pressure and hyperfiltration of the kidney.³³

A review by Martin et al³³ indicated that a high-protein diet was defined as the daily consumption of greater than or equal to 1.5 g/kg/day in adult patients. However, in infants a high protein intake is regarded as 3–4.5 g/kg/day and in children (older than one year), it is known to be 2 g/kg/day actual body weight.⁹

In 1923 the relationship between the level of dietary protein and the rates of urea excretion was first observed and was further supported in a dog model, in which

increased dietary protein intake increased the rate of creatinine and urea excretion in the urine due to resultant changes in GFR. Based on these findings, Van Slyke et al demonstrated that renal blood flow was the basis for GFR-mediated changes in clearance rates in response to increased dietary protein intake. Dietary protein affects GFR, with both acute and chronic increases in consumption increasing GFR.³³

A study by Amore et al³⁴ was conducted on six adult patients with a single kidney without overt renal disease and eight healthy controls to determine whether hyperfiltration induced by an acute response to an oral protein and water load modified the urinary albumin excretion (UAE) in the microalbuminuric range by increasing glomerular filter permeability. Participants were given a 150 g meat-derived protein bolus and 1 l of water and were followed up one hour and four hours later. Investigations included UAE, creatinine clearance and microalbuminuria. At baseline, the participants with one kidney had significantly higher UAE values than the controls. At one-hour follow-up, the UAE values in the single kidney group were significantly higher than in the control group ($p < 0.002$) and an increase in microalbuminuria levels had occurred. High UAE and low creatinine clearance values were maintained over the four-hour observation in participants with one kidney.³⁴

A study by Stribrna et al³⁵ assessed 19 participants with renovascular hypertension and the effect of an acute oral administration of protein (meat snack at 1 g/kg protein) on urinary albumin excretion. Microalbuminuria was recorded in only 31% of the patients, and further results indicated that an acute protein load did not increase albuminuria; however, a significant increase in creatinine clearance was noted. This study recommended 24-hour urine samples for assessment of microalbuminuria.³⁵

The effect of an acute oral protein load (OPL) of 150 g protein on the UAE was assessed by Papagalaniset al³⁶ in subjects who had undergone unilateral nephrectomy more than 10 years ago (18 participants), in subjects who had undergone unilateral nephrectomy less than 10 years ago (21 participants) and in a healthy control group (16 participants). Urine samples were collected and assessed three hours before and after the OPL. At baseline, the UAE in participants who had undergone a nephrectomy more than 10 years ago was higher than the other two groups. The UAE increased significantly after the OPL in subjects who had undergone the nephrectomy less than 10 years ago. The study also suggested that the risk of developing renal insufficiency with a solitary kidney increased in time for more than 10 years, with this increase in risk appearing to follow a progressive compensatory increase in GFR of the remnant kidney during the early years following nephrectomy.³⁶

Research has therefore been done on the effect of protein on renal function in healthy individuals as well as in persons with renal disease and/or solitary kidneys. What can be concluded is that high protein provision directly influences GFR and thus renal function and that over time, renal function in patients with solitary kidneys deteriorates.

Dietary protein provision in patients with renal failure must be strictly controlled and modified according to treatment provided, such as conservative management, peritoneal dialysis or haemodialysis.

Table 2.4 below depicts protein (per kg body weight per day) guidelines for the child and adult with chronic renal failure.³⁸

Table 2.4: Nutritional guidelines for the child³⁷ and adult with chronic renal failure^{38,39,40}

| Age group | Predialysis Protein (g/kg/day) | Peritoneal dialysis Protein(g/kg/day) | Haemodialysis Protein (g/kg/day) |
|---------------------|---|--|---|
| Preterm | 2.5–3.0 | 3.0–4.0 | 3.0 |
| 0.0–0.5 yrs | 1.5–2.1 | 2.1–3.0 | 2.1 |
| 0.5–1.0 yrs | 1.5–1.8 | 2.0–3.0 | 1.5–2.0 |
| 1.0–2.0 yrs | 1.0–1.8 | 2.0–3.0 | 1.5–1.8 |
| 2.0–puberty | 1.0–1.5 | 1.5–2.0 | 1.0–1.5 |
| Pubertal | 1.0–1.5 | 1.4–1.8 | 1.0–1.5 |
| Postpubertal | 1.0–1.5 | 1.3–1.5 | 1.0–1.5 |
| Adults | 0.6–0.75 ³⁸ | 1.3 ³⁹ | 1.2 ⁴⁰ |

One must bear in mind that these guidelines are for patients with diagnosed renal failure and should be implemented for long-term correct nutritional management of patients with such a diagnosis.

Patients being treated for nephroblastoma are not usually in renal failure, and they have high energy and protein requirements. Patients who present with nephroblastoma in South Africa are usually malnourished. Nephroblastoma patients are managed as oncology patients for whom the nutritional provision depends on their nutritional status as well as their needs for growth and development. In a retrospective study done by Holzinger et al,²⁵ 37 nephroblastoma patients' nutritional management and their response to appropriate clinical nutrition were assessed. The median age of the patient population was 47.5 months, with the median daily protein provision being 64.6 g.²⁵ This study demonstrated that early aggressive nutritional support and frequent nutritional assessments were beneficial to patients with nephroblastoma, with nutritional status being enhanced by the nutritional interventions used in the study.

Potential kidney damage is difficult to assess and quantify and the probability of the potential becoming actual is uncertain. In adult and paediatric patients without kidney failure, the recommended dietary reference intakes are applicable.⁴¹

2.12 CONCLUSION

Patients presenting with nephroblastoma require intense medical management, including surgical resection, pre- and post operative chemotherapy as well as possible radiotherapy. Impaired nutrition has an important impact on the overall survival and prognosis of this patient population.

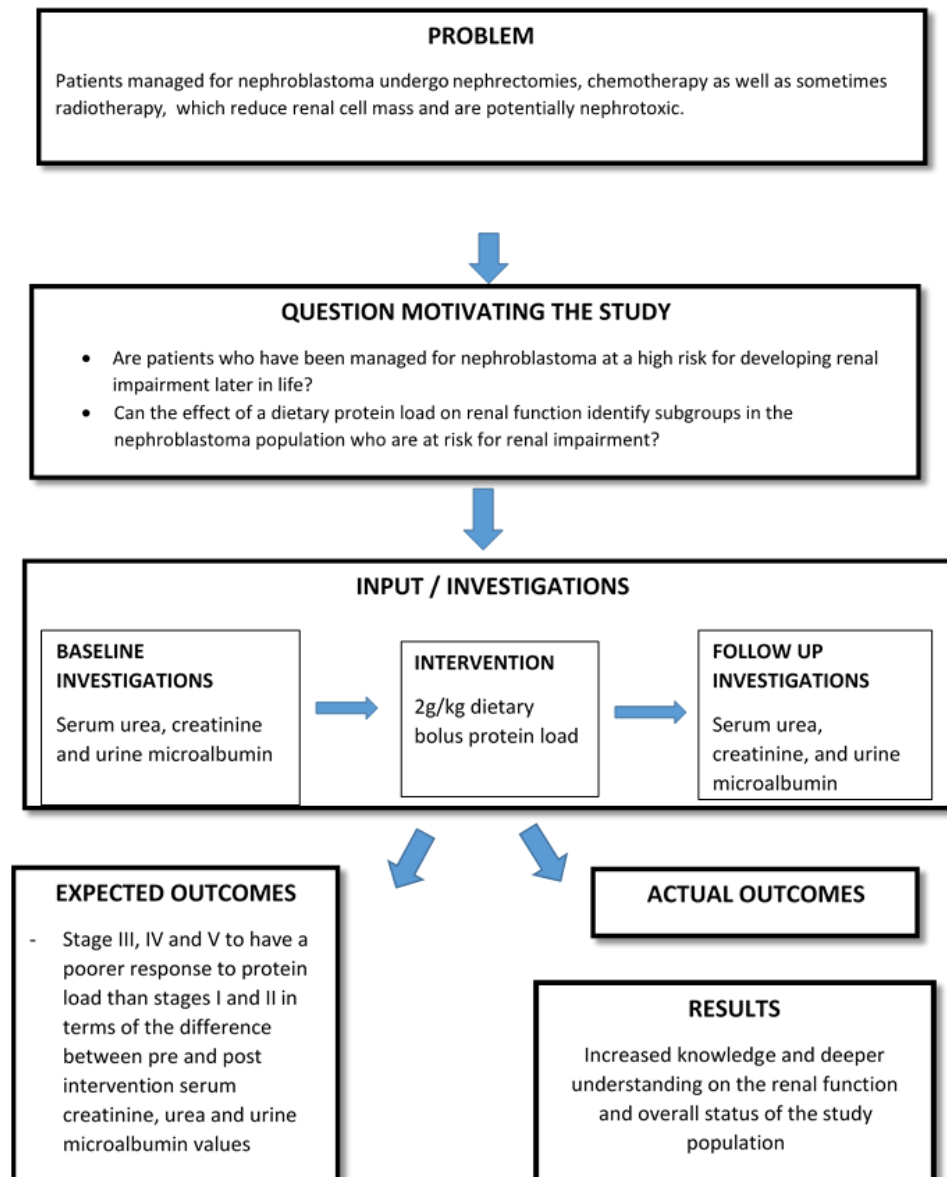
Many aspects of the management of nephroblastoma may contribute to renal impairment in Wilms' tumour patients, and it can be seen that patients who have been managed for nephroblastoma have sub-optimal amounts of kidney tissue. Patients with a solitary kidney develop hypertrophy of the remaining kidney in an attempt to compensate for the workload of the kidney that was surgically removed.

CHAPTER 3: METHODOLOGY

3.1 RESEARCH AIM

To determine the renal handling of a once-off bolus dietary protein load in patients treated for nephroblastoma

3.1.1 Conceptual Framework



3.2 SPECIFIC OBJECTIVES

The objective of the study was to assess the following:

- The effect that the ingestion of a once-off bolus dietary protein load had on patients managed for nephroblastoma in terms of the following:
 - The possible increase in blood urea and creatinine biochemical values.
 - The degree of microalbuminuria.
- Whether the different stages of nephroblastoma (stages I–V) responded differently to the bolus dietary protein load in terms of suspected elevated urea and creatinine levels.
- The effect of maturation status of the patients (pre-/post-pubescent) on the renal handling of a once-off bolus dietary protein load.
- The relationship between the renal handling of a once-off bolus dietary protein load and the blood pressure of patients managed for nephroblastoma.
- The effect of time since diagnosis on the renal handling of a once-off dietary protein load.
- The possible relationship between specific treatment modalities used in the management of nephroblastoma and renal handling of a once-off bolus dietary protein load.

3.3 STUDY PLAN

Study domain: Quantitative

Study design: Non-randomised intervention study in which patients served as their own control before and after a protein load.

3.4 STUDY POPULATION

The study population was gathered from nephroblastoma patients who attended the Paediatric Oncology Clinic at IALCH. This clinic serves all patients who have been managed for nephroblastoma in KZN and who attend the clinic as part of routine monitoring. Despite the clinic being called the 'Paediatric Oncology Clinic', patients who are classified as adults are seen here if they have been managed for nephroblastoma as children. The majority of patients who attend this clinic are ethnic Africans, with Indian and Caucasian patients being uncommon. Patients attending this clinic reside in rural and urban areas, and one can make the assumption that patients attending this clinic generally come from middle- to low-income backgrounds. The service area for this clinic is the whole province of KZN, but private patients are not seen at the clinic. Patients who attend this clinic can speak either English or Zulu, regardless of their culture. Approximately 4–6 patients who have been managed for nephroblastoma are seen at the Paediatric Oncology Clinic per week, with approximately 55 patients being followed up at the clinic per year during the time of the study. Data gathering occurred from May to November 2010. The aim was to obtain 3 – 4 participants per week for a 4 month period providing a population of approximately 48 – 55 participants. This target was not achieved in four months, hence data gathering was extended to seven months to enlarge the study population as much as possible.

3.5 SAMPLING STRATEGY

All patients who attended the clinic and had been managed for nephroblastoma were approached by the primary researcher together with an interpreter (if required).

Those who met the inclusion criteria were asked to participate in the study.

3.6 INCLUSION AND EXCLUSION CRITERIA

3.6.1 Inclusion Criteria

- Patients of any age, ethnicity and gender who had been managed for nephroblastoma and who attended their clinic appointments.
- Patients who had undergone some degree of nephrectomy and/or chemotherapy and/or radiotherapy in their treatment for nephroblastoma.
- Patients who provided written informed consent.
- Patients who spoke either English or Zulu, or who spoke any other language but could communicate with the help of an interpreter and who were willing to sign the informed consent form in either English or Zulu.

3.6.2 Exclusion Criteria

- Patients managed for nephroblastoma who had consequently had kidney transplantation due to renal failure.
- Patients with Denys-Drash syndrome
- Patients diagnosed with chronic renal failure.

3.7 INTERVENTION

After baseline blood and urine samples had been taken, participants were provided with a bolus dietary protein load of 2 g/kg of their body weight, as 2g/kg exceeds the dietary reference intake for children and constitutes a high protein load in both paediatrics and adults.³⁰ Nutren Junior®, a supplement with known protein content (Table 3.1), was used in this study. Protifar®, a modular protein supplement, was added to the standard supplement to reach the required protein load for each participant if the amount required exceeded what was provided by 250 ml of Nutren Junior. This additional protein was added by the researcher in each case. The total amount of protein required differed among patients and was based on their individual weights. Participants were required to consume the full supplement provided.

The same supplement was given to adult and paediatric participants. The volume of supplement varied depending on the total amount of protein that was required to be provided to each patient. The researcher aimed to provide the smallest volume containing the correct amount of protein to reduce excessive volumes consumed (considered > 500 ml for this study) in older adolescents and adults. This was achieved by providing a 250 ml volume of Nutren Junior® supplement enriched with sufficient Protifar® to meet the participants' requirements. However; more than 250 ml was required for some participants.⁴² Table 3.1 provides information regarding the protein content of the supplements.

Table 3.1: Protein provision by Nutren Junior and Protifar^{42, 43}

| Product | Volume | Proteincontent |
|-----------------------------|----------------|----------------|
| Nutren Junior ⁴³ | 250 ml serving | 7.4 g |
| Protifar ⁴² | 5 g scoop | 2.2 g |

Protifar supplement was only added when the calculated required amount of protein exceeded what was provided by 250 ml of Nutren Junior.

After four hours follow-up, urine and blood samples were taken on each participant. During this four-hour period, all routine clinical, biochemical and radiological (chest X-ray and/or abdominal ultrasound) data were gathered. Throughout this period, participants were asked not to eat or drink. However, if young children needed to eat within the time frame and it was not possible to wait until after the follow-up blood samples, the researcher was informed. Every effort to ensure that the child did not consume a high-protein snack during the testing time period was made so as not to influence the results on the follow-up urine and blood tests. The data of patients who did eat during the study (as reported by themselves or their parent/guardian) were still gathered and interpreted in the results due to the small study population.

Clinic appointment times were from 14:00 onwards on a Tuesday, and all participants were seen on their scheduled visits to the clinic. No participants were requested to attend the clinic on a day other than their appointment day for inclusion in the study.

3.8 DATA COLLECTION METHODOLOGY

3.8.1 General Data

The study took place in the Paediatric Oncology Clinic at IALCH. Data were collected over a six-month period (May 2010– November 2010). Data were collected using a structured data gathering sheet that was developed for the study (Addendum 6).

3.8.2 Data Gathered

3.8.2.1 Sociodemographic data

Information was gathering during an interview with the study participants or from their hospital files. The following data were collected:

- Age and date of birth
- Gender

3.8.2.2 Nephroblastoma history and management

The information below was obtained from the patients' hospital files:

- Age at diagnosis
- Stage of disease at diagnosis
- Treatment protocol
 - Chemotherapy agents, dosages and duration
 - Radiotherapy dosages and duration
 - Surgical resection and degree of kidney resection
- Comorbidities

3.8.3 Anthropometrical Data⁴⁴

The weight and height of each participant were measured for this study. The weight was required to determine the protein provision required per individual (a pre determined 2 g/kg protein bolus). The height was required for assessing the blood pressure of the paediatric participants.

The primary researcher conducted all anthropometrical measurements on the study participants. All measurements were done using standardised techniques and the

equipment described below. Due to the effect of clothing on the validity of measurements, patients were asked to remove any excess layers of clothing to reduce measurement error. All anthropometrical measurements were taken in a private room to ensure privacy for the patients.

3.8.3.1 Weight^{44,45}

Participants older than two years:

Weight was measured using a standardised electronic scale: SECA Scale (Volke and Halke Hamburg). The same scale was used throughout the data collection process. For children older than two years and adults, weight was measured to the nearest 0.1 kg. Weight was measured with the participant standing in the middle of the scales platform, without any support. The weight of each individual needed to be equally distributed on both feet. Weight was measured on arrival of the patients to the clinic in the morning of their assessment to reduce diurnal variation. Patients were wearing minimal clothing and no shoes. One measurement was taken per participant

Participants younger than two years:

Weight was measured using a SECA 727 electronic pan-type paediatric scale. Weight was measured to the nearest 0.01 kg. If participants were infants, they were weighed lying down in the middle of the scale, without clothes, and the weight of their diaper was subtracted. One measurement was taken per participant.

3.8.3.2 Height⁴⁴

Participants older than two years:

Standing height was measured using the stadiometer incorporated with the electronic scale: SECA Scale (Volke and Halke Hamburg). The study subjects were barefoot, and any head-dressing or head ornaments had been removed before the measurement was taken. The subjects stood with their heels together, arms by their sides, legs straight, shoulders relaxed and head in the Frankfort horizontal plane. The measurement was taken to the nearest centimetre (cm). One measurement was taken for each participant.

Participants younger than two years:

Length was measured using a measuring device with a stationary headboard and a moveable footboard, which were perpendicular to the backboard. Measurements were recorded to the nearest 0.1 cm. Subjects lay in the supine position, with the Frankfort plane perpendicular to the backboard. The subjects' shoulders and buttocks touched the backboard, the legs were straight and the shoulders and hips were at right angles to the long axis of the body with the feet flat against the footboard. One measurement per participant was taken.

The patient population was divided into three sub-groups namely: 0 – 5 years, 5 – 19 years and > 20 years of age. The 0 – 5 years and 5 – 19 year age groups anthropometrics were assessed according to the WHO growth charts (Addendum 1)⁴⁶

Sub-group 0 – 5 years had gender specific weight for height (W/H) and height for age (H/A) assessed to determine if patients were wasted or stunted. Sub-group 5 – 19 years were assessed for gender specific Body Mass Index (BMI) for age (BMI/A) to

determine if they were overweight or underweight. Adults > 20 years of age had their BMI assessed to assess if underweight, normal or overweight.

3.8.4 Biochemical Data

On admission to the clinic and after signing the informed consent form, participants were sent to the phlebotomist and blood specimens were taken for baseline serum urea and creatinine analysis. A 1 ml blood sample was required for the paediatric participants and a 5 ml sample for adults. After four hours, the procedure was repeated. Blood urea and creatinine were compared to the reference values of the reporting laboratory. This was situated within the hospital, ensuring immediate specimen delivery. Similarly, spot urine samples for microalbuminuria were taken at baseline and after four hours. The laboratory methods used for biochemical analysis are described in Table 3.2 below

Table 3.2: Analytical methodology of biochemical tests

| Test | Analytical methodology |
|------------------|---|
| Urea | Urease with GLDH ⁴⁷ |
| Creatinine | Jaffé alkaline picurate, kinetic with blank rate correction ⁴⁸ |
| Microalbuminuria | Polyethylene glycol enhanced immunoturbidimetric method ⁴⁹ |

GLDH (glutamate dehydrogenase)

All urine samples were taken by the primary researcher to the laboratory on each data collection day. The process for microalbuminuria analysis as indicated by personal correspondence with the National Health Laboratory Service (NHLS) at IALCH is that each urine sample is first assessed with a urine dipstick for the presence of protein in the urine. If protein is present, analysis for microalbuminuria is

not indicated, and if protein is not present, microalbuminuria is tested for. Protein in the urine is assessed in three categories:

1+ equivalent to \pm 30 mg/dl or 0.3 g/l

2+ equivalent to \pm 100 mg/dl or 1 g/l

3+ equivalent to \pm 300 mg/dl or 3 g/l

Microalbuminuria is defined as the presence of albumin in the urine at levels that are higher than normal but lower than those detected by standard protein dipsticks.¹

3.8.5 Clinical Assessment

All participants (paediatric and adult) were examined by a paediatric surgery registrar during their clinic visit, and the following data were recorded in the medical files:

- Abdominal examination for tumour recurrences (yes/no categories).
- Interpretation of chest X-ray and ultrasound for tumour recurrence (yes/no categories).
- Blood pressure value.
- Maturation status (participants were classified as either pre- or post-pubescent).

For patients < 20 years, blood pressure was interpreted according to percentile charts available: Assessing Blood Pressure for Boys and Girls by Age and Height (Addenda 2 and 3).⁵⁰ This tool is used routinely by the Department of Paediatric Surgery at IALCH. It evaluates diastolic and systolic pressure by age and height and classifies the blood pressure into percentiles. For adult patients > 20 years, blood

pressure was compared to the norm of 120/80 and was classified as normotensive or hypertensive, as detailed in Table 3.3 below.

Table 3.3: Adult blood pressure criteria⁵¹

| Blood pressure | Systolic (mmHg) | Systolic (mmHg) |
|----------------|-----------------|-----------------|
| Normotensive | 120 | 80 |
| Hypertensive | ≥ 140 | ≥ 90 |

mmHg = millimetre of mercury

3.8.6 Procedure For Data Collection

On arrival at the clinic, patients were approached by the primary researcher regarding participation in the study. Those patients/parents or guardians of the patient who agreed to participate signed an informed consent form.

Blood samples were taken by the clinic's phlebotomists for the initial baseline and follow-up blood values four hours later. The volume of blood required for a paediatric urea and creatinine blood test was a 1 ml sample and for adults a 5 ml sample. The urine samples required for the microalbuminuria were two single random urine samples –one upon admittance into the study, which was the initial baseline sample, and the other gathered four hours after the first sample had been provided. Table 3.4 describes the reference values provided for serum urea and creatinine values depending on the age groups of the participants. The participants' results were compared to the reference value provided by the NHLS for the age of the study participants (Table 3.4).

Table3.4: The difference in urea and creatinine reference values from NHLS analysis

| Age of participants | Reference range urea (mmol/l) | Reference range creatinine (mmol/l) |
|---------------------|-------------------------------|-------------------------------------|
| 0–12 years | 1.8–6.4 | 27–62 |
| >13 years | 2.1–7.1 | 44–88 |

The urine results were analysed according to the results provided by the laboratory, described in Section 3.8.4.

3.8.7 Statistical Analysis

All data gathered were entered into a database developed by the primary researcher on Excel for statistical analysis. A statistician appointment by SU was consulted for data analysis, and the results obtained are given below. Frequency tables and histograms were used to describe the nominal variables. Descriptive statistics were used to describe the location parameters such as means and medians, and variation parameters such as quartiles and standard deviation were used to describe the variation in the data.

Repeated measures analysis of variance (RMANOVA) was used to determine whether there was a significant difference between pre- and post intervention serum urea, creatinine and urine microalbumin values. RMANOVA is similar to paired t-tests but gives more information about the pre- and post distributions of the variables involved. To compare continuous variables versus several groups or treatments, one-way analysis of variance (ANOVA) was used, and if the residuals were not normally distributed, Kruskal-Wallis tests were used. This approach was used to determine whether there was a significant effect of the different stages of nephroblastoma in response to the dietary protein load.

ANOVA for two groups or Mann-Whitney U tests were similarly used to determine whether there was a significant effect of the maturation status of patients on the renal handling of the population. These tests were also used to determine the relationship of certain chemotherapy agents and the renal function of the population group.

To compare relationships between two nominal variables, crosstabulation statistics with the maximum likelihood chi-square test or Pearson's chi-square test were used. This approach was used to assess the relationship between the nominal responses between the effect of the protein load on serum urea, creatinine or urine microalbumin protein load and the blood pressure and also to determine whether the relationship between high post intervention biochemical values and the time since diagnosis was significant.

ANOVA was used to determine whether the application of post intervention serum urea, creatinine and urine microalbumin values had an impact on the time since diagnosis. Since the residuals were not normally distributed, the analyses were repeated non-parametrically with Mann-Whitney tests.

3.9 ETHICS APPROVAL

Ethics approval was sought from the Committee for Human Research, SU (NO09/08/222), and the Department of Health, KZN (Reference: HRKM059-10). All participants were clearly informed of the reasons for the study, the procedures they or their child would be subjected to as well as the scope of the information required by the researcher.

Participants were informed in either English or isiZulu. The primary researcher used the help of a nursing staff member fluent in isiZulu who was allocated to the clinic

every Tuesday over the course of data gathering. The isiZulu-speaking staff member helped the primary researcher with translation from English to isiZulu and isiZulu to English if required to facilitate communication between the researcher and participants.

Participants were allocated a study number upon entering into the study, and all data gathered were treated as strictly confidential.

All willing participants and/or their parents or guardians signed informed consent forms in either English or isiZulu. Each participant or their parent or guardian kept a copy of the informed consent form, and the primary researcher retained her own copy for record purposes. Children older than seven years of age had to assent to participating in the study prior to their enrolment. Informed consent and assent forms are included as Addendum 4 (English) and 5 (isiZulu) respectfully.

CHAPTER 4: RESULTS

4.1 SAMPLE SIZE

Thirty-four participants who had been previously managed for nephroblastoma were admitted into the study between May and November 2010 and gave their full informed consent in either English or isiZulu.

None were excluded due to the exclusion criteria; however, three patients and their parents refused to participate in the study.

The Centre for Statistical analysis was contacted regarding a power analysis to determine the Effect size (Es) of the study population. The statistical Es between the study population of the thesis (N=34) compared to the annual study population of the clinic (N= 55), which would have been the maximum size of the study population, had data gathering been extended for a full year was assessed.

For dependent samples (i.e. pre and post intervention values) the Es for N=55 was 0.447 and for N=34, the Es was 0.574. For independent samples the Es for N=55 was 0.624 and for N=34 the Es was 0.8

Effect sizes of less than 0.6 and at most 0.75 have been recommended by The Centre for Statistical Analysis. Our study therefore had an appropriate Es for dependent variables and was lacking in power with independent variables.

4.2 DESCRIPTIVE CHARACTERISTICS OF PARTICIPANTS

The descriptive statistics of the study population are depicted in Table 4.1.

Table 4.1: Descriptive statistics of the study population at baseline

| Variable | N | Mean | Median | Minimum | Maximum | Lower quartile | Upper quartile | Standard deviation |
|--|----|--------|--------|---------|---------|----------------|----------------|--------------------|
| Age (months) | 34 | 92.09 | 79 | 24 | 276 | 57 | 120 | 55.24 |
| Weight (kg) | 34 | 23.96 | 19.60 | 9.60 | 65.40 | 17.00 | 25.40 | 12.50 |
| Height (cm) | 34 | 115.83 | 113.25 | 85.00 | 159.00 | 101.50 | 124.00 | 19.54 |
| Diagnosis age (months) | 34 | 41.06 | 36.00 | 10.00 | 108.00 | 22.00 | 56.00 | 26.68 |
| Age for metastases (months) | 8 | 46.63 | 41.00 | 20.00 | 68.00 | 34.50 | 67.00 | 18.36 |
| Radiotherapy dosage (Gy) | 14 | 17.91 | 15 | 12 | 31.50 | 14.00 | 15.00 | 7.39 |
| Systolic BP (mmol/Hg) | 32 | 106.41 | 108.5 | 75.0 | 159.0 | 94.5 | 117.5 | 16.93 |
| Diastolic BP (mmol/Hg) | 32 | 56.28 | 58.0 | 35.0 | 76.0 | 48.0 | 63.0 | 10.64 |
| Time from diagnosis to study (months) | 34 | 51.03 | 33.00 | 9.0 | 252.00 | 18.00 | 61.00 | 52.61 |
| Preingestion urea (mmol/l) | 32 | 4.51 | 4.35 | 2.6 | 8.7 | 3.6 | 5.4 | 1.38 |
| Preingestion creatinine (μ mol/l) | 33 | 64.94 | 68.0 | 28.0 | 98.0 | 45.0 | 81.0 | 20.39 |
| Preingestion microalbumin (mg/mmol) | 18 | 2.89 | 1.23 | 0.15 | 14.94 | 0.61 | 3.92 | 3.61 |

N = Number of participants

4.2.1 SocioDemographic Data

4.2.1.1 Age

Of the 34 participants who were included in this study, 97% (N = 33) were under the age of 20 years and 3% (N = 1) was 23 years of age. There were two participants 18 years and older. The majority of patients presenting to the clinic were minors, with 86% (N =29) of participants being 150 months of age (12.5 years) or younger.

4.2.1.2 Gender, race and pubertal status

Figure 4.1 below illustrates the diversity of the population in terms of race, gender and pubertal status (pre- or post-pubescent).

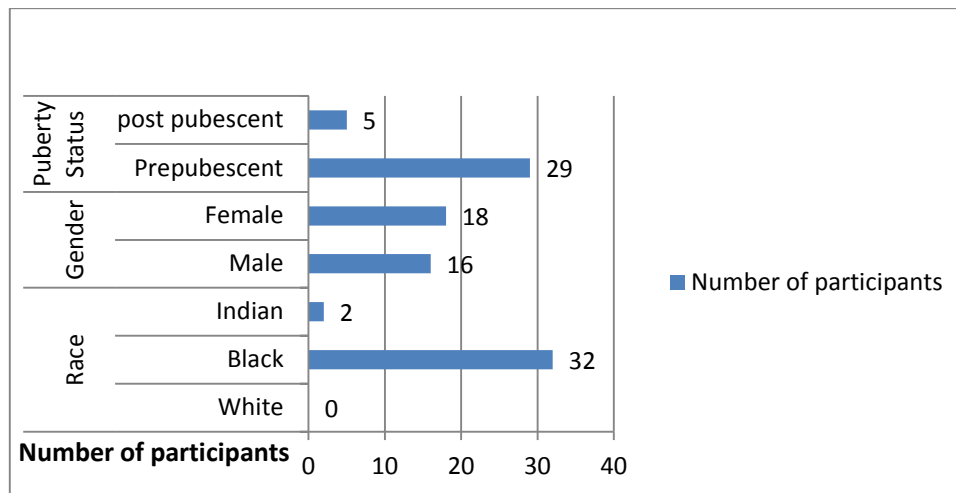


Figure 4.1: The diversity of pubertal status, gender and race of the study population

The population was relatively evenly distributed in terms of gender, with 53% (N= 18) being female. The majority of the population was pre-pubescent. Ninety-four percent (N= 32) of the study population were ethnic African and 6% (N= 2) were Indian.

No white or coloured participants presented to the clinic during the period of data gathering.

4.2.2 Nephroblastoma History And Management

4.2.2.1 Age at diagnosis

The mean age of participants at diagnosis was 41 months, and the median age was 36 months. The age of diagnosis varied, with the youngest age at diagnosis being 10 months and the oldest age being 108 months (nine years).

4.2.2.2 Stage of disease at diagnosis

All stages of nephroblastoma were represented in the study, as seen in Figure 4.2 below. Stage II was the predominant stage in this study population, and 20% (N = 7) of the study population had been diagnosed with Stage V nephroblastoma.

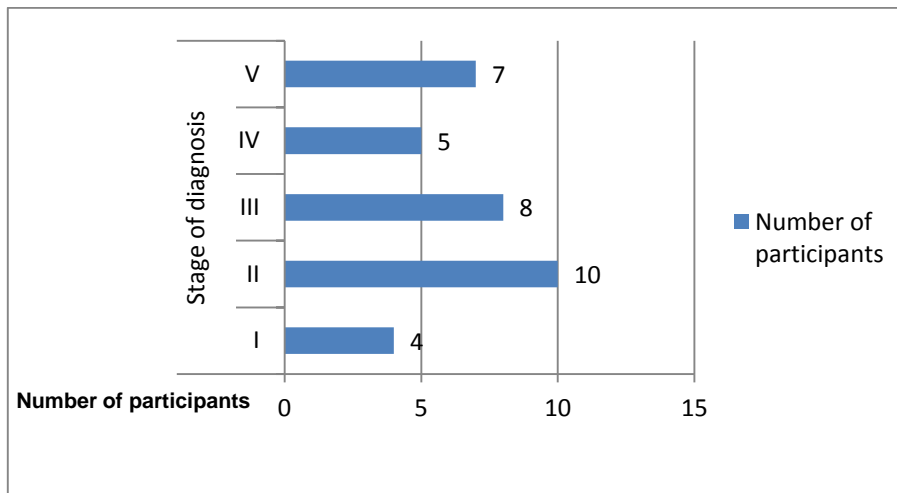


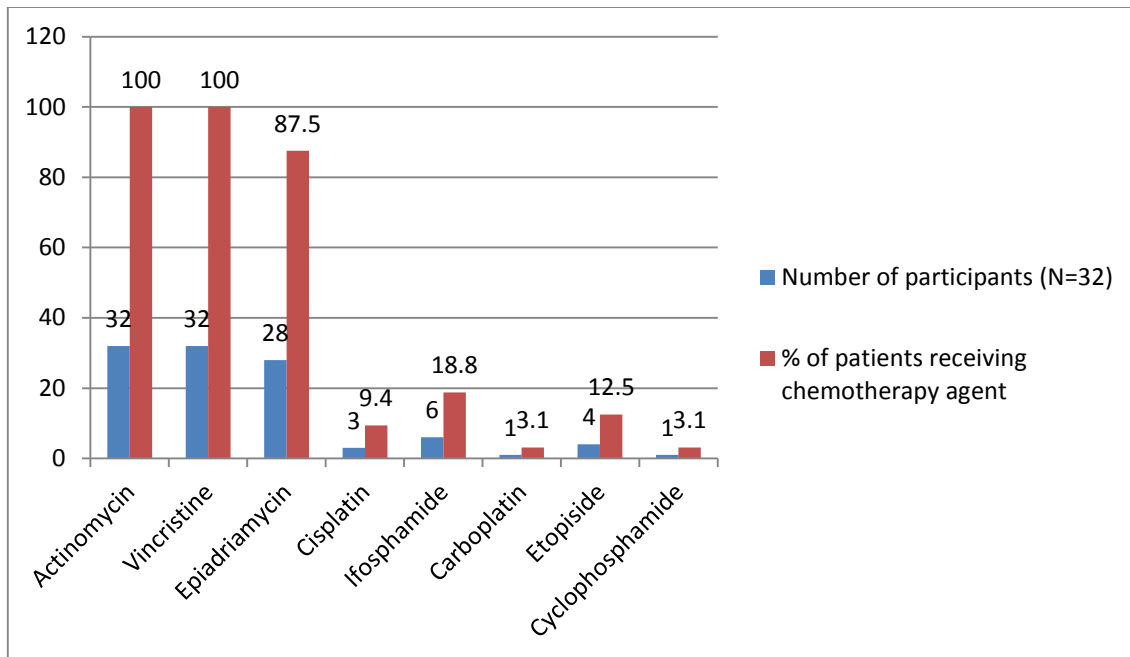
Figure 4.2: The distribution of study participants amongst the different stages of nephroblastoma

4.2.3 Treatment Protocol

4.2.3.1 Chemotherapy agents used in the management of nephroblastoma

Out of the 34 participants, 32 subjects had received chemotherapy and two had not. The most commonly used chemotherapy agents were actinomycin-D, vincristine and epiadriamycin. Cisplatin, ifosfamide, carboplatin, etoposide and cyclophosphamide were less commonly used therapeutic agents. Of the 32 participants who had received chemotherapy, 28 had completed all the chemotherapy and four had not completed the therapy. Reasons for not completing chemotherapy were not noted for this study.

The chemotherapies used in the treatment of the participants are illustrated in Figure 4.3 below.



N = Number of participants

Figure 4.3: Distribution of chemotherapy agents amongst the study population

4.2.3.2 Radiotherapy used in the management of nephroblastoma

Just less than half (N = 14; 41%) of the study population had received radiotherapy as part of their medical management. Five participants (14%) had received lung radiotherapy, 12 (35%) had received abdominal radiotherapy and one (3%) had received additional radiotherapy to the spine.

Of the 14 participants (41%) who had received radiotherapy, seven (50% of the radiotherapy population) had received a radiotherapy dose of 15 Gy. A relatively wide range of radiotherapy dosages had been provided to the 14 participants, ranging from 12 Gy (N = 2; 14%) up to 31 Gy (N = 3; 21%).

4.2.3.3 Surgical resection in the management of nephroblastoma

All participants had undergone surgical resection to some degree in the management of their nephroblastoma. Left nephrectomies (N = 19; 55%) were more common than right nephrectomies (N = 15; 44%). Two (6%) participants had had a left kidney tumorectomy, and four (12%) participants had had a right kidney tumorectomy. Therefore, out of the 34 participants, 18% (N = 6) had had a nephrectomy and contralateral tumorectomy compared to 82% (N = 28) who had only had a unilateral nephrectomy. None of the participants had had a bilateral nephrectomy.

4.2.3.4 Prevalence of metastases in the history of management

Twenty-three percent (N = 8) of the total study population had presented with metastases some time during their management or follow-up assessments for nephroblastoma. Four (12%) of these participants had had metastases upon initial diagnosis, and four (12%) had developed metastases during their treatment or follow-up phase.

The age of participants when their metastases developed was between 20 months and 68 months. Two participants (6%) had developed metastases at the age of 68 months and two (6%) at the age of 41 months.

Of the different areas assessed for metastases namely lung, brain, bone and regional (abdominal including the liver), seven (21%) participants who had metastases had developed them in the lung. Furthermore, three of the seven with metastases to the lungs had also developed abdominal metastases (kidney or liver or abdomen). One patient (3%) presented with abdominal metastases only.

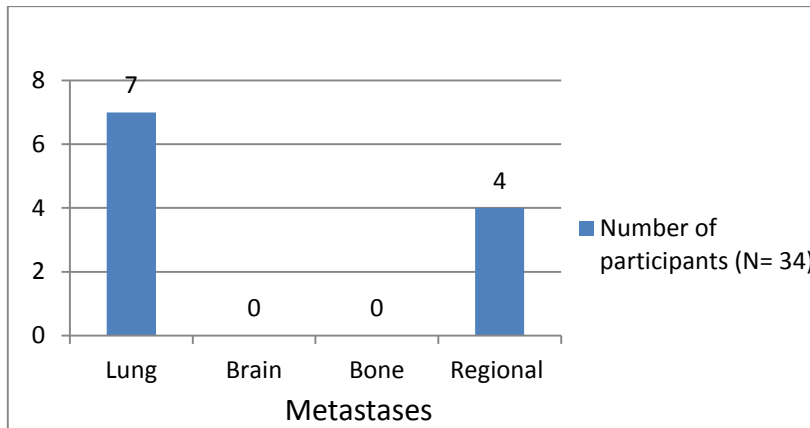


Figure 4.4: The distribution of metastases amongst the study population

4.2.4 Biochemical Data at Baseline

Not all the participants had biochemical data for all the biochemical parameters at baseline and after the protein load. Although blood samples were taken from all participants in the study at baseline and after protein loading, some biochemical values were reported by the laboratory as 'inadequate sample drawn' or hemolysis. Not all urine samples yielded a microalbumin result. Table 4.2 depicts the descriptive characteristics of baseline biochemical data.

Despite not all participants having had conclusive results for all biochemical values, all values available were assessed, including incomplete data sets, and analysed for descriptive statistics due to the small study population.

Table 4.2: Descriptive characteristics of biochemical data at baseline and blood pressure

| Variable | N | Mean | Median | Minimum | Maximum | Lower quartile | Upper quartile | Standard deviation | Reference range |
|-------------------------------------|----|------------|--------|---------|---------|----------------|----------------|--------------------|-----------------|
| Preingestion urea (mmol/l) | 32 | 4.51 | 4.35 | 2.6 | 8.7 | 3.6 | 5.4 | 1.38 | 1.8–6.4 |
| Preingestion creatinine (µmol/l) | 33 | 64.94 | 68.0 | 28.0 | 98.0 | 45.0 | 81.0 | 20.39 | 27–62 |
| Preingestion microalbumin (mg/mmol) | 18 | 2.89 | 1.23 | 0.15 | 14.94 | 0.61 | 3.92 | 3.61 | 0–3.5 |
| Systolic BP (mmol/Hg) | 32 | 106.4 1 | 108.5 | 75.0 | 159.0 | 94.5 | 117.5 | 16.93 | See addenda |
| Diastolic BP (mmol/Hg) | 32 | 56.28 | 58.0 | 35.0 | 76.0 | 48.0 | 63.0 | 10.64 | See addenda |

N = Number of participants**4.2.4.1 Serum urea analysis**

Thirty-two participants (94%) in total had pre ingestion urea results. Only one (3%) of these participants presented with a high urea level before protein ingestion.

4.2.4.2 Serum creatinine analysis

Thirty-three (97%) participants had pre-ingestion creatinine values analysed. Of the 33 participants, 54% presented with high creatinine pre intervention values, which one could interpret as possible baseline renal insufficiency. However, no patients had been clinically diagnosed with renal insufficiency.

4.2.4.3 Urine microalbumin analysis

If a participant presented with protein in their urine detected by a urine dipstick in the laboratory, the analysis for microalbumin did not occur as per NHLS testing standards.

Out of the 34 samples of urine provided for preingestion microalbumin, only 18 samples (53%) were assessed for microalbumin. Ten of the 34 (29%) participants presented with protein in their urine, and six (18%) of the 34 results came back with microalbumin not being detected. Of the 18 samples assessed for microalbumin, 33% (N = 6) had a high microalbumin value at baseline. Therefore, 16 participants presented with protein or a high microalbumin level in their urine at baseline. This could possibly indicate the presence of renal impairment in a portion of the study population prior to intervention. Table 4.7 describes the before- and after-intervention prevalence of protein and microalbumin in the participants' urine samples.

4.2.5 Clinical Data

4.2.5.1 Blood pressure

The blood pressure of each participant was assessed by the primary researcher according to percentile charts used for BP for boys and girls by age and height (Addendum 2, 3). Adult participant blood pressure was compared to adult blood pressure criteria, as stipulated in Table 3.3. The descriptive statistics are highlighted in Table 4.1. In this study, patients were classified as normotensive, prehypertensive or hypertensive as per their blood pressure category. However, this was not a confirmed medical diagnosis of the hypertensive state of participants but was merely a classification for the purpose of the study.

Thirty-two (94%) of the 34 participants had their blood pressure taken and assessed. The reasons for two participants not having BP taken by the clinic are unknown.

Fifty percent (N = 16) of the population presented with normal blood pressure at their clinic visit. Twenty-five percent (N=8) had blood pressure values that were classified as prehypertensive, and 25 percent (N = 8) had hypertensive values.

4.2.5.2 Chest X-rays, ultrasounds and computed tomography scans

During the clinic visits over the duration of data gathering, 32 (95%) of the 34 participants had a chest X-ray done. One participant (3%) had an abnormal chest X-ray presentation. Data gathered only included normal or abnormal radiological findings. Thirty-one participants (91%) had a normal appearance. Thirty-two participants (94%) in total also went for abdominal ultrasound tests. Thirty participants (88%) had a normal ultrasound screen; however, two participants (6%) were assessed to have abnormal ultrasound screens. Only two participants (6%) over the whole data-gathering period had surveillance abdominal computed tomography (CT) scans. Both these scans were classified as normal.

4.2.6 Nutritional Status

Patients' nutritional status on the day of the study was assessed and results are represented below.

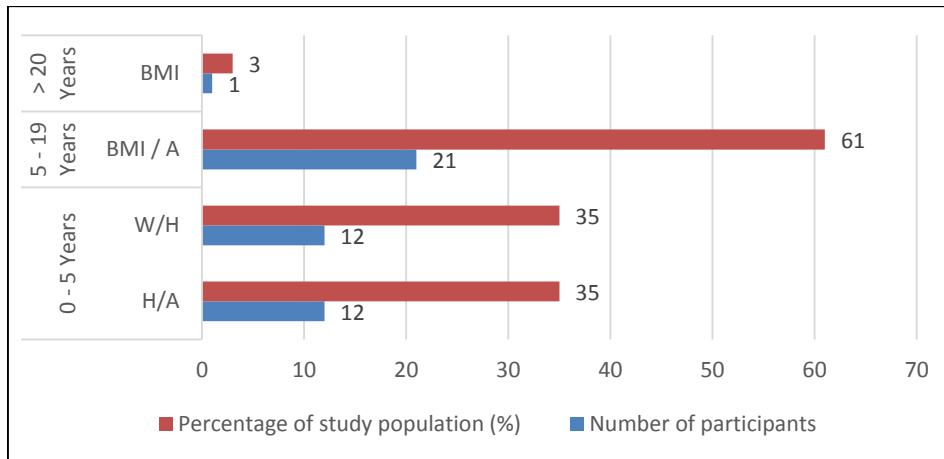


Figure 4.5: The distribution of the different parameters of nutritional assessment used in the study population

The largest sub-group for nutritional assessment was the 5 – 19 years category, followed by 0 – 5 years and then > 20 years of age.

Table 4.3 below addresses how the study population was distributed amongst the WHO nutritional status classification categories.

Table 4.3: Descriptive data on the nutritional status of the population according to WHO charts⁴⁶

| Sub group | Nutritional assessment | <-3 Z score | <-2 Z score | <-1 Z score | <0 Z score | <+1 Z score | <+2 Z score | >+2 Z score | <+3 Z Score |
|------------------------|------------------------|----------------|----------------|----------------|---------------|----------------|----------------|----------------|----------------|
| 0 – 5 years N = 12 | W/H | - | - | 1 (8%) | 1 (8%) | 4 (33%) | 5 (42%) | - | 1 (8%) |
| | H/A | - | 2 (17%) | - | 8 (66%) | - | 2 (17%) | - | - |
| 5 – 19 years N = 21 | BMI /A | - | 2 (9%) | - | 12 (57%) | 5 (24%) | 1 (5%) | 1 (5%) | - |

In the 0 – 5 years age group, only N=2 (17%) of the participants were moderately stunted, with the remainder of the participants having a normal height for age. Only one participant in this age group N=1 (8%) was mildly wasted and the rest of the sub-population well nourished. No children were severely wasted (< -3 Z score W/H).

In the 5 – 19 years age group, N=2 (9%) were classified as thin (< -2 BMI/age), 17 (81%) as normal BMI for age ($< +1$, > -1 BMI/age), 1 (5%) as overweight ($< +2$ BMI/age) and 1 (5%) as obese ($> +2$ BMI/age).

The one adult (> 20 years) had a BMI of 20.3 which was classified as normal.

4.3 RESULTS FROM PROTEIN LOADING

All participants were provided with a supplement to drink after their baseline bloods and urine sample had been taken. This supplement consisted of Nutren Junior supplemented with Protifar to meet each participant's protein supplement provision requirement of 2 g/kg. The mean volume intake of the supplement consumed was 90%, indicating that the majority of patients did consume the full required supplement volume (Table 4.4). The minimum amount of the supplement consumed was 50% of the provided volume (N = 4). However, on average the general consumption of the provided supplement was good, with 73% of the study population consuming 100% of their supplement.

Table 4.4: A breakdown of the volume of protein shake drunk by the study participants

| Percentage of protein shake consumed | Number of participants (%) |
|--------------------------------------|----------------------------|
| 0–49% | 0 (0%) |
| 50– 74% | 6 (18%) |
| 75–100% | 28 (82%) |

The data of patients who ate additional foodstuffs during the study (as reported by themselves or their parent/guardian) were still gathered and interpreted due to the small study population. Information on what they ate is depicted in Table 4.5 below.

Table 4.5: Information on which study participants had additional foodstuffs to eat during their data gathering, reported by themselves or the parent guardian

| Participants who consumed additional food | Food consumed | Protein content of the food eaten | |
|---|--|-----------------------------------|------------|
| | | Per 100 g | Per packet |
| Participant 16 | One small packet of Cheese Naks (22 g) | 5.0 g | 1.1 g |
| Participant 20 | One small packet of Flings crisps (12 g) | 6.6 g | 0.8 g |

Participants who did not consume their entire supplement were still included in the study due to the small number of participants as well as the fact that excluding participants who did not complete the supplement was not stipulated in the protocol for the study. Similarly, participants who ate additional foodstuffs during the intervention period were also included, and the effect on their overall protein load is noted in Table 4.6 below. As seen in Table 4.6, participants still received between 1 and 2 g/kg bolus protein load for this study, with most of the population consuming 2 g/kg protein. However, the impact of this incomplete data set on study outcomes needs to be considered when interpreting results. If a larger study population were available, one could have focused more on including only the participants who consumed 100% of their supplement in this study, which might have made the observed differences more significant.

Table 4.6: A comparison between protein prescribed and provided versus intake for the study

| Participant | Weight (kg) | Protein provided from Nutren Junior and Protifar to meet 2 g/kg | Volume of protein shake drunk (%) | Protein provided from additional foodstuffs | Total protein intake (g/kg) |
|--------------------|--------------------|--|--|--|------------------------------------|
| 1 | 13.6 | 27.2 | 50 | 0 | 1.0 |
| 2 | 18.4 | 36.8 | 75 | 0 | 1.5 |
| 3 | 25.4 | 50.8 | 70 | 0 | 1.4 |
| 4 | 19 | 38 | 100 | 0 | 2.0 |
| 5 | 44 | 88 | 75 | 0 | 1.5 |
| 6 | 19.8 | 39.6 | 100 | 0 | 2.0 |
| 7 | 17.8 | 35.6 | 75 | 0 | 1.5 |
| 8 | 16.1 | 32.2 | 100 | 0 | 2.0 |
| 9 | 17.1 | 34.2 | 100 | 0 | 2.0 |
| 10 | 25.6 | 51.2 | 50 | 0 | 1.0 |
| 11 | 18.8 | 37.6 | 100 | 0 | 2.0 |
| 12 | 17 | 34 | 100 | 0 | 2.0 |
| 13 | 54.8 | 109.6 | 100 | 0 | 2.0 |
| 14 | 45.6 | 91.2 | 100 | 0 | 2.0 |
| 15 | 9.6 | 19.2 | 100 | 0 | 2.0 |
| 16 | 29.2 | 58.4 | 100 | 1.1 | 2.04 |
| 17 | 19 | 38 | 100 | 0 | 2.0 |
| 18 | 13.4 | 26.8 | 100 | 0 | 2.0 |
| 19 | 18.6 | 37.2 | 100 | 0 | 2.0 |
| 20 | 20.4 | 40.8 | 100 | 0.8 | 2.04 |
| 21 | 16.4 | 32.8 | 100 | 0 | 2.0 |
| 22 | 22.6 | 45.2 | 50 | 0 | 1.0 |
| 23 | 19.8 | 39.6 | 100 | 0 | 2.0 |
| 24 | 14.2 | 28.4 | 100 | 0 | 2.0 |
| 25 | 19.6 | 39.2 | 100 | 0 | 2.0 |
| 26 | 22.5 | 45 | 100 | 0 | 2.0 |
| 27 | 25 | 50 | 100 | 0 | 2.0 |
| 28 | 65.4 | 98.1 | 100 | 0 | 1.5 |
| 29 | 23.6 | 47.2 | 100 | 0 | 2.0 |
| 30 | 19.6 | 39.2 | 100 | 0 | 2.0 |
| 31 | 44.6 | 88.2 | 100 | 0 | 2.0 |
| 32 | 16 | 32 | 60 | 0 | 1.2 |
| 33 | 27.6 | 55.2 | 100 | 0 | 2.0 |
| 34 | 14.7 | 29.4 | 50 | 0 | 1.0 |

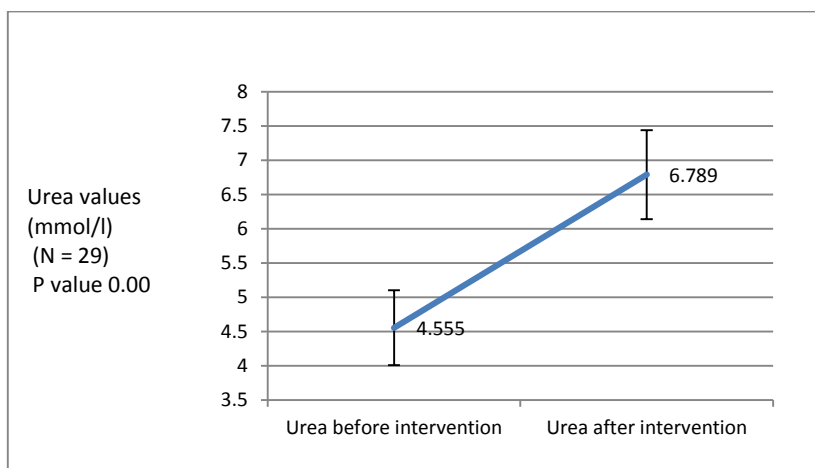
4.4 EFFECT OF PROTEIN LOADING ON STUDY OUTCOMES

4.4.1 The Effect of a Once-Off Bolus Dietary Protein Load on the Renal Handling of Patients Managed for Nephroblastoma

RMANOVA was used to determine whether there was a significant difference in serum urea, creatinine and urine microalbumin levels between pre-and post intervention in subjects for whom both pre- and post ingestion data were available for each specific variable.

Ninety-five percent confidence intervals were used to display differences between pre- and post intervention means, and a significance level of 5% was used in hypothesis testing.

The resultant repeated ANOVA for the difference in urea indicated that there was a significant increase in serum urea levels after protein loading, as seen in Figure 4.6 below ($p < 0.001$).

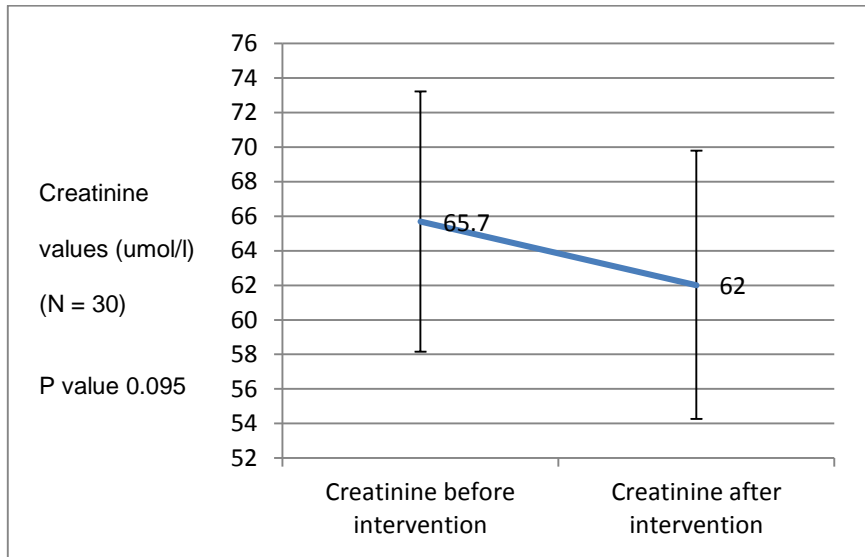


Vertical bars denote 0.95 confidence intervals

N = Number of participants

Figure 4.6: Difference between before and after intervention serum urea values

Thirty participants (88%) had both pre- and post intervention serum creatinine levels available. There was no significant change in mean serum creatinine level before and after intervention ($p = 0.095$). Values achieved are shown in Figure 4.7.



Vertical bars denote 0.95 confidence intervals

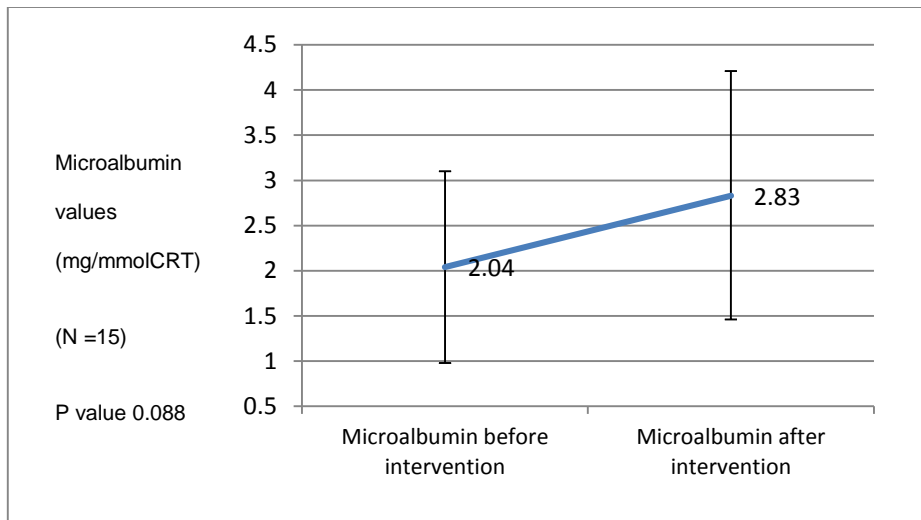
N = Number of participants

Figure 4.7: Difference between before-and after-intervention serum creatinine values of the population.

Only 15 values for microalbumin were assessed due to some urine samples not being assessed for microalbumin as a result of protein particles being present in the urine. Therefore, only 15 participants (44%) had before- and after-intervention microalbumin values available for analysis (analyses using paired t-tests). This differs from descriptive statistics, which describe baseline values, with 18 participants (53%) having microalbumin values available for interpretation.

The mean pre intervention microalbumin value was 2.04 mg/mmolCRT compared to the mean post intervention microalbumin value of 2.83 mg/mmolCRT. Although there was a slight increase in the level of microalbuminuria after protein loading, the

p-value derived from this test was 0.088, indicating that pre- and post intervention microalbumin values did not differ significantly.



Vertical bars denote 0.95 confidence intervals

N = Number of participants

Figure 4.8: The difference between before- and after-intervention urine microalbumin values of the population

Table 4.7 below indicates the urine analyses amongst the study participants before and after intervention.

Table 4.7: Description of before- and after-intervention urine analyses

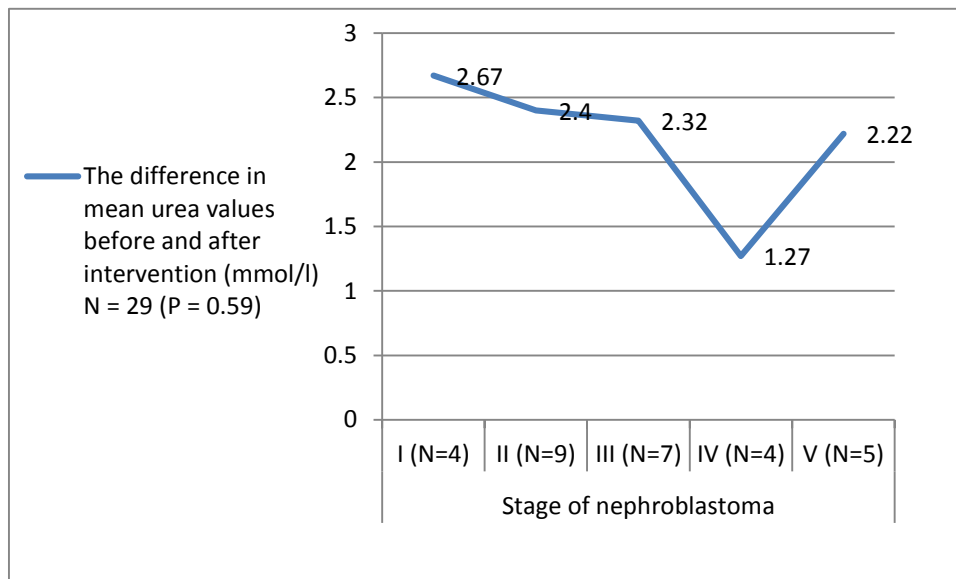
| Number of participants | Before intervention (N) | After intervention (N) |
|------------------------------|-------------------------|------------------------|
| Urine samples collected | 34 | 34 |
| Microalbumin detected | 18 (high levels N = 6) | 20 (high levels N = 9) |
| Protein present in the urine | 10 | 9 |
| No microalbumin detected | 6 | 5 |

N = Number of participants

4.4.2 Effect of the Stages of Nephroblastoma on the Response to a Bolus Dietary Protein Load

4.4.2.1 The difference in mean serum urea before and after protein loading

The mean differences between pre- and post intervention urea values were assessed over the different stages of nephroblastoma and are shown in Figure 4.9 below.



N = Number of participants

Figure 4.9:The difference in mean serum urea values before and after intervention according to the stages of nephroblastoma

ANOVA was used to compare the differences between pre- and post intervention values over the different stages of nephroblastoma. If the residuals were not normally distributed, Kruskal-Wallis tests were used.

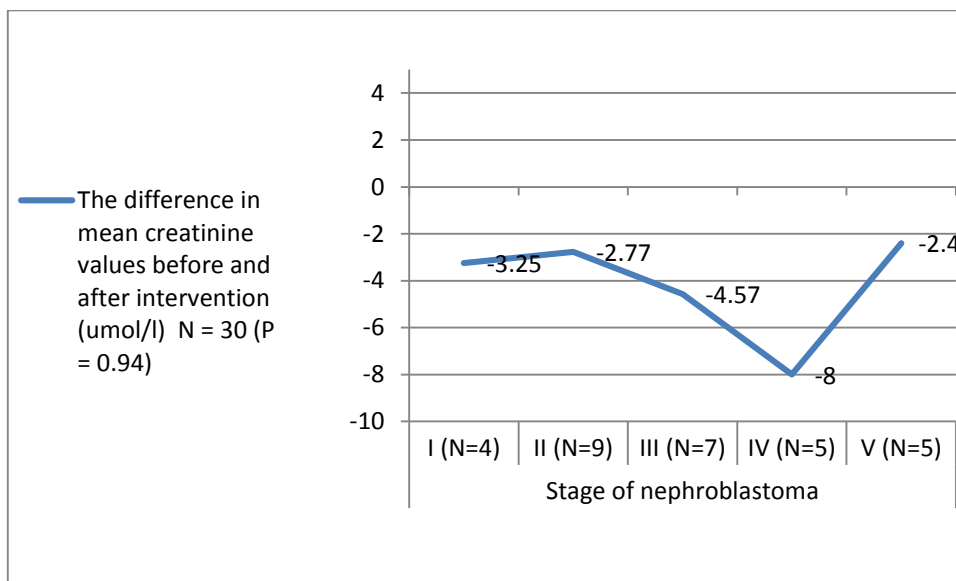
The Kruskal-Wallis method confirmed the non significant differences over the stages as found with ANOVA. ANOVA yielded a p-value of 0.59 and the Kruskal-Wallis test a value of 0.72. The difference in urea values before and after protein loading according to the diagnosis stage was therefore not significant. The number of participants in each stage was, however, very small.

4.4.2.2 The difference in mean serum creatinine values before and after protein loading

The difference in mean serum creatinine values before and after intervention in each stage of nephroblastoma is shown in Figure 4.10.

ANOVA yielded a p-value of 0.94, and the Kruskal-Wallis test similarly gave a p-value of 0.70, which proved that the relationship between stage of nephroblastoma and serum creatinine value was statistically insignificant.

The pre-protein ingestion creatinine levels were actually higher than the post ingestion values (explaining the negative values), but these changes were not significant. It can also be seen that Stage IV participants had the largest mean value for differences in creatinine values, being -8.00 though insignificant.

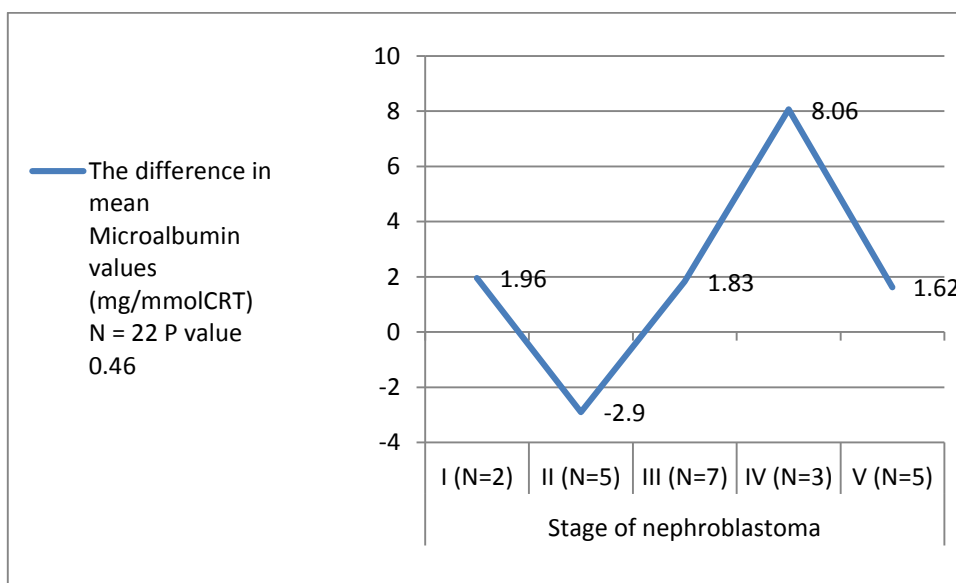


N = Number of participants

Figure 4.10: The difference in mean serum creatinine values before and after intervention according to the stages of nephroblastoma

4.4.2.3 The difference in mean microalbuminuria before and after protein loading

There was no significant difference in the difference in mean microalbumin values before and after protein loading across the five stages of nephroblastoma (ANOVA yielded a p-value of $p = 0.46$ and the Kruskal-Wallis test one of $p = 0.18$). A small population of 22 participants was available for this analysis as that was the number of participants who had microalbumin values across the different stages of nephroblastoma. As in the case of serum creatinine, stage IV nephroblastoma had the biggest but not significant difference between pre- and post intervention mean values, as shown in Figure 4.11.



N = Number of participants

Figure 4.11: The difference in mean urine microalbumin values before and after intervention according to the stages of nephroblastoma

4.4.3 The Effect of Maturation Status of the Patients on the Renal Handling of a Once-Off Bolus Dietary Protein Load

This objective investigated the effect of maturation status on the difference in mean pre- and post intervention urea, creatinine and microalbuminuria levels. This was done to determine whether post-pubescent participants showed a greater difference between the before and after mean values compared to prepubescent participants.

The results are depicted in Table 4.8 below:

Table 4.8: The statistical relationship between the difference in mean before- and after-intervention serum urea, creatinine and urinary microalbumin values and pubertal status

| Biochemical variable investigated | Mean difference before and after protein loading in prepubescent participants | Mean difference before and after protein loading in post-pubescent participants | P-value Least square means | P-value Mann-Whitney U test |
|--|---|---|----------------------------|-----------------------------|
| Serum urea (mmol/l) (N = 29) | 2.29 (N = 24) | 1.96 (N = 5) | 0.60 | 0.49 |
| Serum creatinine (umol/l) (N = 30) | -4.92 (N = 25) | 0.20 (N = 5) | 0.37 | 0.10 |
| Microalbuminuria (mg/mmolCRT) (N = 22) | 2.5 (N = 20) | -7.78 (N = 2) | 0.07 | 0.05 |

N = Number of participants

There was no significant difference between pre- and post-pubescent categories when assessing the difference between pre- and post intervention serum urea and serum creatinine values. Values were obtained using Mann-Whitney U tests.

The difference in mean urine microalbumin values between pre- and post-pubescent participants was borderline significant. This could indicate that post-pubescent participants had a significantly larger difference in mean microalbumin values

compared to prepubescent participants. Post-pubescent participants had progressed through puberty and thus a large growth spurt in their lives, which might have impacted their renal ability to handle a large protein load, hence the large difference between before- and after-intervention mean values. However, one needs to interpret this with caution as the size of the post-pubescent group for differences in mean microalbumin was considerably smaller than that of the prepubescent group (N = 2 compared to N = 20).

4.4.4 The Relationship between the Renal Handling of a Once-Off Bolus Dietary Protein Load and the Blood Pressure in Patients Managed for Nephroblastoma

This objective was assessed using crosstabulation statistics using the maximum likelihood (ML) chi-square test, by comparing the results of participants with normal blood pressure and those who presented with hypertension or prehypertension in terms of the effect on pre- and post intervention serum urea, creatinine and microalbuminuria values.

The results obtained are detailed in Table 4.9 below:

Table 4.9: A summary of the participants who were normotensive, prehypertensive or hypertensive and who presented with normal or high serum urea and creatinine and microalbuminuria before and after intervention

| | Blood pressure classification | | | P-value (Pearson's chi square; ML chi square) |
|--------------------------------|-------------------------------|-----------------|--------------|---|
| | Normal BP | Prehypertensive | Hypertensive | |
| Serum urea | | | | |
| Before intervention (N = 30) | | | | 0.45 |
| Normal blood value (N = 29) | 13 | 8 | 8 | |
| Increased blood value (N = 1) | 1 | 0 | 0 | |
| After intervention (N = 29) | | | | 0.71 |
| Normal blood value (N = 12) | 7 | 3 | 2 | |
| Increased blood value (N = 17) | 8 | 4 | 5 | |
| Serum creatinine | | | | |
| Before intervention (N = 31) | | | | 0.11 |
| Normal blood value (N = 13) | 8 | 4 | 1 | |
| Increased blood value (N = 18) | 7 | 4 | 7 | |
| After intervention (N = 29) | | | | 0.32 |
| Normal blood value (N = 15) | 8 | 4 | 3 | |
| Increased blood value (N = 14) | 7 | 3 | 4 | |
| Microalbuminuria | | | | |
| Before intervention (N = 17) | | | | 0.85 |
| Normal blood value (N = 11) | 5 | 2 | 4 | |
| Increased blood value (N = 6) | 2 | 1 | 3 | |
| After intervention (N = 19) | | | | 0.44 |
| Normal blood value (N = 10) | 6 | 2 | 2 | |
| Increased blood value (N = 9) | 3 | 2 | 4 | |

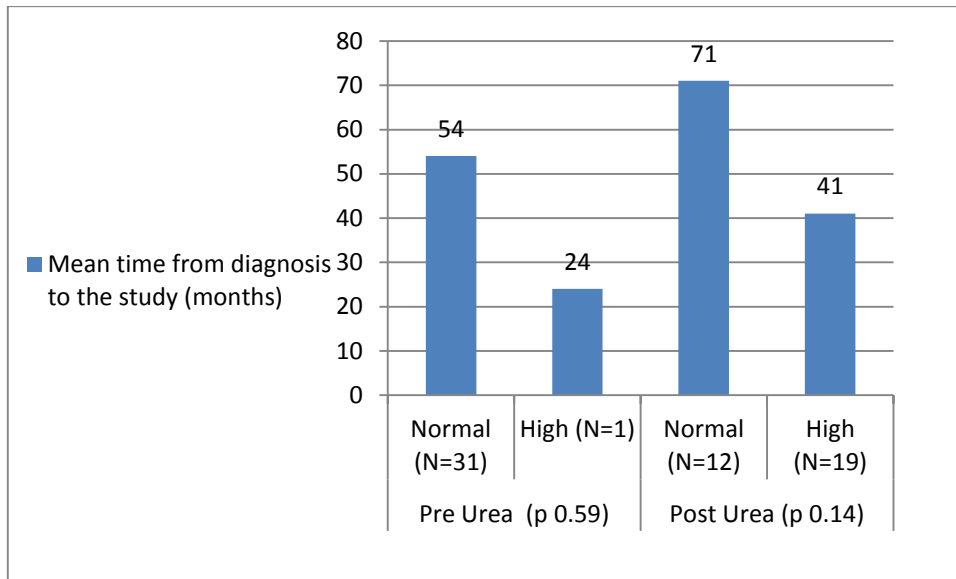
N = Number of participants

ML = Maximum likelihood

There was no statistically significant correlation between the presence of hypertension or prehypertension and increases in post ingestion serum urea, creatinine or microalbumin values. The sub-population analysed for microalbumin was much smaller than those for blood urea and creatinine, and this must be considered when interpreting the results.

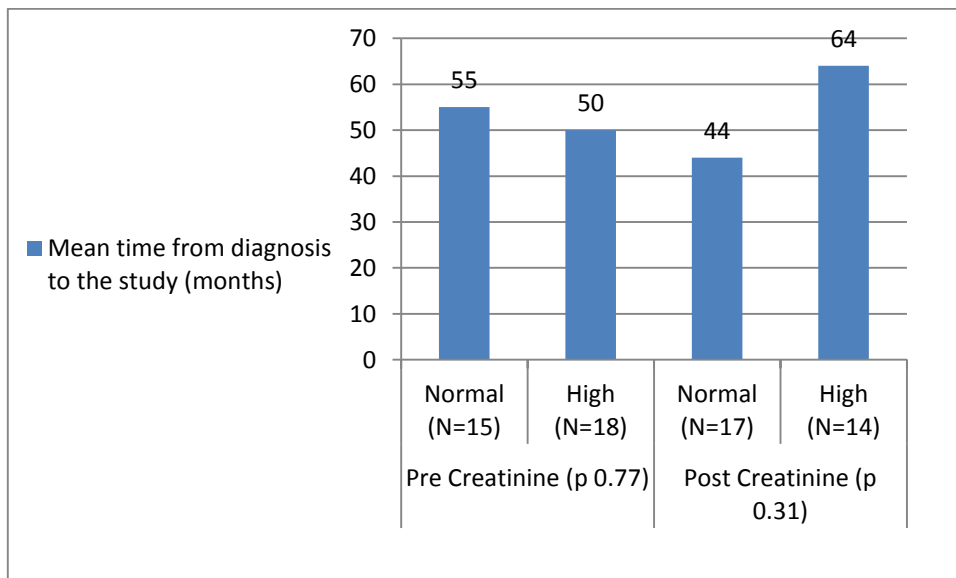
4.4.5 The Effect of Time Since Diagnosis on the Renal Handling of a Once-Off Bolus Dietary Protein Load

The statistical relationships between participants who presented with normal or high pre- and post intervention serum urea, creatinine and urine microalbumin values and their mean time since diagnosis were assessed to determine whether participants who presented with high pre- and especially post intervention biochemical values had a higher mean time since diagnosis than participants with normal biochemical values. All three variables (urea, creatinine and microalbumin) were assessed independently using ANOVA and Mann-Whitney tests to determine the relationship between high biochemical values before and after protein loading and time since diagnosis. ANOVA was used, and statistical significance was set at a p-value of < 0.05 . The difference between mean time since diagnosis pre and post intervention and normal or high serum urea, creatinine and microalbumin values was not proven statistically significant. The results obtained are described in figures 4.12, 4.13 and 4.14 below.



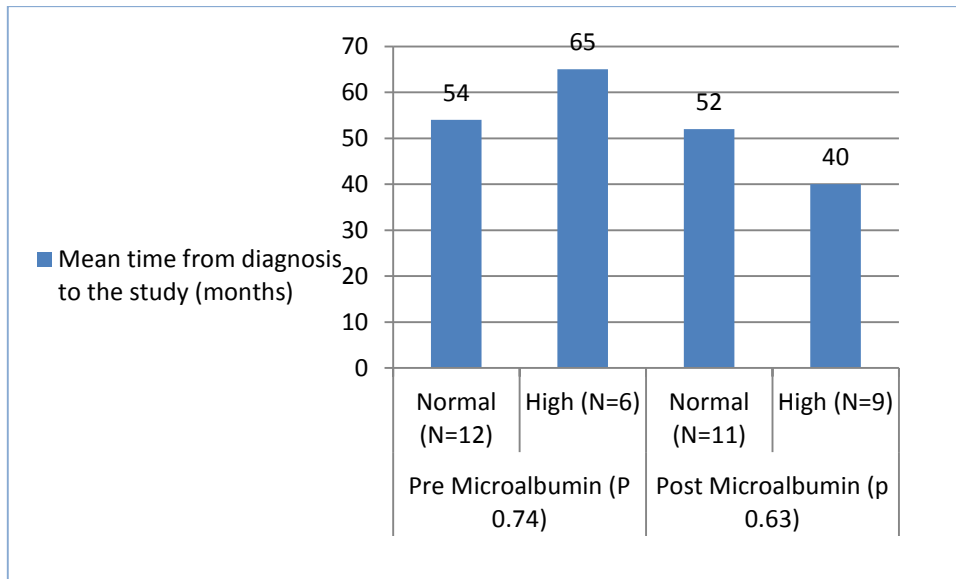
N = Number of participants

Figure 4.12: The statistical relationship between normal and high before- and after-intervention serum urea values and the mean time since diagnosis of the study population



N = Number of participants

Figure 4.13: The statistical relationship between normal and high before- and after-intervention serum creatinine values and the mean time since diagnosis of the study population.



N = Number of participants

Figure 4.14: The statistical relationship between normal and high before- and after-intervention urine microalbumin values and the mean time since diagnosis of the study population

4.4.6 The Relationship between Specific Treatment Agents Used in the Management of Nephroblastoma and the Renal Handling of a Once-Off Bolus Dietary Protein Load

The difference between pre- and post intervention urea, creatinine and microalbumin was compared using ANOVA for two groups or Mann-Whitney U tests between participants who had received ifosfamide or cisplatin and those who had not. A very small subpopulation of the study group had received cisplatin and/or ifosfamide, as indicated in figures 4.15, 4.16 and 4.17 below, which should be taken into consideration in the interpretation of the results.

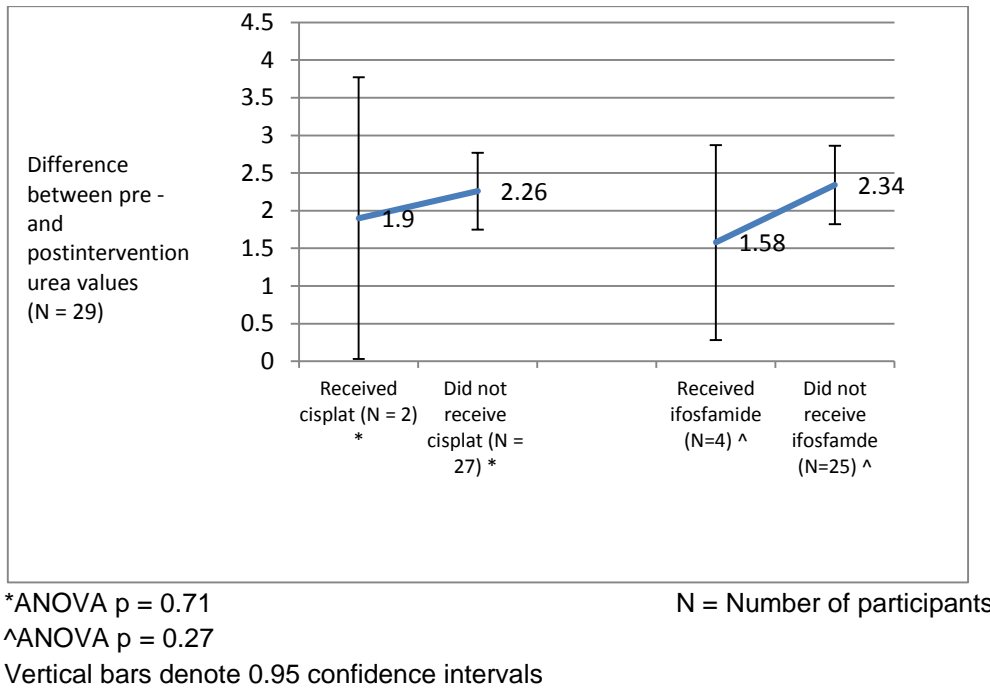
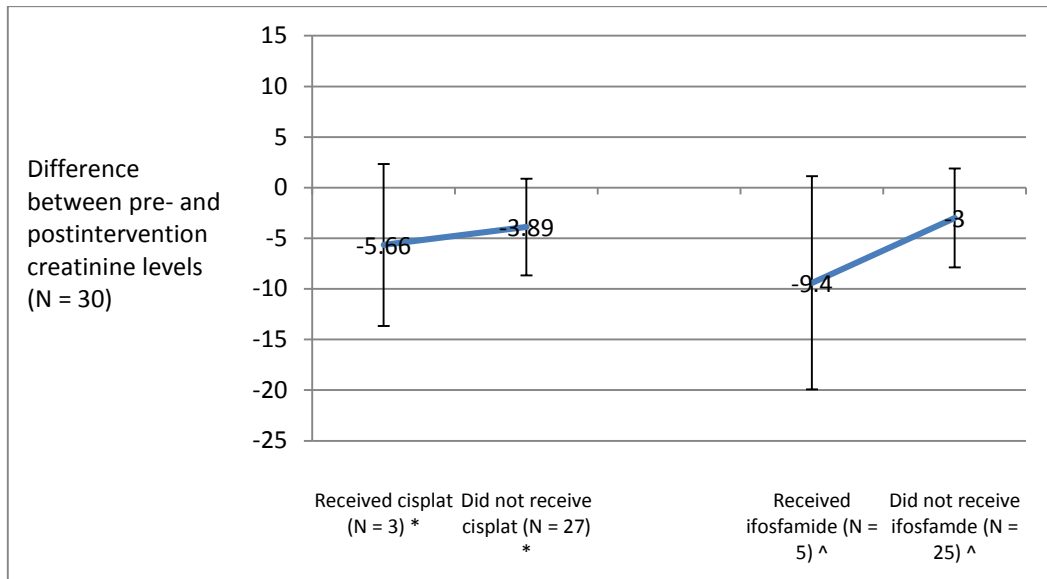


Figure 4.15: The association between the difference in before- and after-intervention serum urea values in participants who had received cisplatin and ifosfamide and those who had not

No significant relationship was found between participants who had received cisplatin and/or ifosfamide with having a larger difference between pre- and post intervention serum urea, creatinine and microalbumin values. The size of the population of participants who had received cisplatin and ifosfamide must be considered when interpreting these results.



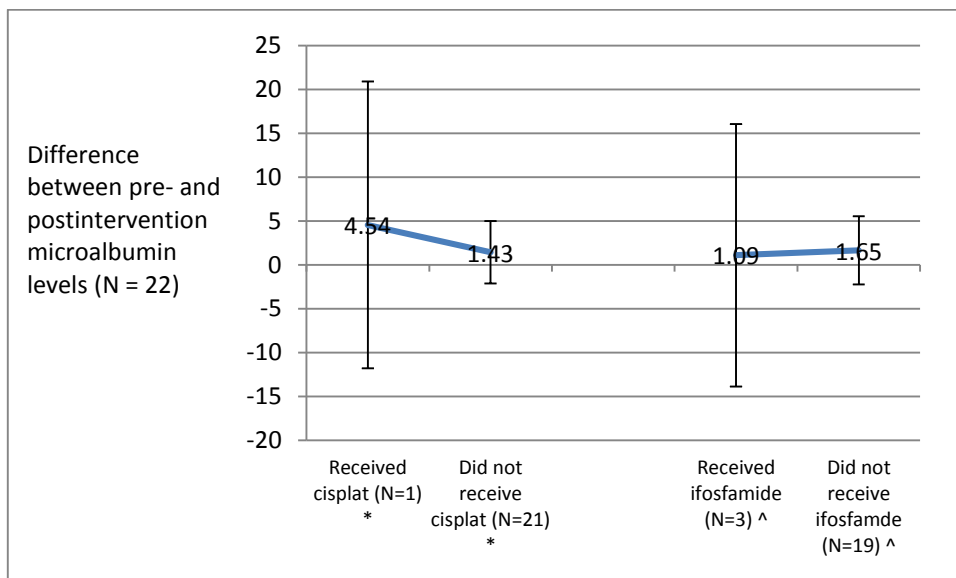
*ANOVA $p = 0.8$

N = Number of participants

^ANOVA $p = 0.26$

Vertical bars denote 0.95 confidence intervals

Figure 4.16: The association between the difference in before- and after-intervention serum creatinine values in participants who had received cisplatin and ifosfamide and those who had not



*ANOVA $p = 0.7$

N = Number of participants

^ANOVA $p = 0.91$

Vertical bars denote 0.95 confidence intervals

Figure 4.17: The association between the difference in before- and after-intervention in urine microalbumin values in participants who had received cisplatin and ifosfamide and those who had not

CHAPTER 5: DISCUSSION

The aim of the study was to determine renal handling of a once-off dietary protein load in patients managed for nephroblastoma in terms of the objects set out for the study.

This was a cross-sectional descriptive study conducted at IALCH over a period of seven months in 2010. The descriptive statistics of this study provide some valuable insight into the study population. There were 34 participants included in the study. None of the participants included had been diagnosed with renal impairment, hypertension or renal failure.

5.1 THE EFFECT OF A ONCE-OFF BOLUS DIETARY PROTEIN LOAD ON THE RENAL HANDLING OF PATIENTS MANAGED FOR NEPHROBLASTOMA IN TERMS OF CHANGES IN SERUM UREA, CREATININE AND URINARY PROTEIN

All participants had blood and urine taken for pre- and post intervention serum urea, creatinine and urine microalbumin levels.

A significant increase between pre- and post intervention serum urea values occurred, indicating a possible degree of impairment of the renal function in response to the dietary protein load; however, there was no significant difference between pre- and post intervention serum creatinine values. Despite no significant difference, one would expect the post intervention serum creatinine value to be higher than the pre intervention value, as with the urea trend, as increased dietary protein intake increases the rate of creatinine and urea excretion due to resultant changes in GFR.³³ However, the mean pre intervention serum creatinine value was higher for

the study population than the post intervention value. This could possibly indicate a degree of renal impairment already present in the study population at baseline, but further increased post intervention serum creatinine values would then be expected. Cozzi et al¹⁹ confirmed in 2012 that 20–40% of children with unilateral Wilms' tumour treated with nephrectomy presented with Stage II chronic kidney disease; however, such chronic kidney disease was not seen in this study at baseline.

A very small subpopulation was analysed for the difference between pre- and post intervention mean microalbumin values, with no significant change in microalbuminuria after intervention. No studies for nephroblastoma populations on this subject could be found, however Green reported that microalbuminuria or proteinuria was reported in 0 – 36% of Wilms tumour survivors with an overall prevalence of 14.8% in those who received radiotherapy and 7.8% in those who did not. This was seen without patients receiving a high dietary protein load. This degree of presence of microalbuminuria was not detected in our study population.¹⁷ However, similar results occurred in a study of 19 patients with renovascular hypertension and the effect of a protein load (1 g/kg body weight) on urinary albumin excretion. After administration of that acute protein load, microalbuminuria was recorded in 31% of the participants and the study concluded that an acute protein load did not increase albuminuria.³⁵ Another study, however; suggested that adult patients with a single kidney with reduced renal function reserve presented with a significant ($p < 0.002$) increase in microalbuminuria following oral protein (150 g meat-derived protein bolus) and 1 l water load compared to control subjects. This study included six participants and eight controls.³⁴ Perhaps with the present study, a significant value would be achieved in a larger study population. Overall, the study

population did not handle dietary protein load as expected, with one expecting to see most post intervention values to be higher than pre intervention values, as dietary protein affects GFR, with both acute and chronic increases in consumption increasing GFR.³³

5.2 THE EFFECT OF THE DIFFERENT STAGES OF NEPHROBLASTOMA ON THE RESPONSE TO A BOLUS DIETARY PROTEIN LOAD

This objective determined whether participants from different diagnostic stages of nephroblastoma responded differently to the bolus dietary protein load in terms of the difference in values of urea, creatinine and microalbuminuria before and after intervention. One would expect participants with Stage IV or V nephroblastoma to possibly have a larger difference between pre- and post intervention values, considering that these subpopulations often have undergone further surgical resections than the other three stages (with Stage V often involving a nephrectomy as well as a tumorectomy, i.e. the removal of more renal mass) as well as radiotherapy and further chemotherapy agents, which negatively influence renal function.^{12,13,16,17,20} A study published in 2013 by Cozzi et al¹⁸ assessed the renal function adaptation up to the fifth decade after treatment of children with a unilateral renal tumour (not necessarily Wilms' tumour); the estimated GFR was used to measure renal function. This study showed no significant differences in mean GFR between patients treated by three-drug chemotherapy and/or radiotherapy and patients treated by nephrectomy and two-drug chemotherapy. Different measurements were used compared to the present study; however, the non-

significant relationship between two- and three-drug chemotherapy and/or radiotherapy on renal function is important to note, as it differs from other literature that shows the influence of certain chemotherapies and radiotherapy on renal function in terms of GFR.¹⁸

Stage I nephroblastoma participants had the largest difference in mean urea values before and after intervention, compared to Stage IV nephroblastoma participants who had the smallest difference. The Stage IV nephroblastoma subpopulation had the biggest difference between pre- and post intervention mean serum creatinine levels as well as microalbumin values, which was expected, but this was not statistically significant.

The different stages of nephroblastoma did not all respond similarly to a bolus dietary protein load in terms of a significant difference between pre- and post intervention mean urea, creatinine and microalbumin values. Uniformity in response to the dietary protein load across the different stages of nephroblastoma was expected, with the difference in mean pre- and post intervention serum urea, creatinine and microalbumin values expected to be raised for Stage IV or V nephroblastoma patients. One cannot conclude from the findings that one specific stage of nephroblastoma responds more intensely to a dietary protein load compared to others, as no statistical relationships have been proven.

5.3 THE EFFECT OF MATURATION STATUS OF THE PATIENTS ON THE RENAL HANDLING OF A ONCE-OFF BOLUS DIETARY PROTEIN LOAD

This objective was to detect whether post-pubescent participants presented with a larger difference between pre- and post intervention biochemical values than

prepubescent participants and to determine whether this association was statistically significant.

There was no significant difference between the mean pre- and post intervention serum urea and creatinine values in pre- and post-pubescent participants. There was a very large yet insignificant difference between the mean pre- and post intervention serum creatinine values in the pre-pubescent subpopulation. This subpopulation was much larger than the post-pubescent group.

Cozzi et al¹⁸ found a direct association between aging and increasing number of patients with decreased renal function after nephrectomy for unilateral renal tumour during childhood. This study assessed renal functional adaptation up to the fifth decade after treatment, which differs from the present study that compared only pre and post-pubescent participants, none of which were in their fifth decade after treatment.

The difference in the mean pre- and post intervention microalbumin values in the post-pubescent group was of borderline significance ($p = 0.05$). This could be interpreted as meaning that participants who are post-pubescent and whose kidneys have undergone stress during puberty have responded poorly to the dietary protein load, with a borderline significantly higher post intervention microalbumin value being found. This may indicate a degree of renal impairment in post-pubescent participants, highlighted by their response to a bolus dietary protein load in terms of microalbuminuria. This however; was not supported by post-pubescent participants' post intervention serum and creatinine values.

There were study limitations affecting this objective. The main problem was that the subgroups between pre- and post-pubescent participants were very different, with the post-pubescent population consisting of only five participants for urea and creatinine and only two participants for microalbumin due to limited microalbumin data. The results should therefore be interpreted with caution.

5.4 THE RELATIONSHIP BETWEEN THE RENAL HANDLING OF A ONCE-OFF BOLUS DIETARY PROTEIN LOAD AND BLOOD PRESSURE IN PATIENTS MANAGED FOR NEPHROBLASTOMA

Brenner's theory indicates that reduced nephron mass leads to hyperfiltration and hypertrophy of remaining nephrons, resulting in progressive deterioration of renal function with proteinuria and hypertension.⁵²

Participants who presented with high pre-intervention creatinine and urea values (values exceeding the normal range) had a higher prevalence of prehypertension and hypertension than participants who had a normal pre-ingestion creatinine and urea value. Statistical tests however; proved the association between raised serum creatinine and urea values and increased blood pressure statistically insignificant.

There was a high (50%) but non significant prevalence of hypertension amongst participants with a high post intervention microalbumin value. However, the sub-population for microalbumin assessment was much smaller than that for urea and creatinine, so these results should be interpreted with caution. A study by Shirzai et al⁵² assessed the serum cystatin, serum creatinine, microalbumin and B2 microglobulin levels in 24-hour urine and the relation to ambulatory blood pressure

parameters of children with a solitary kidney compared to healthy controls. The results showed that children with solitary kidneys had a normal GFR and blood pressure but higher urinary microalbumin excretions in long-term follow-up, with a significant urinary microalbumin excretion in patients living with a solitary kidney for more than five years. The authors speculate that urinary microalbumin occurred due to hyperfiltration in the long run before hypertension developed and GFR decreased. This therefore emphasises the need to monitor urinary microalbumin in children with solitary kidneys to detect kidney function deterioration before hypertension develops.⁵² The longitudinal progression of chronic kidney disease, and therefore its associated hypertension can better be interpreted using serum creatinine, or cystatin rather than GFR, and where proteinuria is present, to monitor for progression of renal function.¹⁷

5.5 THE EFFECT OF TIME SINCE DIAGNOSIS ON THE RENAL HANDLING OF A ONCE-OFF DIETARY PROTEIN LOAD

This objective wished to determine whether time since medical management affected the renal protein handling of the participants and therefore contributed towards the overall determination of renal function in these patients.

The difference between time since diagnosis and pre- and post ingestion normal and high urea values was not statistically significant. The assumption that the longer the time since diagnosis and management is the poorer the renal response to a dietary protein load and therefore perhaps the poorer the renal function is cannot be confirmed in this study population. Larger studies in populations elsewhere have confirmed deterioration of renal function in a solitary kidney or in patients after nephroblastoma management over time.^{18,52} A Review on the evaluation of renal

function after successful treatment for unilateral non-syndromic Wilms tumour patients reviewed 19 studies. Eleven studies including participants who had received abdominal irradiation and 8 studies not including participants with abdominal irradiation. Their duration of follow up and the percentage of participants with proteinuria/microalbuminuria and the percentage with decreased GFR was assessed. These reports showed that the longer the median or mean duration of follow up, the higher the percentage of patients with proteinuria / microalbuminuria or decreased GFR. However this review did not conclude any direct statistical relationship between duration of follow up (i.e. time since diagnosis) and renal function. The 20 year cumulative risk of end stage renal disease among syndromic Wilms ranged from 43 – 83% but the 20 year cumulative risk of less severe degrees of renal dysfunction among non-syndromic Wilms' was classified as small.¹⁷

5.6 THE RELATIONSHIP BETWEEN SPECIFIC TREATMENT AGENTS USED IN THE MANAGEMENT OF NEPHROBLASTOMA AND THE EFFECT ON RENAL HANDLING OF A ONCE-OFF BOLUS DIETARY PROTEIN LOAD

The researcher set out to determine whether participants who had received cisplatin or ifosfamide in their medical management would demonstrate a greater difference between pre- and post intervention creatinine, urea and microalbumin values than those participants who had not received these agents. This investigation was based on the assumption that participants who had received renal toxic chemotherapy agents and abdominal radiotherapy would have a poorer renal response to a large dietary protein load than those who had not received renal toxic chemotherapy or radiotherapy.^{5,12} This relationship could not be confirmed in the study population as the difference failed to reach statistical significance. However, it can be seen that

often the overall mean difference between pre- and post intervention values is larger for those who have received ifosphamide or cisplatin than those who have not. Similarly, a study assessing renal function adaptation after treatment of children with unilateral renal tumours (including but not limited to Wilms' tumour) over five decades found no significant differences in post nephrectomy renal function adaptation between patients who did or did not have chemotherapy and/or radiotherapy.¹⁸ The groups receiving ifosfamide and cisplatin were considerably smaller than the groups who did not receive these chemotherapy agents as part of their overall medical management for nephroblastoma.

5.7 LIMITATIONS OF THE STUDY

There was no control group used in this study. The use of a control group would have allowed for a better comparison of the nephroblastoma population to a study population without nephroblastoma. If controls were used in this study, a matched number of controls for the study population would be recommended. The use of a control group was not in the scope of this study.

The study population was small, resulting in small subpopulation groups for analysis. A larger study population may have bigger statistical power to identify significant findings.

The study population assessed (N = 34) was not as diverse as the complete population who presents itself to the clinic on an annual basis (it was estimated at the time of data gathering that 55 participants attended the outpatient clinic annually). Perhaps participants from a wider age range and more diverse ethnic backgrounds could have been included if the data gathering had occurred over the entire year.

Data sets collected were not always complete for every participant, as reported in the methodology and results for biochemical analyses, which might have affected the interpretation of the study results. The result was that for some variables, the sample size was smaller than the total study sample.

Studies looking at long-term renal function in solitary kidneys and after management of specific conditions such as Wilms' tumour may span decades.¹⁸ The mean time from diagnosis to the current study was 51 months (four years), and the study did not assess longitudinal data but made only a cross-sectional analysis. A longitudinal study of the same population group assessing renal function over decades could provide a clearer picture than a once-off response to a dietary protein load.

Not all participants consumed 100% of the required supplementation drink provided for the study; however, participants did consume between 1 and 2 g/kg protein, with the majority consuming the required volume of their drink. However, the results of this study need to be interpreted with this in mind, and for future studies, analysing participants who only consumed 100% of their required shake may improve the statistical validity of the results.

The study did not identify the difference between HIV positive and negative participants as well as participants who had TB either during their management or during their follow up and therefore during the study intervention. HIV and TB are important contributing factors to the overall morbidity and mortality of patients in South Africa, and the knowledge of their influence on the renal function of patients managed for Nephroblastoma would have contributed significantly to the findings of the study. The inclusion of HIV and TB involvement in future studies is recommended.

CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS

6.1 CONCLUSIONS

The aim of the study was to determine the overall renal handling of a once-off dietary protein load in patients managed for nephroblastoma. The study was unable to statistically prove that participants managed for nephroblastoma had poor renal handling of a once-off dietary protein load in terms of the objectives specified.

More specifically, there was a significant increase between pre- and post intervention serum urea values, indicating a possibly impaired renal response of the participants' kidneys to the dietary protein load. However, no significant difference was noted between the pre- and post intervention serum creatinine and urine microalbumin values.

No significant effects were found for the following:

- The different stages of nephroblastoma and participants' response to the dietary protein load.
- The effect of maturation status on the renal handling of a protein load in terms of participants' pre- and post intervention serum and urine biochemical values.
- The renal handling of a once-off bolus dietary protein load and the blood pressure of patients managed for nephroblastoma.
- The effect of time since diagnosis and the response to a protein load in terms of pre- and post intervention serum urea, creatinine and urine microalbumin values.
- The effect of ifosphamide and cisplatin on the response to a dietary protein load.

6.2 RECOMMENDATIONS

It is recommended that a larger and more representative study population be assessed and that further tests and indicators be used to determine renal function after management of nephroblastoma, especially of a South African population as many studies are conducted in first world countries.

Although this study was unable to prove that participants with nephroblastoma presented with renal impairment after receiving a large dietary protein load, awareness has been created around this study population and its renal function in response to a dietary protein load. Routine follow-up outpatient clinic care should include an aspect of assessing baseline renal function (serum urea and creatinine) at each visit to develop a longitudinal data set for each patient on how their renal function adapts over time as well as to monitor for renal insufficiency if or when it presents itself.

This study was conducted on South African participants and most of them from lower socioeconomic backgrounds. Neither the nutritional status nor the HIV/tuberculosis (TB) status of the participants were included, all of which would have further implications on the renal function of the participants, as HIV-associated nephropathy and malnutrition (including malnutrition associated with HIV and TB) all impact renal function negatively. The reality is that malnutrition, HIV/AIDS as well as TB are prevalent in South Africa, and thus these factors should definitely be included in further studies if the results are to be compared and perhaps utilised in the South African nephroblastoma population.

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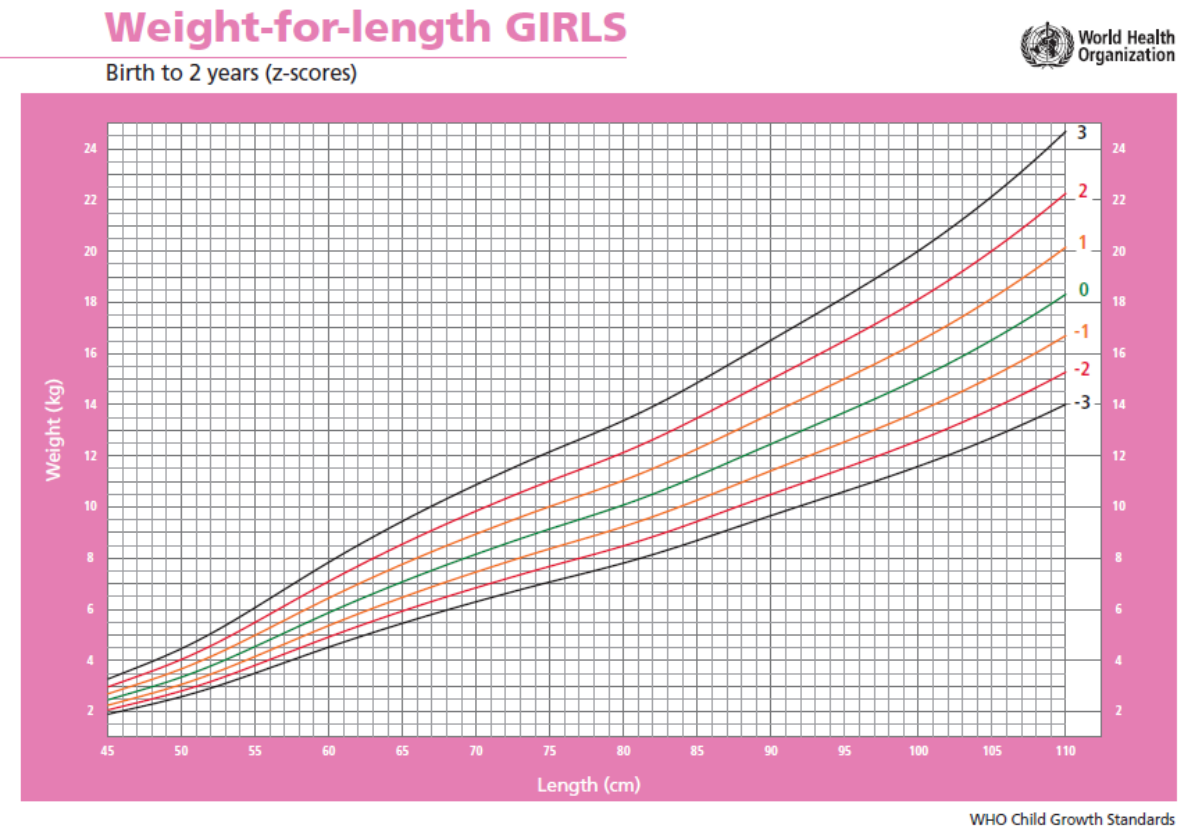
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ADDENDA

ADDENDUM 1: WHO GROWTH CHARTS

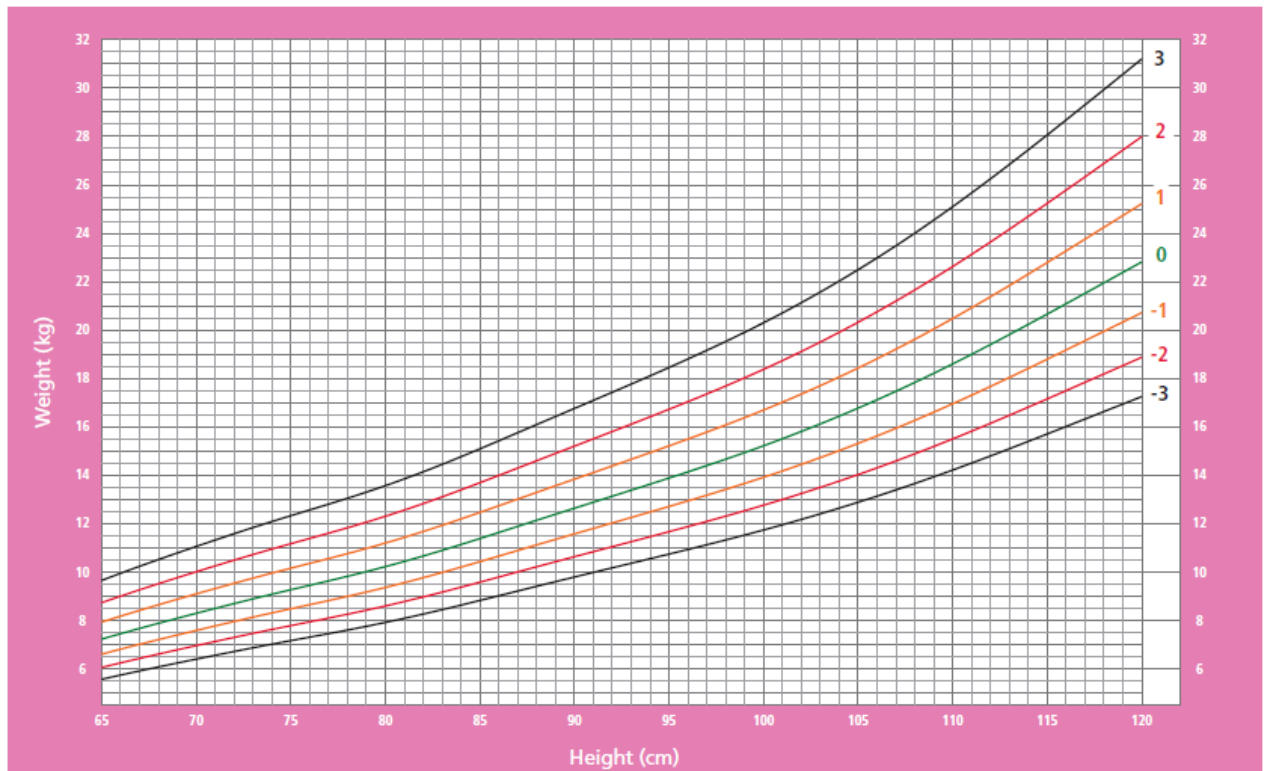
- Weight for length girls



- **Weight for height girls**

Weight-for-Height GIRLS

2 to 5 years (z-scores)

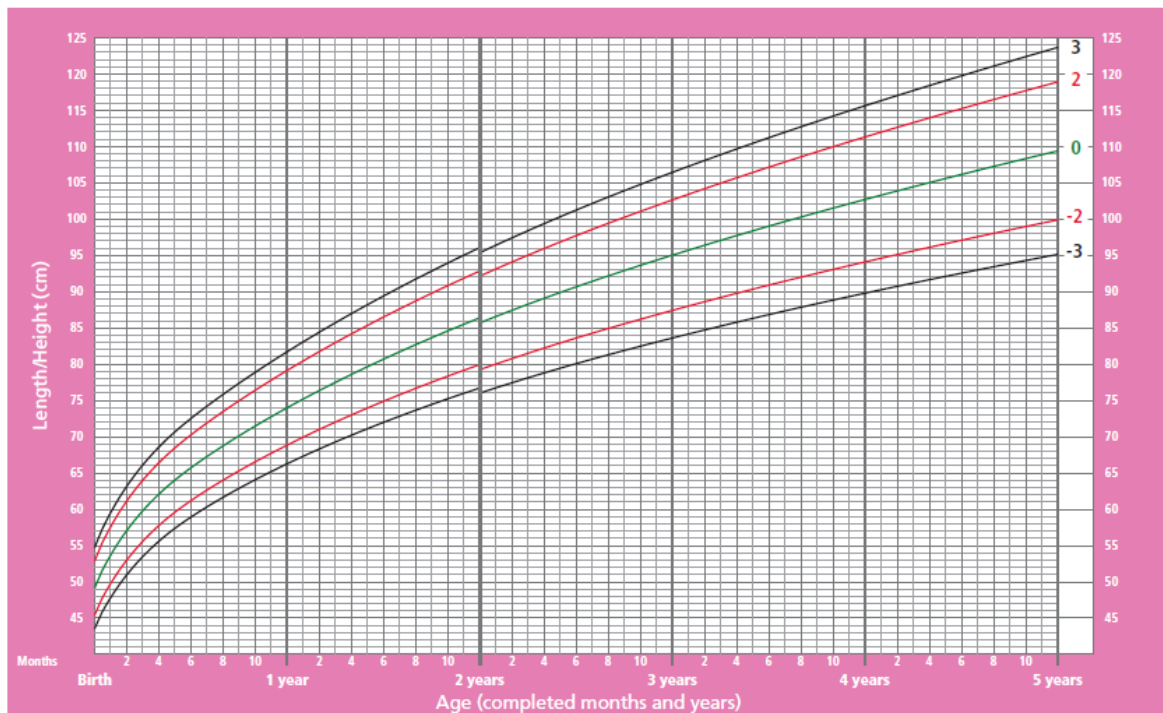


WHO Child Growth Standards

- Length / height for age girls

Length/height-for-age GIRLS

Birth to 5 years (z-scores)

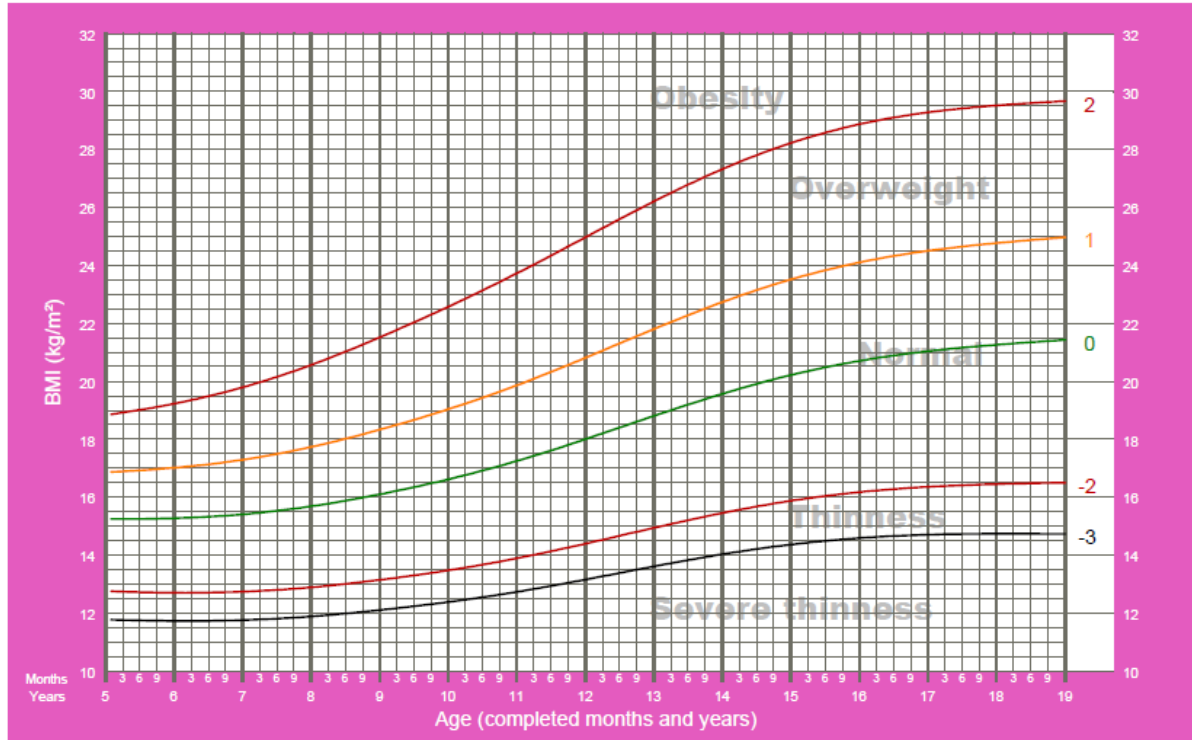


WHO Child Growth Standards

- BMI for age girls

BMI-for-age GIRLS

5 to 19 years (z-scores)

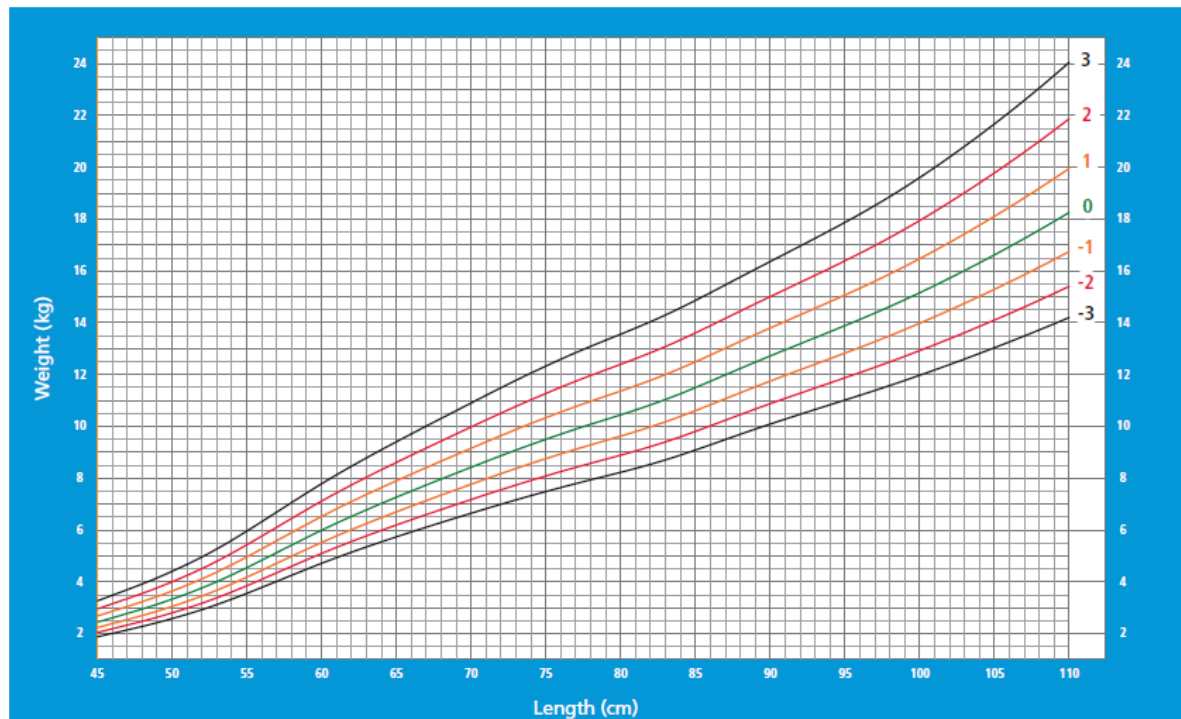


2007 WHO Reference

- Weight for length boys

Weight-for-length BOYS

Birth to 2 years (z-scores)

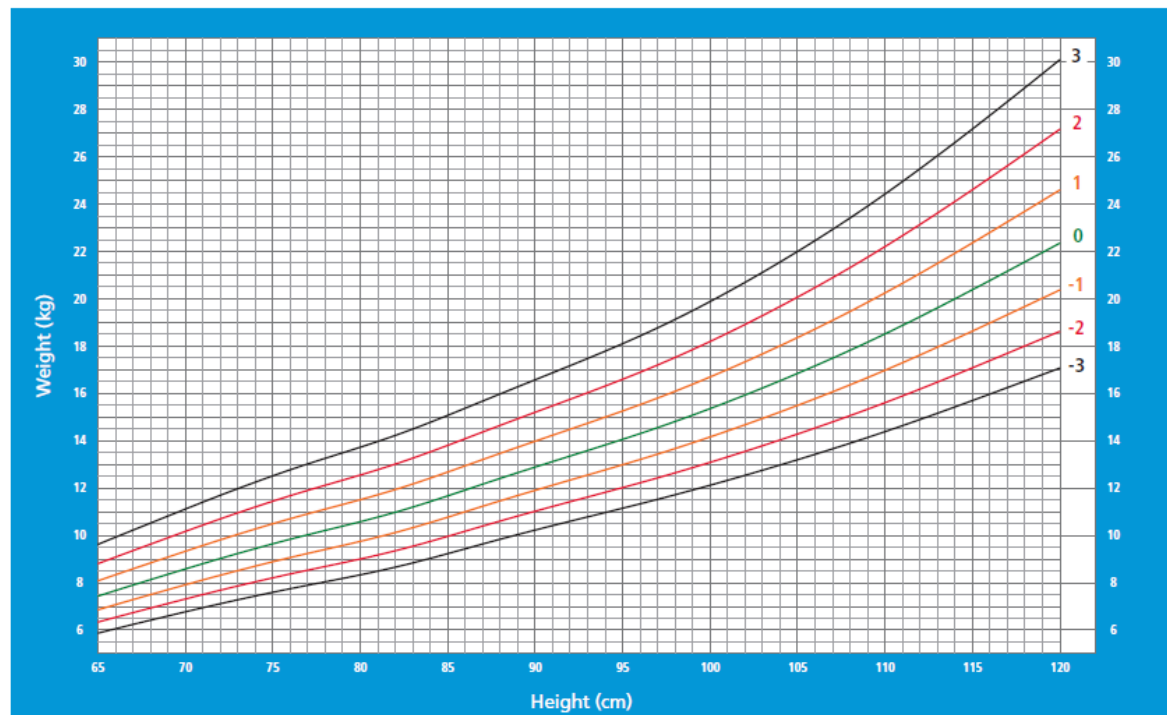


WHO Child Growth Standards

- Weight for height boys

Weight-for-height BOYS

2 to 5 years (z-scores)

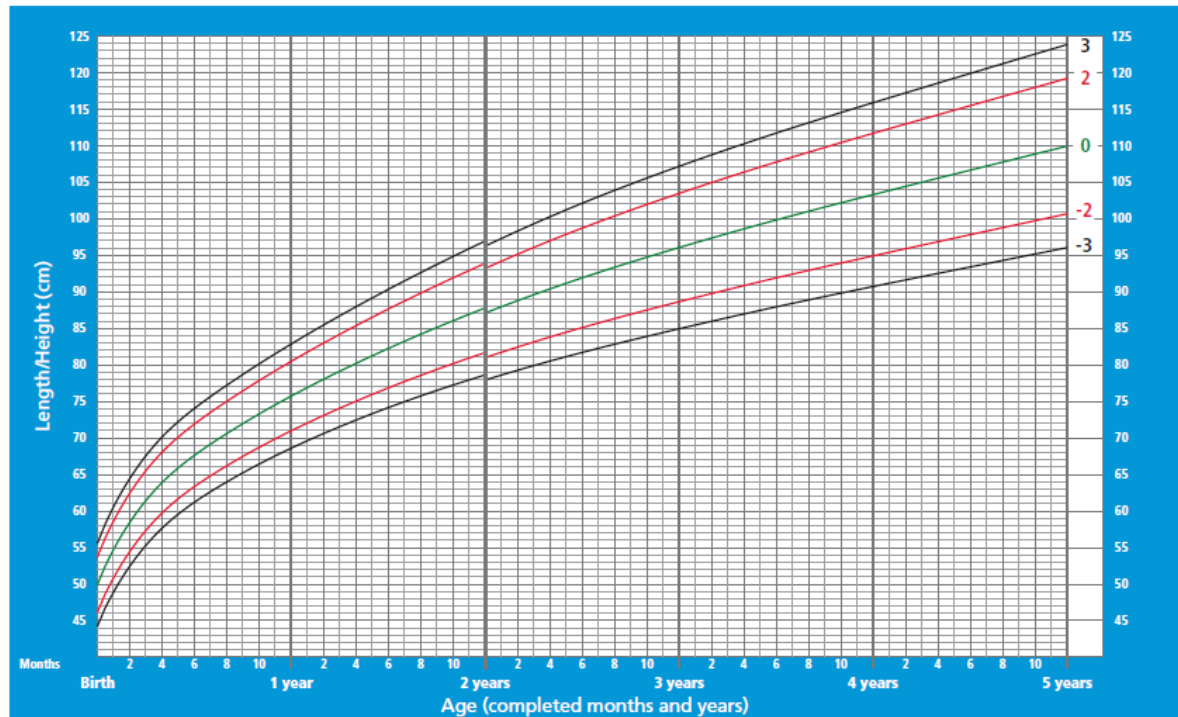


WHO Child Growth Standards

- Length / height for age boys

Length/height-for-age BOYS

Birth to 5 years (z-scores)

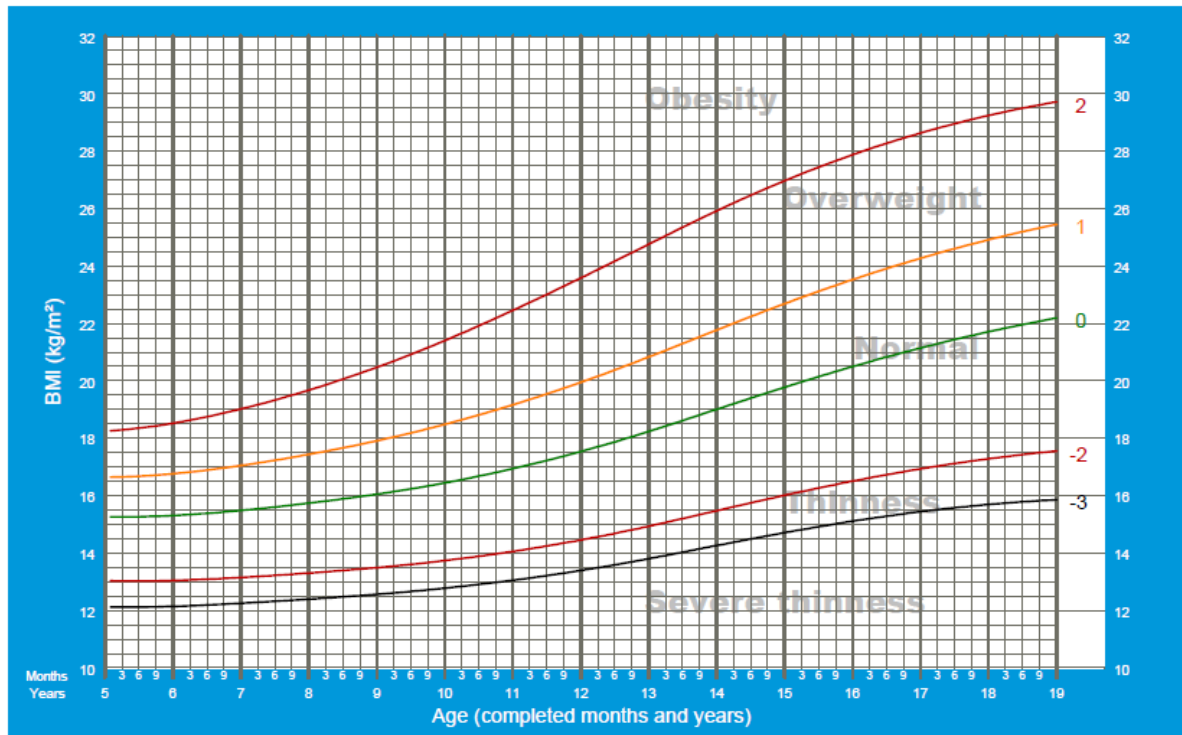


WHO Child Growth Standards

- BMI for age boys

BMI-for-age BOYS

5 to 19 years (z-scores)



2007 WHO Reference

ADDENDUM 2: BLOOD PRESSURE LEVELS FOR BOYS BY AGE AND HEIGHT PERCENTILES

Blood Pressure Levels for Boys by Age and Height Percentile

| Age (Year) | BP Percentile ↓ | Systolic BP (mmHg) | | | | | | | Diastolic BP (mmHg) | | | | | | |
|---------------|-----------------------|--------------------------|------|------|------|------|------|------|--------------------------|------|------|------|------|------|------|
| | | ← Percentile of Height → | | | | | | | ← Percentile of Height → | | | | | | |
| | | 5th | 10th | 25th | 50th | 75th | 90th | 95th | 5th | 10th | 25th | 50th | 75th | 90th | 95th |
| 1 | 50th | 80 | 81 | 83 | 85 | 87 | 88 | 89 | 34 | 35 | 36 | 37 | 38 | 39 | 39 |
| | 90th | 94 | 95 | 97 | 99 | 100 | 102 | 103 | 49 | 50 | 51 | 52 | 53 | 53 | 54 |
| | 95th | 98 | 99 | 101 | 103 | 104 | 106 | 106 | 54 | 54 | 55 | 56 | 57 | 58 | 58 |
| | 99th | 105 | 106 | 108 | 110 | 112 | 113 | 114 | 61 | 62 | 63 | 64 | 65 | 66 | 66 |
| 2 | 50th | 84 | 85 | 87 | 88 | 90 | 92 | 92 | 39 | 40 | 41 | 42 | 43 | 44 | 44 |
| | 90th | 97 | 99 | 100 | 102 | 104 | 105 | 106 | 54 | 55 | 56 | 57 | 58 | 58 | 59 |
| | 95th | 101 | 102 | 104 | 106 | 108 | 109 | 110 | 59 | 59 | 60 | 61 | 62 | 63 | 63 |
| | 99th | 109 | 110 | 111 | 113 | 115 | 117 | 117 | 66 | 67 | 68 | 69 | 70 | 71 | 71 |
| 3 | 50th | 86 | 87 | 89 | 91 | 93 | 94 | 95 | 44 | 44 | 45 | 46 | 47 | 48 | 48 |
| | 90th | 100 | 101 | 103 | 105 | 107 | 108 | 109 | 59 | 59 | 60 | 61 | 62 | 63 | 63 |
| | 95th | 104 | 105 | 107 | 109 | 110 | 112 | 113 | 63 | 63 | 64 | 65 | 66 | 67 | 67 |
| | 99th | 111 | 112 | 114 | 116 | 118 | 119 | 120 | 71 | 71 | 72 | 73 | 74 | 75 | 75 |
| 4 | 50th | 88 | 89 | 91 | 93 | 95 | 96 | 97 | 47 | 48 | 49 | 50 | 51 | 51 | 52 |
| | 90th | 102 | 103 | 105 | 107 | 109 | 110 | 111 | 62 | 63 | 64 | 65 | 66 | 66 | 67 |
| | 95th | 106 | 107 | 109 | 111 | 112 | 114 | 115 | 66 | 67 | 68 | 69 | 70 | 71 | 71 |
| | 99th | 113 | 114 | 116 | 118 | 120 | 121 | 122 | 74 | 75 | 76 | 77 | 78 | 78 | 79 |
| 5 | 50th | 90 | 91 | 93 | 95 | 96 | 98 | 98 | 50 | 51 | 52 | 53 | 54 | 55 | 55 |
| | 90th | 104 | 105 | 106 | 108 | 110 | 111 | 112 | 65 | 66 | 67 | 68 | 69 | 69 | 70 |
| | 95th | 108 | 109 | 110 | 112 | 114 | 115 | 116 | 69 | 70 | 71 | 72 | 73 | 74 | 74 |
| | 99th | 115 | 116 | 118 | 120 | 121 | 123 | 123 | 77 | 78 | 79 | 80 | 81 | 81 | 82 |
| 6 | 50th | 91 | 92 | 94 | 96 | 98 | 99 | 100 | 53 | 53 | 54 | 55 | 56 | 57 | 57 |
| | 90th | 105 | 106 | 108 | 110 | 111 | 113 | 113 | 68 | 68 | 69 | 70 | 71 | 72 | 72 |
| | 95th | 109 | 110 | 112 | 114 | 115 | 117 | 117 | 72 | 72 | 73 | 74 | 75 | 76 | 76 |
| | 99th | 116 | 117 | 119 | 121 | 123 | 124 | 125 | 80 | 80 | 81 | 82 | 83 | 84 | 84 |
| 7 | 50th | 92 | 94 | 95 | 97 | 99 | 100 | 101 | 55 | 55 | 56 | 57 | 58 | 59 | 59 |
| | 90th | 106 | 107 | 109 | 111 | 113 | 114 | 115 | 70 | 70 | 71 | 72 | 73 | 74 | 74 |
| | 95th | 110 | 111 | 113 | 115 | 117 | 118 | 119 | 74 | 74 | 75 | 76 | 77 | 78 | 78 |
| | 99th | 117 | 118 | 120 | 122 | 124 | 125 | 126 | 82 | 82 | 83 | 84 | 85 | 86 | 86 |
| 8 | 50th | 94 | 95 | 97 | 99 | 100 | 102 | 102 | 56 | 57 | 58 | 59 | 60 | 60 | 61 |
| | 90th | 107 | 109 | 110 | 112 | 114 | 115 | 116 | 71 | 72 | 72 | 73 | 74 | 75 | 76 |
| | 95th | 111 | 112 | 114 | 116 | 118 | 119 | 120 | 75 | 76 | 77 | 78 | 79 | 79 | 80 |
| | 99th | 119 | 120 | 122 | 123 | 125 | 127 | 127 | 83 | 84 | 85 | 86 | 87 | 87 | 88 |
| 9 | 50th | 95 | 96 | 98 | 100 | 102 | 103 | 104 | 57 | 58 | 59 | 60 | 61 | 61 | 62 |
| | 90th | 109 | 110 | 112 | 114 | 115 | 117 | 118 | 72 | 73 | 74 | 75 | 76 | 76 | 77 |
| | 95th | 113 | 114 | 116 | 118 | 119 | 121 | 121 | 76 | 77 | 78 | 79 | 80 | 81 | 81 |
| | 99th | 120 | 121 | 123 | 125 | 127 | 128 | 129 | 84 | 85 | 86 | 87 | 88 | 88 | 89 |
| 10 | 50th | 97 | 98 | 100 | 102 | 103 | 105 | 106 | 58 | 59 | 60 | 61 | 61 | 62 | 63 |
| | 90th | 111 | 112 | 114 | 115 | 117 | 119 | 119 | 73 | 73 | 74 | 75 | 76 | 77 | 78 |
| | 95th | 115 | 116 | 117 | 119 | 121 | 122 | 123 | 77 | 78 | 79 | 80 | 81 | 81 | 82 |
| | 99th | 122 | 123 | 125 | 127 | 128 | 130 | 130 | 85 | 86 | 86 | 88 | 88 | 89 | 90 |

Blood Pressure Levels for Boys by Age and Height Percentile (Continued)

| Age (Year) | BP Percentile ↓ | Systolic BP (mmHg) | | | | | | | Diastolic BP (mmHg) | | | | | | |
|---------------|-----------------------|--------------------------|------|------|------|------|------|------|--------------------------|------|------|------|------|------|------|
| | | ← Percentile of Height → | | | | | | | ← Percentile of Height → | | | | | | |
| | | 5th | 10th | 25th | 50th | 75th | 90th | 95th | 5th | 10th | 25th | 50th | 75th | 90th | 95th |
| 11 | 50th | 99 | 100 | 102 | 104 | 105 | 107 | 107 | 59 | 59 | 60 | 61 | 62 | 63 | 63 |
| | 90th | 113 | 114 | 115 | 117 | 119 | 120 | 121 | 74 | 74 | 75 | 76 | 77 | 78 | 78 |
| | 95th | 117 | 118 | 119 | 121 | 123 | 124 | 125 | 78 | 78 | 79 | 80 | 81 | 82 | 82 |
| | 99th | 124 | 125 | 127 | 129 | 130 | 132 | 132 | 86 | 86 | 87 | 88 | 89 | 90 | 90 |
| 12 | 50th | 101 | 102 | 104 | 106 | 108 | 109 | 110 | 59 | 60 | 61 | 62 | 63 | 63 | 64 |
| | 90th | 115 | 116 | 118 | 120 | 121 | 123 | 123 | 74 | 75 | 75 | 76 | 77 | 78 | 79 |
| | 95th | 119 | 120 | 122 | 123 | 125 | 127 | 127 | 78 | 79 | 80 | 81 | 82 | 82 | 83 |
| | 99th | 126 | 127 | 129 | 131 | 133 | 134 | 135 | 86 | 87 | 88 | 89 | 90 | 90 | 91 |
| 13 | 50th | 104 | 105 | 106 | 108 | 110 | 111 | 112 | 60 | 60 | 61 | 62 | 63 | 64 | 64 |
| | 90th | 117 | 118 | 120 | 122 | 124 | 125 | 126 | 75 | 75 | 76 | 77 | 78 | 79 | 79 |
| | 95th | 121 | 122 | 124 | 126 | 128 | 129 | 130 | 79 | 79 | 80 | 81 | 82 | 83 | 83 |
| | 99th | 128 | 130 | 131 | 133 | 135 | 136 | 137 | 87 | 87 | 88 | 89 | 90 | 91 | 91 |
| 14 | 50th | 106 | 107 | 109 | 111 | 113 | 114 | 115 | 60 | 61 | 62 | 63 | 64 | 65 | 65 |
| | 90th | 120 | 121 | 123 | 125 | 126 | 128 | 128 | 75 | 76 | 77 | 78 | 79 | 79 | 80 |
| | 95th | 124 | 125 | 127 | 128 | 130 | 132 | 132 | 80 | 80 | 81 | 82 | 83 | 84 | 84 |
| | 99th | 131 | 132 | 134 | 136 | 138 | 139 | 140 | 87 | 88 | 89 | 90 | 91 | 92 | 92 |
| 15 | 50th | 109 | 110 | 112 | 113 | 115 | 117 | 117 | 61 | 62 | 63 | 64 | 65 | 66 | 66 |
| | 90th | 122 | 124 | 125 | 127 | 129 | 130 | 131 | 76 | 77 | 78 | 79 | 80 | 80 | 81 |
| | 95th | 126 | 127 | 129 | 131 | 133 | 134 | 135 | 81 | 81 | 82 | 83 | 84 | 85 | 85 |
| | 99th | 134 | 135 | 136 | 138 | 140 | 142 | 142 | 88 | 89 | 90 | 91 | 92 | 93 | 93 |
| 16 | 50th | 111 | 112 | 114 | 116 | 118 | 119 | 120 | 63 | 63 | 64 | 65 | 66 | 67 | 67 |
| | 90th | 125 | 126 | 128 | 130 | 131 | 133 | 134 | 78 | 78 | 79 | 80 | 81 | 82 | 82 |
| | 95th | 129 | 130 | 132 | 134 | 135 | 137 | 137 | 82 | 83 | 83 | 84 | 85 | 86 | 87 |
| | 99th | 136 | 137 | 139 | 141 | 143 | 144 | 145 | 90 | 90 | 91 | 92 | 93 | 94 | 94 |
| 17 | 50th | 114 | 115 | 116 | 118 | 120 | 121 | 122 | 65 | 66 | 66 | 67 | 68 | 69 | 70 |
| | 90th | 127 | 128 | 130 | 132 | 134 | 135 | 136 | 80 | 80 | 81 | 82 | 83 | 84 | 84 |
| | 95th | 131 | 132 | 134 | 136 | 138 | 139 | 140 | 84 | 85 | 86 | 87 | 87 | 88 | 89 |
| | 99th | 139 | 140 | 141 | 143 | 145 | 146 | 147 | 92 | 93 | 93 | 94 | 95 | 96 | 97 |

BP, blood pressure

* The 90th percentile is 1.28 SD, 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean.

For research purposes, the standard deviations in Appendix Table B-1 allow one to compute BP Z-scores and percentiles for boys with height percentiles given in Table 3 (i.e., the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles). These height percentiles must be converted to height Z-scores given by (5% = -1.645; 10% = -1.28; 25% = -0.68; 50% = 0; 75% = 0.68; 90% = 1.28; 95% = 1.645) and then computed according to the methodology in steps 2-4 described in Appendix B. For children with height percentiles other than these, follow steps 1-4 as described in Appendix B.

ADDENDUM 3: BLOOD PRESSURE LEVELS FOR GIRLS BY AGE AND HEIGHT PERCENTILES

Blood Pressure Levels for Girls by Age and Height Percentile

| Age (Year) | BP Percentile ↓ | Systolic BP (mmHg) | | | | | | | | Diastolic BP (mmHg) | | | | | | | |
|---------------|-----------------------|--------------------------|------|------|------|------|------|------|--|--------------------------|------|------|------|------|------|------|--|
| | | ← Percentile of Height → | | | | | | | | ← Percentile of Height → | | | | | | | |
| | | 5th | 10th | 25th | 50th | 75th | 90th | 95th | | 5th | 10th | 25th | 50th | 75th | 90th | 95th | |
| 1 | 50th | 83 | 84 | 85 | 86 | 88 | 89 | 90 | | 38 | 39 | 39 | 40 | 41 | 41 | 42 | |
| | 90th | 97 | 97 | 98 | 100 | 101 | 102 | 103 | | 52 | 53 | 53 | 54 | 55 | 55 | 56 | |
| | 95th | 100 | 101 | 102 | 104 | 105 | 106 | 107 | | 56 | 57 | 57 | 58 | 59 | 59 | 60 | |
| | 99th | 108 | 108 | 109 | 111 | 112 | 113 | 114 | | 64 | 64 | 65 | 65 | 66 | 67 | 67 | |
| 2 | 50th | 85 | 85 | 87 | 88 | 89 | 91 | 91 | | 43 | 44 | 44 | 45 | 46 | 46 | 47 | |
| | 90th | 98 | 99 | 100 | 101 | 103 | 104 | 105 | | 57 | 58 | 58 | 59 | 60 | 61 | 61 | |
| | 95th | 102 | 103 | 104 | 105 | 107 | 108 | 109 | | 61 | 62 | 62 | 63 | 64 | 65 | 65 | |
| | 99th | 109 | 110 | 111 | 112 | 114 | 115 | 116 | | 69 | 69 | 70 | 70 | 71 | 72 | 72 | |
| 3 | 50th | 86 | 87 | 88 | 89 | 91 | 92 | 93 | | 47 | 48 | 48 | 49 | 50 | 50 | 51 | |
| | 90th | 100 | 100 | 102 | 103 | 104 | 106 | 106 | | 61 | 62 | 62 | 63 | 64 | 64 | 65 | |
| | 95th | 104 | 104 | 105 | 107 | 108 | 109 | 110 | | 65 | 66 | 66 | 67 | 68 | 68 | 69 | |
| | 99th | 111 | 111 | 113 | 114 | 115 | 116 | 117 | | 73 | 73 | 74 | 74 | 75 | 76 | 76 | |
| 4 | 50th | 88 | 88 | 90 | 91 | 92 | 94 | 94 | | 50 | 50 | 51 | 52 | 52 | 53 | 54 | |
| | 90th | 101 | 102 | 103 | 104 | 106 | 107 | 108 | | 64 | 64 | 65 | 66 | 67 | 67 | 68 | |
| | 95th | 105 | 106 | 107 | 108 | 110 | 111 | 112 | | 68 | 68 | 69 | 70 | 71 | 71 | 72 | |
| | 99th | 112 | 113 | 114 | 115 | 117 | 118 | 119 | | 76 | 76 | 76 | 77 | 78 | 79 | 79 | |
| 5 | 50th | 89 | 90 | 91 | 93 | 94 | 95 | 96 | | 52 | 53 | 53 | 54 | 55 | 55 | 56 | |
| | 90th | 103 | 103 | 105 | 106 | 107 | 109 | 109 | | 66 | 67 | 67 | 68 | 69 | 69 | 70 | |
| | 95th | 107 | 107 | 108 | 110 | 111 | 112 | 113 | | 70 | 71 | 71 | 72 | 73 | 73 | 74 | |
| | 99th | 114 | 114 | 116 | 117 | 118 | 120 | 120 | | 78 | 78 | 79 | 79 | 80 | 81 | 81 | |
| 6 | 50th | 91 | 92 | 93 | 94 | 96 | 97 | 98 | | 54 | 54 | 55 | 56 | 56 | 57 | 58 | |
| | 90th | 104 | 105 | 106 | 108 | 109 | 110 | 111 | | 68 | 68 | 69 | 70 | 70 | 71 | 72 | |
| | 95th | 108 | 109 | 110 | 111 | 113 | 114 | 115 | | 72 | 72 | 73 | 74 | 74 | 75 | 76 | |
| | 99th | 115 | 116 | 117 | 119 | 120 | 121 | 122 | | 80 | 80 | 80 | 81 | 82 | 83 | 83 | |
| 7 | 50th | 93 | 93 | 95 | 96 | 97 | 99 | 99 | | 55 | 56 | 56 | 57 | 58 | 58 | 59 | |
| | 90th | 106 | 107 | 108 | 109 | 111 | 112 | 113 | | 69 | 70 | 70 | 71 | 72 | 72 | 73 | |
| | 95th | 110 | 111 | 112 | 113 | 115 | 116 | 116 | | 73 | 74 | 74 | 75 | 76 | 76 | 77 | |
| | 99th | 117 | 118 | 119 | 120 | 122 | 123 | 124 | | 81 | 81 | 82 | 82 | 83 | 84 | 84 | |
| 8 | 50th | 95 | 95 | 96 | 98 | 99 | 100 | 101 | | 57 | 57 | 57 | 58 | 59 | 60 | 60 | |
| | 90th | 108 | 109 | 110 | 111 | 113 | 114 | 114 | | 71 | 71 | 71 | 72 | 73 | 74 | 74 | |
| | 95th | 112 | 112 | 114 | 115 | 116 | 118 | 118 | | 75 | 75 | 75 | 76 | 77 | 78 | 78 | |
| | 99th | 119 | 120 | 121 | 122 | 123 | 125 | 125 | | 82 | 82 | 83 | 83 | 84 | 85 | 86 | |
| 9 | 50th | 96 | 97 | 98 | 100 | 101 | 102 | 103 | | 58 | 58 | 58 | 59 | 60 | 61 | 61 | |
| | 90th | 110 | 110 | 112 | 113 | 114 | 116 | 116 | | 72 | 72 | 72 | 73 | 74 | 75 | 75 | |
| | 95th | 114 | 114 | 115 | 117 | 118 | 119 | 120 | | 76 | 76 | 76 | 77 | 78 | 79 | 79 | |
| | 99th | 121 | 121 | 123 | 124 | 125 | 127 | 127 | | 83 | 83 | 84 | 84 | 85 | 86 | 87 | |
| 10 | 50th | 98 | 99 | 100 | 102 | 103 | 104 | 105 | | 59 | 59 | 59 | 60 | 61 | 62 | 62 | |
| | 90th | 112 | 112 | 114 | 115 | 116 | 118 | 118 | | 73 | 73 | 73 | 74 | 75 | 76 | 76 | |
| | 95th | 116 | 116 | 117 | 119 | 120 | 121 | 122 | | 77 | 77 | 77 | 78 | 79 | 80 | 80 | |
| | 99th | 123 | 123 | 125 | 126 | 127 | 129 | 129 | | 84 | 84 | 85 | 86 | 86 | 87 | 88 | |

Blood Pressure Levels for Girls by Age and Height Percentile (Continued)

| Age (Year) | BP Percentile ↓ | Systolic BP (mmHg) | | | | | | | Diastolic BP (mmHg) | | | | | | |
|---------------|-----------------------|--------------------------|------|------|------|------|------|------|--------------------------|------|------|------|------|------|------|
| | | ← Percentile of Height → | | | | | | | ← Percentile of Height → | | | | | | |
| | | 5th | 10th | 25th | 50th | 75th | 90th | 95th | 5th | 10th | 25th | 50th | 75th | 90th | 95th |
| 11 | 50th | 100 | 101 | 102 | 103 | 105 | 106 | 107 | 60 | 60 | 60 | 61 | 62 | 63 | 63 |
| | 90th | 114 | 114 | 116 | 117 | 118 | 119 | 120 | 74 | 74 | 74 | 75 | 76 | 77 | 77 |
| | 95th | 118 | 118 | 119 | 121 | 122 | 123 | 124 | 78 | 78 | 78 | 79 | 80 | 81 | 81 |
| | 99th | 125 | 125 | 126 | 128 | 129 | 130 | 131 | 85 | 85 | 86 | 87 | 87 | 88 | 89 |
| 12 | 50th | 102 | 103 | 104 | 105 | 107 | 108 | 109 | 61 | 61 | 61 | 62 | 63 | 64 | 64 |
| | 90th | 116 | 116 | 117 | 119 | 120 | 121 | 122 | 75 | 75 | 75 | 76 | 77 | 78 | 78 |
| | 95th | 119 | 120 | 121 | 123 | 124 | 125 | 126 | 79 | 79 | 79 | 80 | 81 | 82 | 82 |
| | 99th | 127 | 127 | 128 | 130 | 131 | 132 | 133 | 86 | 86 | 87 | 88 | 88 | 89 | 90 |
| 13 | 50th | 104 | 105 | 106 | 107 | 109 | 110 | 110 | 62 | 62 | 62 | 63 | 64 | 65 | 65 |
| | 90th | 117 | 118 | 119 | 121 | 122 | 123 | 124 | 76 | 76 | 76 | 77 | 78 | 79 | 79 |
| | 95th | 121 | 122 | 123 | 124 | 126 | 127 | 128 | 80 | 80 | 80 | 81 | 82 | 83 | 83 |
| | 99th | 128 | 129 | 130 | 132 | 133 | 134 | 135 | 87 | 87 | 88 | 89 | 89 | 90 | 91 |
| 14 | 50th | 106 | 106 | 107 | 109 | 110 | 111 | 112 | 63 | 63 | 63 | 64 | 65 | 66 | 66 |
| | 90th | 119 | 120 | 121 | 122 | 124 | 125 | 125 | 77 | 77 | 77 | 78 | 79 | 80 | 80 |
| | 95th | 123 | 123 | 125 | 126 | 127 | 129 | 129 | 81 | 81 | 81 | 82 | 83 | 84 | 84 |
| | 99th | 130 | 131 | 132 | 133 | 135 | 136 | 136 | 88 | 88 | 89 | 90 | 90 | 91 | 92 |
| 15 | 50th | 107 | 108 | 109 | 110 | 111 | 113 | 113 | 64 | 64 | 64 | 65 | 66 | 67 | 67 |
| | 90th | 120 | 121 | 122 | 123 | 125 | 126 | 127 | 78 | 78 | 78 | 79 | 80 | 81 | 81 |
| | 95th | 124 | 125 | 126 | 127 | 129 | 130 | 131 | 82 | 82 | 82 | 83 | 84 | 85 | 85 |
| | 99th | 131 | 132 | 133 | 134 | 136 | 137 | 138 | 89 | 89 | 90 | 91 | 91 | 92 | 93 |
| 16 | 50th | 108 | 108 | 110 | 111 | 112 | 114 | 114 | 64 | 64 | 65 | 66 | 66 | 67 | 68 |
| | 90th | 121 | 122 | 123 | 124 | 126 | 127 | 128 | 78 | 78 | 79 | 80 | 81 | 81 | 82 |
| | 95th | 125 | 126 | 127 | 128 | 130 | 131 | 132 | 82 | 82 | 83 | 84 | 85 | 85 | 86 |
| | 99th | 132 | 133 | 134 | 135 | 137 | 138 | 139 | 90 | 90 | 90 | 91 | 92 | 93 | 93 |
| 17 | 50th | 108 | 109 | 110 | 111 | 113 | 114 | 115 | 64 | 65 | 65 | 66 | 67 | 67 | 68 |
| | 90th | 122 | 122 | 123 | 125 | 126 | 127 | 128 | 78 | 79 | 79 | 80 | 81 | 81 | 82 |
| | 95th | 125 | 126 | 127 | 129 | 130 | 131 | 132 | 82 | 83 | 83 | 84 | 85 | 85 | 86 |
| | 99th | 133 | 133 | 134 | 136 | 137 | 138 | 139 | 90 | 90 | 91 | 91 | 92 | 93 | 93 |

BP, blood pressure

* The 90th percentile is 1.28 SD, 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean.

For research purposes, the standard deviations in Appendix Table B-1 allow one to compute BP Z-scores and percentiles for girls with height percentiles given in Table 4 (i.e., the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles). These height percentiles must be converted to height Z-scores given by (5% = -1.645; 10% = -1.28; 25% = -0.68; 50% = 0; 75% = 0.68; 90% = 1.28; 95% = 1.645) and then computed according to the methodology in steps 2-4 described in Appendix B. For children with height percentiles other than these, follow steps 1-4 as described in Appendix B.

ADDENDUM 4: INFORMED CONSENT FORMS ENGLISH

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM (ADULTS)

Title: Assessing the renal handling of a dietary protein load in patients managed for Nephroblastoma

Reference Number:

Principal Investigator: Claire Goodall

Address: IALCH Dietetics Department

Contact Number: 031 240 1645

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study researcher or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is entirely voluntary and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the Committee for Human Research at Stellenbosch University and will be conducted according to the ethical guidelines and principles of the International Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this study about?

This study will try to determine if patients who have had Nephroblastoma and have been treated for it run a risk of developing kidney impairment / failure later on in life. Some chemotherapy drugs and radiotherapy can cause serious damage and harm to normal body tissue, including kidney tissue. This study wants to determine if a high protein oral intake influences the way the kidney functions as a high dietary protein load is presumed to “stress the remaining kidney(s)”. We hope to be able to see if a blood test and a urine test will show us how the kidney is affected by the protein.

Why have you been invited to participate?

You have been invited to be part of our study as you have had Nephroblastoma and have received treatment for the tumor.

What procedures will be done?

You will have the same standard tests done as with your routine clinic visits. These include:

- Abdominal Ultrasound
- Chest X-Ray
- Visit by the Paediatric Surgeons in the Oncology clinic
- Weight and height
- Blood pressure

Additional tests which will be done for the purpose of the study

- two blood tests (one when you arrive at the oncology clinic and one 4 hours later at an exact time given to you by the researcher)
- two urine tests (one when you arrive at the oncology clinic and one 4 hours later at an exact time given to you by the researcher)
- 2 further body measurements: Arm circumference and triceps skinfold measurement

You will be asked to drink a Nutritional supplement provided by the researcher. The total volume of supplement provided will have to be consumed by you.

What will your responsibilities be?

Your responsibilities will be to ensure that you are at the Oncology clinic at the appropriate times as provided by the researcher for all the necessary procedures.

Will you benefit from taking part in this research?

You will not benefit directly from this research but by participating in this study, you will be helping us gain new knowledge about the possible risks for further kidney problems later on in your and other patients' lives. All information gathered will be included into your clinic file for future reference.

If you do not agree to take part, what alternatives do you have?

You will still have your normal clinic appointment at the Oncology clinic. You will still have procedures done as deemed necessary by the attending doctors.

Who will have access to your medical records?

Only the main researcher who is a qualified dietician working at the hospital, as well as the attending doctors working at the Pediatric Oncology clinic on the day of the appointment will have access to your records. All information collected will be treated as confidential and protected and your identity will remain unknown to anybody else.

You will receive a copy of this information and consent form for your own records

Declaration by participant

By signing below, I _____ agree to take part in a research study entitled:
Assessing the renal handling of a dietary protein load in patients managed for Nephroblastoma

I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is voluntary and I have not been pressurized to take part.
- I may choose to leave the study at any time and will not be penalized or prejudiced in any way.
- I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.

Signed at _____ on _____

Signature of Participant

Signature of Witness

Declaration by Investigator

I Claire Goodall declare that:

- I explained the information in this document to _____
- I encouraged him / her to ask questions and took adequate time to answer them.
- I am satisfied that he / she adequately understands all aspects of the research, as discussed above
- I did / did not use an Interpreter (if interpreter was used – to sign the declaration below)

Signed at _____ on _____

Signature of Investigator

Signature of Witness

Declaration by Interpreter

I _____ declare that:

- I assisted the investigator Claire Goodall to explain the information in this document to _____ using the language medium Isi-Zulu
- We encouraged him / her to ask questions and took adequate time to answer them
- I conveyed a factually correct version of what was related to me
- I am satisfied that the participant fully understands the content of this informed consent document and has had all his / her questions satisfactorily answered.

Signed at _____ on _____

Signature of Interpreter

Signature of Witness

**PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM FOR USE BY PARENTS/ LEGAL
GUARDIANS**

Title: Assessing the renal handling of a dietary protein load in patients managed for Nephroblastoma

Reference Number: NO09/08/22

Principal Investigator: Claire Garrett

Address: IALCH Dietetics Department

Contact Number: 031 240 1645

Your child is being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the researcher any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how your child could be involved. Also, your child's participation is entirely voluntary and you are free to decline to participate. If you say no, this will not affect you or your child negatively in any way whatsoever. You are also free to withdraw him / her from the study at any point, even if you do initially agree to let him / her take part.

This study has been approved by the Committee for Human Research at Stellenbosch University and will be conducted according to the ethical guidelines and principles of the International Declaration of

Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this study about?

This study will try to determine if patients who have had Nephroblastoma (the kidney cancer which your child has been treated for) and have been treated for it run a risk of developing kidney problems or kidney failure later on in life. Some chemotherapy drugs, and radiotherapy used to treat Nephroblastoma can cause serious damage and harm to normal body tissue, including kidney tissue. This study wants to see if a once-off high protein oral intake in the form of a nice tasting “milk shake” changes the way the kidney functions as a high amount of protein from food is thought to “stress the remaining kidney(s)”. We hope to be able to see if a blood test and a urine test will show us how the kidney is affected by the high protein intake.

Why has your child been invited to participate?

Your child has been invited to be part of our study as he / she has had Nephroblastoma and has received treatment for the tumor.

What procedures will be done?

Your child will have the same standard tests done as with his previous clinic visits. These include:

- Abdominal Ultrasound (known as the “sound test”)
- Chest X-Ray
- Visit by the Paediatric Surgeons in the Oncology clinic
- Weight and height (this measures how much your child weighs and how tall he/she is)
- Blood pressure

Additional tests which will be done for the purpose of the study

- two blood tests (one when your child arrives at the oncology clinic and one 4 hours later at an exact time given to you by the researcher).
- two urine tests (one when your child arrives at the oncology clinic and one 4 hours later at an exact time given to you by the researcher)

Your child will be asked to drink a 250ml vanilla flavored Nutritional supplement provided by the researcher. The total volume of supplement provided will need to be drunk by your child. Your child will also be asked not to eat or drink any further food or drink (apart from water) from the time after drinking the “milk shake” until the second time the blood is taken. This will be about a 4 hour period. However if your child is very hungry or you feel that he / she must eat something during this time period, please inform the researcher regarding your decision.

What will your responsibilities be?

Your responsibilities will be to make sure that your child is at the Oncology clinic at the appropriate times as provided by the researcher for all the necessary procedures. If in the unlikely event that injury results as a direct consequence of the research, please inform the researcher and paediatric oncology clinic immediately.

Potential risks involved with this study

As a participant in the study your child will be asked to drink a “milkshake” provided by the researcher. There will be a specific amount of protein in this milkshake, which the researcher will provide. Depending on the weight of your child, he / she may have to drink a large volume of this shake, which may make him / her feel full and perhaps nauseous. We do not know how your child’s kidneys will react to the protein; that is what we are trying to find out by doing this study, however the risk of doing damage to his / her kidneys by drinking this once off “milk shake” is incredibly small, as he / she currently doesn’t have kidney failure.

Blood will have to be taken from your child twice. This may cause a small amount of discomfort, however only a small amount of blood is required.

Both procedures (drinking the milkshake, and having blood taken) hold very small risks in doing your child harm – as described above.

Please feel free to talk to the researcher if you have any further questions regarding this matter.

Will your child benefit from taking part in this research?

Your child will not benefit immediately from this research but by participating in this study, he / she will be helping us gain new knowledge about the possible risks for further kidney problems later on in his / her life. All information gathered will be included into your child's clinic file for future reference.

If you do not agree to allow your child to take part, what alternatives does your child have?

Your child will still have their normal clinic appointment at the Oncology clinic. He / she will still have procedures done as deemed necessary by the attending doctors.

Who will have access to your child's medical records?

Only the main researcher who is a qualified dietician working at the hospital, as well as the attending Doctors working at the Pediatric Oncology clinic on the day of the appointment will have access to your child's record. All information collected will be treated as confidential and protected and your identity will remain anonymous.

There is a possibility that study auditors may need to inspect the research records at a given date in the future, however your child's identity will not be compromised.

There is no monetary reward for your child participating in the study, nor will it cost you anything for the child to be in the study.

You can contact the Committee for Human Research at 021-938 9207 if you have any concerns or complaints that have not been adequately addressed by the study researcher.

You will receive a copy of this information and consent form for your own records.

Assent of Minor (if > 7 years)

I (Name of Child)_____ have been invited to take part in the above research project.

- The study dietician / nurse and my parents have explained the details of the study to me and I understand what they have said to me
- They have also explained that my blood will be taken on two occasions and my urine taken on two occasions when I am asked to give it
- I also know that I am free to withdraw from the study at any time if I am unhappy
- By writing my name below, I voluntary agree to take part in this research project. I confirm that I have not been forced either by my parents or doctor to take part.

Name of Child

Independent Witness

Declaration by parent / legal guardian

By signing below, I _____ agree to allow my child _____ who is _____ years old, to take part in a research study entitled: Assessing the renal handling of a dietary protein load in patients managed for Nephroblastoma

I declare that:

- I have read or had read to me this information and consent form and that it is written in a language with which I am fluent and comfortable.
- If my child is older than 7 years, he / she must agree to take part in the study and his / her ASSENT must be recorded on this form (see above).
- I have had a chance to ask questions, and all my questions have been adequately answered.
- I understand that taking part in this study is voluntary and I have not been pressurized to let my child take part.
- I may choose to withdraw my child from the study at any time and my child will not be penalized or prejudiced in any way.
- My child may be asked to leave the study before it has finished in the study doctor or researcher feels it is in my child's best interests, or if my child does not follow the study plan as agreed to.

Signed at (Place) _____ on Date: _____

Signature of Parent / Legal Guardian

Signature of Witness

Declaration by Investigator

I Claire Garrett declare that:

- I explained the information in this document to: _____
- I encouraged him / her to ask questions and took adequate time to answer them.
- I am satisfied that he / she adequately understands all aspects of the research as discussed above
- I did / did not use an interpreter

Signed at (place) _____ on Date: _____

Signature of Investigator

Signature of Witness

Declaration by Interpreter

I (name) _____ declare that:

- I assisted Claire Garrett to explain the information in this document to _____ using the language IsiZulu
- We encouraged him / her to ask questions and took adequate time to answer them.
- I conveyed a factually correct version of what was related to me.
- I am satisfied that the parent / legal guardian fully understands the content of this informed consent document and has had all his / her questions answered satisfactorily.

Signed at (place) _____ on Date: _____

Signature of Interpreter

Signature of Witness

ADDENDUM 5: INFORMED CONSENT FORMS ISI-ZULU

INCWAJANA EQUKETHE ULWAZI OLUPHATHELENE NABANTU ABAZOBAMBA IQHAZA

KANYE NEFOMU LEMVUME (ABANTU ABADALA)

Isihloko: Ukuhlolwa kwendlela izinso ezikwazi ukumelana ngayo nomthamo wezakhamzimba ezingamaphrotheyini atholakala ekudleni kwiziguli ezilashelwa umdlavuzwa wezinso (*Nephroblastoma*)

Inombolo Eyireferense: NO09/08/22

Umcwaniyi Oyinhloko: ClaireGarrett

Ikheli: IALCH Dietetics Department

Inombolo Yocingo :031 240 1645

Uyamenywa ukuthi ubambe iqhaza kulo mklamo (iphrojekthi) wocwaniyi. Siyacela ukuthi ufundisise ulwazi oluqukethe kule ncwajana ezokuchazela ngemininingwane yalolu cwaniyi. Siyacela futhi ukuthi ubuze umcwaniyi noma udokotela imibuzo mayelana nezinto ongaziqondisisi kahle kulolu cwaniyi. Kusemqoka kakhulu ukuthi uzigculise ngokuphelele ukuthi uyaqondisisa ukuthi luphathelele nani lolu cwaniyi kanye nendlela ongazimbandakanya ngayo kulona. Futhi kumele uqonde ukuthi ukubamba kwakho iqhaza kulolu cwaniyi yinto oyenza ngentando yakho, awuphoqeelwe futhi unelungelo eligcwele lokwenqaba ukubamba iqhaza. Uma uthi cha awufuni ukubamba iqhaza, lokho ngeke kube nomthelela ongemuhle kuwena. Ungahoxa noma ninikulolu cwaniyi, noma ngabe ubuvumile ekuqaleni ukubamba iqhaza.

Lolu cwaniyi lwamukelwe yiKomidi Lwezocwaniyi Oluphathelele Nabantu eNyuvesi yase-Stellenbosch futhi luzokwenziwa ngokulandela imihlahlandlela kanye nemigomo yokuziphatha ngokwenkambiso efanele Yesitatimende Somhlaba saseHelsinki, Imihlahlandlela yaseNingizimu

Afrika Yokuziphatha Ngendlela Efanele Kwezokwelapha kanye Nemihlahlandlela Yokuziphatha
Ngokwenkambiso Efanele Kwezocwaningo yoMkhandlu Wocwaningo Lwezokwelapha.

Ngabe luphathelene nani lolu cwaningo?

Lolu cwaningo luzozama ukuthola ukuthi kungenzeka yini ukuthi iziguli eziphethwe yi-Nephroblastoma (umdlavuza wezinso olashelwe wona) futhi ezilashelwe yona zibe sengozini yokuba nezinkinga zezinso noma izinso ezingasebenzi kahle ngokuhamba kwesikhathi. Amanye amakhambi angamakhemikhali (imithi yokwelapha umdlavuza) kanye nohlelo lomshini okhipha imisebe yokushisa amaseli omdlavuza, okusetshenziselwa ukwelapha umdlavuza wezinso, kungenza umonakalo omkhulu futhi kulimaze namathishu omzimba ajwayelekile, kumbandakanya namathishu ezinso. Lolu cwaningo lufuna ukuthola ukuthi ngabe ukuphuza kanye nje vo isiphuzo sobisi esishubile (i-“*milk shake*”) esimnandi esinothe kakhulu ngezakha mzimba ezinamaphrotheyini, kuyayiguqula yini indlela izinso ezisebenza ngayo njengoba kucatshangwa ukuthi umthamo ophezulu wamaphrotheyini ekudleni “ufaka ingcindezi kwi(zi)nso e(zi)sele”. Sinethemba lokuthi sizokwazi ukuthola ukuthi ukuhlolwa kwegazi kanye nokuhlolwa komchamo kuyawuveza yini umthelela wokudla okunotho kakhulu ngamaphrotheyini ezinsweni.

Kungani umenyiwe ukuthi ubambe iqhaza?

Umenyiwe ukuthi ube yingxenye yocwaningo lwethu ngoba uke waphathwa nguMdlavuza Wezinso futhi uke wathola ukwelashelwa isigaxa somdlavuza ezinsweni zakho.

Ukuhlolwa okunjani okuzokwenziwa?

Uzohlolwa ngendlela efana naleyo oyijwayele ohlolwa ngayo uma uvakashele emtholampilo. Lokhu kumbandakanya:

- Uhlelo lwe-*Ultrasound* Yesisu (olwaziwa ngokuthi “ukuhlolwa okuphathelene nemisindo”)
- I-Eksireyi Yesifuba

- Ukuvakashela koDokotela Bezingane emtholampilo woMdlavuza
- Ukuhlolwa kwesisindo sakho kanye nobude bakho
- Ukuhlolwa komfutho wegazi emzimbeni

Okunye ukuhlolwa okuzokwenziwa kulolu cwaningo

- Ukuhlolwa kwegazi kabili (ukuhlolwa kokuqala kuzokwenziwa ngenkathi ufika emtholampilo womdlavuza bese okwesibili kwenziwa emva kwamahora ama-4 ngesikhathi osinikezwe ngumcwaningi).
- Ukuhlolwa komchamo kabili (ukuhlolwa kokuqala kuzokwenziwa ngenkathi ufika emtholampilo womdlavuza bese okwesibili kwenziwa emva kwamahora ama-4 ngesikhathi osinikezwe ngumcwaningi)

Yiziphi izinto okuzomele zenziwe nguwana?

Kuzomele wenze isiqiniseko sokuthi uba seMtholampilo womdlavuza ngesikhathi esifanele osinikezwe ngumcwaningi, futhi nguyena ozokwenza konke ukuhlolwa okudingekayo. Uma kwenzeka into eyivela kancane yokuthi kube khona ukulimala okubangelwe wucwaningo, uyacelwa ukuthi wazise umcwaningi kanye nomtholampilo womdlavuza ngokushesha. Uzobe usunikezwa isiphuzo Esinothe ngezakhamzimba futhi kubalulekile ukuthi usiphuze sonke leso siphuzo osinikeziwe. Uzocelwa futhi ukuthi ungalokothi udle noma uphuze noma yikuphi okunye ukudla noma isiphuzo (ngaphandle kwamanzi) kusukela ngesikhathi onikezwe ngaso isiphuzo esinothe ngezakhamzimba kuze kufike isikhathi sokudonswa kwegazi kwesibili. Lokhu kuzokwenzeka emva kwamahora ama-4. Uma uzizwa ulambe kakhulu noma ubona ukuthi kufanele udle noma uphuze okuthile ngalesi sikhathi, uyacelwa ukuthi wazise umcwaningi.

Ingozi okungenzeka ibe khona kulolu cwaningo

Njengomuntu obamba iqhaza kulolu cwaningo uzocelwa ukuthi uphuze isiphuzo esishubile esinobisi ("i-milkshake") osinikezwe ngumcwaningi. Kulesi siphuzo ozosinikezwa ngumcwaningi kumomthamo okaliwe wamaphrotheyini. Ngokuya kwesisindo somzimba wakho, kungenzeka kudingeke ukuthi uphuze umthamo omkhulu walesi siphuzo sobisi esishubile, lokho kungenza ukuthi isisu sakho sigcwele kakhulu futhi uzizwe sengathi uzophalaza. Asazi ukuthi kuzokwenzekani kwizinso zakho uma

zithola la maphrotheyini; futhi yilokho esizama ukukuthola ngokwenza lolu cwaningo, kodwa yincane kakhulu ingozi yokuthi kungaba khona umonakalo owenzekayo ezinsweni zakho emva kokuphuza lesi “siphuzo sobisi esishubile” kanye nje vo, ngoba njengamanje awunayo inkinga yokungasebenzi kahle kwezinso.

Kuzodonswa igazi emzimbeni wakho kabili. Lokhu kungenzeka kubangele ukuthi uzwe ubuhlungu obuncane emzimbeni, kodwa-ke ungakhathazeki ngoba kudingeka umthamo wegazi omncane nje.

Buncane kakhulu ubungozi bomonakalo ongadalwa yilokhu okubili okuzokwenziwa kuwena (ukuphuza isiphuzo sobisi esishubile, kanye nokudonswa kwegazi) – njengoba kuchaziwe ngenhla.

Kumele ukhulume ngokukhululeka nomcwaningi uma uneminye imibuzo mayelana nalolu daba.

Ngabe ukhona umhlomulo ozowuthola ngokubamba iqhaza kulolu cwaningo?

Awukho umhlomulo ozowuthola ngokushesha emva kwalolu cwaningo kodwa ngokubamba iqhaza kulolu cwaningo, uzosisiza ukuthi sithole ulwazi olusha mayelana nobungozi bezinye izinkinga zezinso okungenzeka zibe khonangokuhamba kwesikhathi empilweni yakho noma ezimpilweni zabanye abantu. Lonke ulwazi oluzotholakala kulolu cwaningo luzofakwa kwifayela yakho yasemtholampilo ukuze lusetshenziswe esikhathini esizayo.

Uma ungavumi ukubamba iqhaza kulolu cwaningo, yikuphi okunye ongakwenza?

Uzoqhubeka nokunikezwa njengenjwayelo izinsuku okumele uvakashele ngazo emtholampilo woMdlavuza. Kuzoqhutshekwa nokuthi kwenziwe kuwena izinhlelo zokukuhlola kanye nokukwepha ezibonwa ngodokotela basemtholampilo njengento esemqoka okumele yenziwe.

Ngubani ozovunyelwa ukubona imininingwane yamarekhodi akho ezempilo?

Ngumcwaningi omkhulu kuphelafuthi ongungcweti oneziqu ezifanele mayelana nemithetho yokudla ukudla okufanele, osebenza esibhedlela, kanye nodokotela abazobe besebenza emtholampilo woMdlavuza Wezingane ngosuku lokuvakashela kwakho emtholampilo, abazovunyelwa ukuthi babone amarekhodi akho. Lonke ulwazi olutholakele luzoba yimfihlo futhi luzovikelwa futhi akhekho omunye umuntu ozonikezwa ulwazi oluqondene nawe futhi akhonjiswe imininingwane yakho.

Kungenzeka kudingeke ukuthi abacwaningi bamabhuku aphaathelene nalolu cwaningo bahlale amarekhodi alolu cwaningo esikhathini esizayo, kodwa-ke ngeke lidalulwe igama lakho.

Awukho umhlomulo oyimali ozonikezwa labo ababambe iqhaza kulolu cwaningo, futhi ngeke ukhokhiswe lutho ngokuba yingxenye yalolu cwaningo.

Ungaxhumana neKomidi Locwaningo Oluphathele Nabantu ngokushayela le nombolo yocingo 021-938 9207 uma kukhona okukukhathazayo noma uma unezikhalazo ezingaxazululwanga ngendlela efanele ngumcwaningi owenza lolu cwaningo.

Uzonikezwa ikhophi equkethe lolu lwazi kanye nefomu lemvume ukuze uzigcinele kona.

Isitatimende esiyisifungo esenziwa ngumuntu obamba iqhaza

Ngokusayinda lapha ngezansi, mina u- _____ ngiyavuma ukubamba iqhaza kucwaningo olunesihloko esithi: Ukuhlolwa kwendlela izinso ezikwazi ukumelana ngayo nomthamo wezakhamzimba ezingamaphrotheyini atholakala ekudleni kwiziguli ezilashelwa umdlavuzwa wezinso (*Nephroblastoma*)

Ngियाqinisekisa ukuthi:

- Ngilufundile noma ngilufundeliwe lolu lwazi kanye nefomu lemvume futhi kubhalwe ngolimi engilwaziyo futhi engingenankinga nalo.
- Nginikeziwe ithuba lokubuza imibuzo futhi yonke imibuzo yami iphendulwe ngendlela egculisayo.
- Ngियाqonda ukuthi ukubamba iqhaza kulolu cwaningo yinto umuntu azenzela yona ngokuthanda kwakhe futhi akekho ongiphokelelile ukuthi ngibambe iqhaza.
- Nginelungelo lokuhoxa kulolu cwaningo noma nini futhi lokho ngeke kuholele ekutheni ngihlawuliswe futhi kuphulwe amalungelo ami noma ngayiphi indlela.

- Kungenzeka ngicelwe ukuthi ngiphume kulolu cwaningo ngaphambi kokuthi luphuthulwe, uma udokotela wocwaningo noma umcwaningi ebona ukuthi lesi senzo singaba nosizo kimina, noma uma ngingalulandeli uhlelo locwaningo okuvunyelwane ngalo.

Kusayindwe e _____ mhlaka _____

Isiginesha Yomuntu Obamba Iqhaza

Isiginesha Yomuntu Ongufakazi

Isitatimende esiyisifungo esenziwa nguMcwaningi

Minau-Claire Garrett ngiyaqinisekisa ukuthi:

- Ngimchazelile u- _____ ulwazi oluqokethwe kule ncwajana.
- Ngimkhuthazile ukuthi abuze imibuzo futhi ngiznikezile isikhathi esanele sokuthi ngiphendule imibuzo.
- Ngigculisekile ukuthi uyakuqonda konke okuphathelele nalolu cwaningo, njengoba kukhulunywa ngakho lapha ngenhla.
- Ngisebenzise / Angimsebenzisanga uTolika (uma kusetshenziswe utolika – kumele asayinde lesi sitatimende esiyisifungo esibhalwe lapha ngezansi

Kusayindwe e _____ mhlaka _____

Isiginesha Yomcwaningi

Isiginesha Yomuntu Ongufakazi

Isitatimende esiyisifungo esenziwa nguTolika

Mina u-_____ ngiyaqinisekisa ukuthi:

- Ngimsizile umcwaningi u- Claire Garrett ukuchazela u- _____ ulwazi oluqukethwe kule ncwajana ngisebenzisa ulimi lwesiZulu

- Simkhuthazile ukuthi abuze imibuzo futhi sizinikezile isikhathi esanele sokuthi siphendule imibuzo yakhe

- Ngimnikeze ulwazi oluyiqiniso futhi oluqondile mayelana nalokho engitshelwe kona

- Ngigculisekile ukuthi lowo obambe iqhaza ukuqonda kahle lokho okuqukethwe kule ncwajana yemvume futhi yonke imibuzo yakhe iphendulwe ngendlela egculisayo.

Kusayindwe e _____ mhlaka _____

Isiginesha kaTolika

Isiginesha Yomuntu Ongufakazi

**INCWAJANA EQUKETHE ULWAZI OLUPHATHELENE NABANTU ABAZOBAMBA IQHAZA
KANYE NEFOMU LEMVUME OKUQONDISWE KUBAZALI/ABAPHATHI BENGANE
ABASEMTHETHWENI**

Isihloko:Ukuhlolwa kwendlela izinso ezikwazi ukumelana ngayo nomthamo wezakhamzimba ezingamaphrotheyini atholakala ekudleni kwiziguli ezilashelwa umdlavuza wezinso (*Nephroblastoma*)

Inombolo Eyireference: NO09/08/22

Umcwaniyi Oyinhloko:ClaireGarrett

Ikheli:IALCH Dietetics Department

Inombolo Yocingo:031 240 1645

Ingane yakho iyaminywa ukuthi ibambe iqhaza kulo mklamo wocwaniyo. Sicela ukuthi ufundisise ulwazi oluqukethe kule ncwajana ezokuchazela ngemininingwane yalolu cwaniyo. Sicela futhi ukuthi ubuze umcwaniyi imibuzo mayelana nanoma iyiphi ingxenye yalolu cwaniyo ongayiqondisisi kahle. Kusemqoka kakhulu ukuthi uzigculise ngokuphelele ukuthi uyaqondisisa ukuthi luphathelene nani lolu cwaniyo kanye nendlela ingane yakho engazibandakanya ngayo kulona. Kumele uqonde futhi ukuthi ukubamba kwengane yakho iqhaza kulolu cwaniyo yinto umuntu azenzela yona ngentando yakhe, akekho ophoqeile futhi unelungelo eligcwele lokwenqaba ukuthi ingane yakho ibambe iqhaza. Uma uthi cha awufuni ukuthi ingane yakho ibambe iqhaza, lokho ngeke kube

nomthelela ongemuhlekuwena noma enganeni yakho. Ungayihoxisa ingane yakho kulolu cwaningo noma nini, noma ngabe ubuvumile ekuqaleni ukuthi ibambe iqhaza.

Lolu cwaningo lwamukelwe yiKomidi Lwezocwaningo Oluphathelene Nabantu eNyuvesi yase-Stellenbosch futhi luzokwenziwa ngokulandela imihlahlandlela kanye nemigomo yokuziphatha ngokwenkambiso efanele Yesitatimende Somhlaba saseHelsinki, Imihlahlandlela yaseNingizimu Afrika Yokuziphatha Ngendlela Efanele Kwezokwelapha kanye Nemihlahlandlela Yokuziphatha Ngokwenkambiso Efanele Kwezocwaningo yoMkhandlu Wocwaningo Lwezokwelapha.

Ngabe luphathelene nani lolu cwaningo?

Lolu cwaningo luzozama ukuthola ukuthi kungenzeka yini ukuthi iziguli eziphethwe yi-Nephroblastoma (umdlavuza wezinso ingane yakho elashelwe wona) futhi ezilashelwe yona zibe sengozini yokuba nezinkinga zezinso noma izinso ezingasebenzi kahle ngokuhamba kwesikhathi. Amanye amakhambi angamakhemikhali (imithi yokwelapha umdlavuza) kanye nohlelo lomshini okhipha imisebe yokushisa amaseli omdlavuza okusetshenziselwa ukwelapha umdlavuza wezinso kungenza umonakalo omkhulu futhi kulimaze namathishu omzimba ajwayelekile, kumbandakanya namathishu ezinso. Lolu cwaningo lufuna ukuthola ukuthi ngabe ukuphuza kanye nje vo isiphuzo sobisi esishubile (i-“*milk shake*”) esimnandi esinothe kakhulu ngezakhamzimba ezinamaphrotheyini kuyayiguqula yini indlela izinso ezisebenza ngayo njengoba kucatshangwa ukuthi umthamo ophezulu wamaphrotheyini ekudleni “ufaka ingcindezi kwi(zi)nso e(zi)sele”. Sinethemba lokuthi sizokwazi ukuthola ukuthi ukuhlolwa kwegazi kanye nokuhlolwa komchamo kuyawuveza yini umthelela wokudla okunotho kakhulu ngamaphrotheyini ezinsweni.

Kunganiimenyiwe ingane yakho ukuthi ibambe iqhaza?

Ingane yakho imenyiwe ukuthi ibe yingxenye yocwaningo lwethu ngoba ike yaphathwa nguMdlavuza Wezinso futhi ike yathola ukwelashelwa isigaxa somdlavuza ezinsweni.

Ukuhlolwa okunjani okuzokwenziwa?

Ingane yakho izohlolwa ngendlela efana naleyo ehlolwe ngayo nesikhathi esedlule ngenkathi ivakashela emtholampilo. Lokhu kumbandakanya:

- Uhlelo lwe-*Ultrasound* Yesisu (olwaziwa ngokuthi “ukuhlolwa okuphathelele nemisindo”)
- I-Eksireyi Yesifuba
- Ukuvakashela koDokotela Bezingane emtholampilo woMdlavuza
- Ukuhlolwa kwesisindo sakho kanye nobude bakho
- Ukuhlolwa komfutho wegazi emzimbeni

Okunye ukuhlolwa okuzokwenziwa kulolu cwaningo

- Ukuhlolwa kwegazi kabili (ukuhlolwa kokuqala kuzokwenziwa ngenkathi ingane yakho ifika emtholampilo woMdlavuza bese okwesibili kwenziwa emva kwamahora ama-4 ngesikhathi osinikezwe ngumcwaningi).
- Ukuhlolwa komchamo kabili (ukuhlolwa kokuqala kuzokwenziwa ngenkathi ingane yakho ifika emtholampilo woMdlavuza bese okwesibili kwenziwa emva kwamahora ama-4 ngesikhathi osinikezwe ngumcwaningi)

Ingane yakho izocelwa ukuthi iphuze isiphuzo esingu- 250ml esinikezwe ngumcwaningi esinongwe nge-*vanilla* futhi Esinothe ngezakhamzimba. Ingane yakho kumele isiphuze sonke leso siphuzo esinikeziwe. Ingane yakho izocelwa futhi ukuthi ingalokothi idle noma iphuze noma yikuphi okunye ukudla noma isiphuzo (ngaphandle kwamanzi) kusukela ngesikhathi ephuze ngaso isiphuzo sobisi “esishubile esinothe ngezakhamzimba” kuze kufike isikhathi sokudonswa kwegazi kwesibili. Lokhu kuzokwenzeka emva kwamahora ama-4. Kodwa-ke uma ingane yakho isilambe kakhulu noma ubona ukuthi kufanele idle noma iphuze okuthile ngalesi sikhathi, sicela ukuthi wazise umcwaningi mayelana nesinqumo sakho.

Yiziphi izinto okuzomele zenziwe nguwenana?

Umsebenzi wakho kuzoba ukwenza isiqiniseko sokuthi ingane yakhe isemtholampilo womdlavuzana ngezikhathi ezifanele ozinikezwe ngumcwani ukuze kwenziwe konke ukuhlolwa okudingekayo. Uma kwenzeka kuba khona ukulimala okubangelwe wucwani, okuyinto engavamisile ukwenzeka, uyacelwa ukuthi wazise umcwani kanye nomtholampilo womdlavuzana wezingane ngokushesha.

Ingozi okungenzeka ibe khona kulolu cwani?

Njengomuntu obamba iqhaza kulolu cwani ingane yakho izocelwa ukuthi iphuze isiphuzo sobisi esishubile (“i-milkshake”) esinikezwe ngumcwani. Kulesi siphuzo esizonikezwa ingane yakho ngumcwani kumomthamo okaliwe wamaphrotheyini. Ngokuya kwesisindo somzimba somzimba wengane yakho, kungenzeka kudingekile ukuthi iphuze umthamo omkhulu walesi siphuzo sobisi esishubile, futhi lokho kungenza ukuthi isisu sengane yakho sigcwele kakhulu futhi izizwe sengathi izophalaza. Asazi ukuthi izinso zengane yakho zizophatheka kanjani uma zithola la maphrotheyini; yilokho esizama ukukuthola ngokwenza lolu cwani, kodwa yincane kakhulu ingozi yokuthi kungaba khona umonakalo owenzekayo ezinsweni zengane yakho emva kokuphuza lesi “siphuzo sobisi esishubile” kanye nje vo, ngoba njengamanje ayinayo inkinga yokungasebenzi kahle kwezinsu.

Kuzodonswa igazi emzimbeni wengane yakho kabili. Lokhu kungenzeka kubangele ukuthi izwe ubuhlungu obuncane emzimbeni, kodwa-ke ungakhathazeki ngoba kudingeka umthamo wegazi omncane nje.

Buncane kakhulu ubungozi bomonakalo ongalwa yilokhu okubili okuzokwenziwa enganeni yakho (ukuphuza isiphuzo sobisi esishubile, kanye nokudonswa kwegazi) – njengoba kuchaziwe ngenhla.

Kumele ukhulume ngokukhululeka nomcwani uma uneminye imibuzo mayelana nalolu daba.

Ngabe ukhona umhlomulo ozotholwa yingane yakho ngokubamba iqhaza kulolu cwani?

Awukho umhlomulo ozotholwa yingane yakho ngokushesha emva kwalolu cwani kodwa ngokubamba iqhaza kulolu cwani, ingane yakho izosisiza ukuthi sithole ulwazi olusha mayelana nobungozi bezinye izinkinga zezinsu okungenzeka zibe khonangokuhamba kwesikhathi empilweni

yakhe. Lonke ulwazi oluzotholakala kulolu cwaningo luzofakwa kwifayela yasemtholampilo yengane yakho ukuze lusetshenziswe esikhathini esizayo.

Uma ungavumi ukuthi ingane yakho ibambe iqhaza kulolu cwaningo, yikuphi okunye okumele ikwenze?

Ingane yakho isazoqhubeka nokunikezwa njengenjwayelo izinsuku okumele ivakashele ngazo emtholampilo woMdlavuza. Kuzoqhutshekwa nokuthi kwenziwe izinhlelo zokuxilonga nokwelapha ingane yakho ezibonwa ngodokotela basemtholampilo njengento esemqoka okumele yenziwe.

Ngubani ozovunyelwa ukubona imininingwane yamarekhodi ezempilo engane yakho?

Ngumcwaningi omkhulu kuphela futhi oyingcweti eneziqu zemfundo efanele mayelana nemithetho yokudla ukudla okufanele, osebenza esibhedlela, kanye noDokotela abazobe besebenza emtholampilo woMdlavuza Wezingane ngosuku lokuvakashela kwengane yakho emtholampilo, abazovunyelwa ukuthi babone amarekhodi engane yakho. Lonke ulwazi olutholakele luzoba yimfihlo futhi luzovikelwa futhi akhekho omunye umuntu ozonikezwa ulwazi oluphathelele negama lengane yakho.

Kungenzeka kudingeke ukuthi abacwaningi bamabhuku aphaathelene nalolu cwaningo bahlole amarekhodi aphaathelene nalolu cwaningo esikhathini esizayo, kodwa-ke ngeke lidalulwe igama lengane yakho.

Awukho umhlomulo oyimali ozonikezwa ingane yakho ngokubamba kwayo iqhaza kulolu cwaningo, futhi ngeke ukhokhiswe lutho ngokufakwa kwengane yakho kulolu cwaningo.

Ungaxhumana neKomidi Locwanigo Oluphathelele Nabantu ngokushayela le nombolo yocingo 021 938 9207 uma kukhona okukukhathazayo noma uma unezikhalazo ezingaxazululwanga ngendlela efanele ngumcwaningi owenza lolu cwaningo.

Uzonikezwa ikhophi equkethe lolu lwazi kanye nefomu lemvume ukuze uzigcinele kona.

Imvume Yengane (uma ineminyaka engaphezu kwesi -7)

Mina (Igama Lengane)u-_____ ngimenyiwe ukuthi ngibambe iqhaza kulo mklamo wocwaningo ongenhla.

- Isikhulu salolu cwaningo esiyingcweti kwezokudla / umhlengikazi kanye nabazali bami bangichazelile imininingwane yalolu cwaningo futhi ngiyakuqonda lokho abangichazele kona.
- Bangichazelile futhi ukuthi igazi lami lizodonswa kabili futhi nomchamo wami uzothwathwa amahlandla amabili uma ngicelwa ukuthi nginikele ngawo
- Ngiyazi futhi ukuthi ngingahoxa noma nini kulolu cwaningo uma kukhona into engangigculisi
- Ngokubhala igama lami ngezansi, ngiyazivumela ngokuthanda kwami ukubamba iqhaza kulo mklamo wocwaningo. Ngiaqinisekisa ukuthi abazali bami noma udokotela wami abangiphoqelelanga ukuthi ngibambe iqhaza.

Igama Lengane

Ufakazi Ozimele

Isitatimende esiyisifungo esenziwa ngumzali / umphathi wengane osemthethweni

Ngokusayinda ngezansi, mina u-_____ ngiyayivumela ingane yami u-_____ oneminyaka engu- _____, ukuthi abambe iqhaza kucwaningo olunesihloko esithi: Ukuhlolwa kwendlela izinso ezikwazi ukumelana ngayo nomthamo

wezakhamzimba ezingamaphrotheyini atholakala ekudleni kwiziguli ezilashelwa umdlavuza wezinso
(*Nephroblastoma*)

Ngiyaqinisekisa ukuthi:

- Ngilufundile noma ngilufundeliwe lolu lwazi kanye nefomu lemvume futhi kubhalwe ngolimi engilwaziyo futhi engingenankinga nalo.
- Uma ingane yami ineminyaka eyisi- 7, kumele ivume ukubamba iqhaza ocwaningweni / futhi IMVUME yakhe kumele ibhalwe kuleli fomu (bheka lokhu okubhalwe ngenhla).
- Nginikeziwe ithuba lokubuza imibuzo futhi yonke imibuzo yami iphendulwe ngendlelaegculisayo.
- Ngियाqonda ukuthi ukubamba iqhaza kulolu cwaningo yinto umuntu azenzela yona ngokuthanda kwakhe futhi akekho ongiphoqeletile ukuthi ngivumele ingane yami ukuthi ibambe iqhaza.
- Nginelungelo lokuhoxisa ingane yami kulolu cwaningo noma nini futhi ngeke lokho kuholele ekutheni ngihlawuliswe noma kuphulwe amalungelo ami noma ngayiphi indlela.
- Kungenzeka ikhishwe ingane yami kulolu cwaningo ngaphambi kokuthi luphothulwe uma udokotela wocwaningo noma umcwaningi ebona ukuthi leso senzo singaba nosizokuyona, noma uma ingane yami ingalulandeli uhlelo locwaningo okuvunyelwane ngalo.

Kusayindwe e (Indawo) _____ mhlaka: _____

Isiginesha yoMzali / Umphathi WenganeIsigineshaYomuntu Ongufakazi

Osemthethweni

Isitatimende esiyisifungo esenziwa nguMcwaningi

Minau-Claire Garrett ngiyaqinisekisa ukuthi:

- Ngimchazelile u- _____ ulwazi oluqukethwe kule ncwajana.
- Ngimkhuthazile ukuthi abuze imibuzo futhi ngizinikezile isikhathi esanele sokuthi ngiphendule imibuzo.
- Ngigculisekile ukuthi uyakuqonda konke okuphathelene nalolu cwaningo, njengoba kukhulunywa ngakho lapha ngenhla.
- Ngisebenzise / Angimsebenzisanga uTolika (uma kusetshenziswe utolika – kumele asayinde lesi sitatimende esiyisifungo esibhalwe lapha ngezansi

Kusayindwe e _____ mhlaka _____

Isiginesha Yomcwaningi

Isiginesha Yomuntu Ongufakazi

Isitatimende esiyisifungo esenziwa nguTolika

Mina u- _____ ngiyaqinisekisa ukuthi:

- Ngimsizile umcwaningi u- Claire Garrett ukuchazela u- _____ ulwazi oluqukethwe kule ncwajana ngisebenzisa ulimi lwesiZulu
- Simkhuthazile ukuthi abuze imibuzo futhi sizinikezile isikhathi esanele sokuthi siphendule imibuzo yakhe
- Ngimnikeze ulwazi oluyiqiniso futhi oluqondile mayelana nalokho engitshelwe kona
- Ngigculisekile ukuthi lowo obambe iqhaza ukuqonda kahle lokho okuqukethwe kule ncwajana yemvume futhi yonke imibuzo yakhe iphendulwe ngendlela egculisayo.

Kusayindwe e _____ mhlaka _____

Isiginesha kaTolika

Isiginesha Yomuntu Ongufakazi

ADDENDUM 6: DATA COLLECTION SHEET**ASSESSING THE RENAL HANDLING OF PATIENTS MANAGED****FOR NEPHROBLASTOMA****General Information**

Study Number:

Age:

| | |
|---------------|---------------|
| < 20 years | > 20 years |
|---------------|---------------|

Gender:

Male

Female

Race

Medical History

Date of Diagnosis:

dd

Mm

Yy

Age at diagnosis:

Diagnosis of Nephroblastoma:

Stage

I

II

III

IV

V

Risk profile of
Nephroblastoma:

High

Low

Recurrent Metastases?:

Yes

No

If yes to the above question

Age of recurrent metastases:

Location of recurrence:

lung

Brain

bone

local

**Medical management for
nephroblastoma**

Chemotherapy:

Yes

No

Chemotherapy agents:

Actinomycin

Vincristine

Cisplatin

Ifosphamide

Epirubicin

Carboplatin

Etoposid
eCyclophosphamid
e

Chemotherapy dosages:

| | | |
|---------------|-----|----|
| Radiotherapy: | Yes | No |
|---------------|-----|----|

| | | | |
|----------------------|-------|---------|-------|
| Area of irradiation: | chest | abdomen | spine |
|----------------------|-------|---------|-------|

Radiotherapy dosages:

| | | |
|----------|-----|----|
| Surgery: | Yes | No |
|----------|-----|----|

| | | |
|---------------------|-----------------------|-------------------|
| Surgical resection: | Left nephrectomy | Right nephrectomy |
| | Left tumorectomy | Right tumorectomy |
| | bilateral nephrectomy | |

Anthropometrical Assessment

Weight: _____ kg Height: _____ m

Current Medical Management

Blood pressure: _____ / _____

| | | |
|-----------|--------|----------|
| Chest XR: | Normal | Abnormal |
|-----------|--------|----------|

| | | |
|-------------|--------|----------|
| Ultrasound: | Normal | Abnormal |
|-------------|--------|----------|

| | | |
|----------|--------|----------|
| CT Scan: | Normal | Abnormal |
|----------|--------|----------|

Study Logistics

PROTEIN PROVISION SECTION

Weight = _____ Kg

Protein Provision (2g/kg) required=

Volume of Nutren Junior provided: _____

Protein provision from Nutren Junior: _____

Volume of Protifar provided: _____

Protein provision from Protifar: _____

BIOCHEMICAL SECTION

| <u>Pre-ingestion U&E</u> | | <u>Post- ingestion U&E</u> | |
|---|-------|--------------------------------|-------|
| <u>Date</u> | Time | <u>Date</u> | Time |
| Anion gap | _____ | Anion gap | _____ |
| Chloride | _____ | Chloride | _____ |
| CO2 | _____ | CO2 | _____ |
| Creatinine | _____ | Creatinine | _____ |
| Potassium | _____ | Potassium | _____ |
| Sodium | _____ | Sodium | _____ |
| Urea | _____ | Urea | _____ |
| Pre ingestion urine analysis for microalbuminurea: | | _____ | |
| Post ingestion urine analysis for microalbuminurea: | | _____ | |

ADDENDUM 7: HEALTH RESEARCH ETHICS APPROVAL LETTER



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jou kennisvenoot • your knowledge partner

15 March 2010

MAILED

Ms C Garrett
Department of Human Nutrition
3rd Floor, Clinical building
Stellenbosch University
Tygerberg campus
7505

Dear Ms Garrett

"Assessing the renal handling of a dietary protein load in patients managed for Nephroblastoma."

ETHICS REFERENCE NO: N09/08/222

RE : APPROVED

At a meeting of the Health Research Ethics Committee that was held on 16 September 2009, the above project was approved on condition that further information is submitted.

This information was supplied and the project was finally approved on 15 March 2010 for a period of one year from this date. This project is therefore now registered and you can proceed with the work.

Please quote the above-mentioned project number in ALL future correspondence.

Please note that a progress report (obtainable on the website of our Division: www.sun.ac.za/rds) should be submitted to the Committee before the year has expired. The Committee will then consider the continuation of the project for a further year (if necessary). Annually a number of projects may be selected randomly and subjected to an external audit. Translations of the consent document in the languages applicable to the study participants should be submitted.

Federal Wide Assurance Number: 00001372
Institutional Review Board (IRB) Number: IRB0005239

The Health Research Ethics Committee complies with the SA National Health Act No.61 2003 as it pertains to health research and the United States Code of Federal Regulations Title 45 Part 46. This committee abides by the ethical norms and principles for research, established by the Declaration of Helsinki, the South African Medical Research Council Guidelines as well as the Guidelines for Ethical Research: Principles Structures and Processes 2004 (Department of Health).

Please note that for research at a primary or secondary healthcare facility permission must still be obtained from the relevant authorities (Western Cape Department of Health and/or City Health) to conduct the research as stated in the protocol. Contact persons are Ms Claudette Abrahams at Western Cape Department of Health (healthres@pgwc.gov.za Tel: +27 21 483 9907) and Dr Hélène Visser at City Health (Helene.Visser@capetown.gov.za Tel: +27 21 400 3981). Research that will be conducted at any tertiary academic institution requires approval from the relevant hospital manager. Ethics approval is required BEFORE approval can be obtained from these health authorities.

18 March 2010 12:08

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Approval Date: 15 March 2010

Expiry Date: 15 March 2011

Yours faithfully

MRS MERTRUDE DAVIDS

RESEARCH DEVELOPMENT AND SUPPORT

Tel: 021 938 9207 / E-mail: mertrude@sun.ac.za

Fax: 021 931 3352

18 March 2010 12:08

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