

PAEDIATRIC NEPHROLOGY SERVICES IN SRI LANKA – A JOURNEY FROM INFANCY TO ADOLESCENCE

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Introduction

My interest in renal disorders began during my internship at the Renal Unit of the National Hospital of Sri Lanka, under the supervision of Dr. Suresh Ramachandran. Due to the constraints of manpower at that time, I had the blessing of getting much needed hands on experience in renal procedures while still an intern house officer. This was further strengthened during surgical internship at the Professorial Unit where I developed a desire to manage renal transplant patients, as it was the only transplant centre in existence in the country at that time. With this background I started my career in paediatrics as a Registrar in Paediatrics at Teaching Hospital, Peradeniya, where I was given a free hand to perform procedures and carry out research on renal disorders by my supervising consultants. Even though I had a deep desire to become a paediatric nephrologist, my ambition was not realized as the Postgraduate Institute of Medicine did not recognize paediatric nephrology as a subspeciality at this juncture, and my hopes were temporarily suspended. However, while in training in the United Kingdom I continued my quest to be trained as a paediatric nephrologist. The research work I had performed in Sri Lanka¹⁻⁷, and the good references I had obtained, helped me to secure a Clinical Research Registrar post in Paediatric Nephrology at the Great Ormond Street Children's Hospital (GOSH),

University College London, United Kingdom (UK).

The main responsibilities of this post were to carry out research by investigating many aspects of nephrotic syndrome (NS) under the expert guidance of Dr. Richard Trompeter, Prof. Michael J. Dillon, Dr. William van't Hoff and Dr. Lesley Rees, all extremely eminent personalities in paediatric nephrology. I attended courses in statistics, research protocol development and human resource management to improve my profile as a researcher. The research I conducted in investigating many aspects of nephrotic syndrome have been presented in international scientific forums such as the British Renal Association, International Pediatric Nephrology Association and the Royal College of Paediatrics and Child Health⁸⁻¹³ and published in many international journals such as Paediatric Nephrology, Expert Opinion on Pharmacotherapy, Archives of Disease in Childhood and the Lancet¹⁴⁻²⁰.

In addition to the research work, I conducted two out patient clinics per week, provided advice for regional hospitals on management issues for children with nephrotic syndrome and did on-calls with the renal registrars. I received a wealth of experience in managing diverse renal problems during my stay at the Great Ormond Street Hospital as it was the largest paediatric transplant unit in the UK

and Europe and the final referral centre in the UK.

When I returned to Sri Lanka after 4 years of overseas training in the UK in 2002, paediatric nephrology services in Sri Lanka were in its infancy. The services were in the hands of four general paediatricians who had an interest in paediatric nephrology with many limitations. There was no end stage renal failure programme in the form of dialysis and renal transplantation. As such children with end stage renal disease (ESRD) were offered very little care and a painful end was inevitable. It was amid this background that I began to launch a multi-pronged effort to develop paediatric nephrology services in Sri Lanka. In this endeavour I focused my attention on,

- Initiating a general nephrology clinic at Teaching Hospital, Peradeniya
- Accepting renal patients 24 hours a day, all year round from any part of the country for further in-patient care
- Initiating an End Stage Renal Disease clinic
- Developing a dialysis and transplant programme
- Carrying out credible research with international collaboration to gain national and international recognition
- Obtaining recognition for paediatric nephrology as an important subspeciality in Sri Lanka

Today after a decade, I will present to you a 360 degree review of my efforts in developing paediatric nephrology from infancy to adolescence in Sri Lanka.

Estimating the burden of renal disorders and end stage renal disease (ESRD) in Sri Lanka is difficult because of the dearth of national registries and representative surveys. This was one of the major obstacles in justifying the need for the development of paediatric

nephrology to the Ministry of Health and to the Postgraduate Institute of Medicine. Therefore with the experience I gained in the UK, I developed a database to record renal patients seeking in-patient and out-patient care. I was fully supported by the Heads of my department who allocated one cubicle for in-patient care of renal patients and a slot in the outpatient department on a weekly basis. All patients attending the renal clinic were personally seen by me and in addition these children were provided free access to the paediatric ward. They were able to contact me over the phone or via e-mail for advice. As time went by, the number kept on increasing and today I review between 50 – 100 patients on a weekly basis. Even though there were two other doctors who helped me in the clinic, we sat around one big table to ensure that I could continue to make the management decisions and communicate at least a few words to all the patients. It was encouraging to see the diverse geographical areas of referral scattered all around the country from Hambantota in the south, to Jaffna in the north, to Colombo in the west and Trincomalee in the east, from where children presented to us. It is this that motivated and spurred me to help these children who otherwise would be bereft of hope, with a morbid future looming ahead of them. As children with chronic renal failure need extremely meticulous care, two special clinics are now in operation on a weekly basis for children with ESRD and post renal transplantation.

After 10 years, the review of database revealed information of different renal disorders among substantial numbers of patients.

Steroid Sensitive NS: 905, Steroid Resistant NS: 234, Focal Segmental GN: 146, Membranoproliferative GN: 29, Post Streptococcal GN: 748, Rapidly Progressive

GN: 46, Lupus Nephritis: 28, Chronic Renal Failure: 211.

This can easily be considered as one of the largest series of renal patients from a single centre and some reputed research centres have termed our centre as a gold mine for research. In fact one international multi-centre study which had identified 15 centres including ours to study a genetic link in steroid sensitive NS, allocated 18 months for sample collection. To the surprise of the principle investigator we were able to provide the total number of samples within 10 weeks. Therefore we are now in an ideal platform to launch quality research projects with international collaboration.

In-patient care

In-patient care began in an 8-bed cubicle at the Professorial Paediatric Unit. However it was a challenging task at the beginning as this was additional work for the nurses and junior doctors. More importantly it was a financial burden to the hospital Director as most renal patients needed expensive drugs and consumables. I was fortunate to obtain generous donations from hospitals in the UK in which I had worked before, to sustain the initial period. Patients were accepted from any part of the country, at any time of the day, irrespective of the condition of the patient. For the last 10 years I have been on-call on a daily basis for these patients. With donations from well-wishers, overseas hospitals and with the help of the Ministry of Health, the renal section is now fully equipped and has specified cubicles for patients with NS, general nephrology patients, patients on dialysis and post renal transplantation. The total bed strength is now 30, out of which 10 are high dependency beds. Today the unit is a recognised centre for the local training component in paediatric nephrology and for the paediatric component of adult nephrology

training by the Postgraduate Institute of Medicine. More importantly, we continue to receive referrals from all provinces in Sri Lanka, including Colombo, and thus have become the hub of paediatric nephrology services in Sri Lanka.

End Stage Renal Clinic

The national burden of ESRD is concealed behind statistics, which reflects only the number of people treated and not those who unfortunately die of kidney failure or other related complications. This is particularly the case for developing countries like Sri Lanka, where resources to provide renal replacement therapy (RRT) are severely limited and where substantial under reporting of ESRD probably reflects a vast unmet need. Therefore attention to both the prevention and management of ESRD is required. Successful RRT programmes for children have been established in some developing countries, and are testimony to the viability of such programmes with the appropriate mix of local factors. Dialysis and transplant services need to be affordable, cost-effective and ideally suited to local conditions. The economic and quality-of-life advantages of transplantation make it an attractive modality over dialysis, and coordinated efforts to facilitate safe and ethical transplantation in Sri Lanka was planned.

As the first step, an outpatient clinic for children with chronic renal failure began in 2002. It is possible to either halt or delay the progression to ESRD with careful monitoring and appropriate interventions, which is extremely important in the context of difficulties in providing RRT in Sri Lanka. We started our dialysis programme with peritoneal dialysis using manual exchanges, as we could not afford expensive machines. Haemodialysis was performed with the help of the adult nephrology unit at Teaching

Hospital, Kandy using temporary catheters. However, the lack of a renal transplant programme was a major obstacle for the dialysis programme as the ones who needed long term dialysis or transplantation succumbed to complications like infections during temporary dialysis procedures. This was very distressing to the team.

Sustaining a paediatric renal transplantation programme in a developing country poses many challenges. However, successful transplantation is the gold standard of therapy for children with ESRD. The impediments to success are different and are of greater magnitude than seen with adults, primarily because of differences in aetiology, distinctly different medical and surgical considerations in children, and an enhanced immune response in smaller children. Nevertheless, excellent results can be obtained in paediatric renal transplantation by strict adherence to surgical detail, stringent immunosuppressive management, careful integration of urologic reconstructive surgery with renal transplantation and aggressive fluid management in the small child. The management of these patients by an integrated, skilled and experienced team consisting of medical, surgical and critical care specialists is most important in achieving this success.

In 2004 our unit was visited by Dr. Oswald Fernando, a premier paediatric transplant surgeon in the UK, who offered his services to begin a paediatric renal transplant programme at Peradeniya. We were fortunate to have the services of Prof. Chula Goonasekera, a critical care expert who had had paediatric nephrology training at GOSH for 5 years. The surgical team gave their fullest corporation with Prof. M. D. Lamawansa and Dr. Gamini Buthpitya taking up the challenge of learning transplant surgery.

A superbly coordinated team effort by the Departments of Paediatrics, Surgery and Anaesthesiology, with the help of the transplant surgeon from the UK, provided the much needed impetus to commence the paediatric renal transplant program at the Teaching Hospital, Peradeniya in August 2004. The Head of the Department Prof. Chandra Abeysekera played a pivotal role in coordinating the programme, especially liaising with the adult nephrology unit in Kandy, which provided valuable support in initiating and sustaining this paediatric renal transplant programme.

(The initial results were presented at the Asian Society of Paediatric Nephrology Meeting Beijing China 2006, International Paediatric Transplant Association 2010 Istanbul Turkey, and the full paper was published in the Journal Paediatric Transplantation 2007)

Although the principle of early referral to allow preparation for RRT is well accepted, this is not always easily achieved in clinical practice. Timely referral provides the opportunity to plan for RRT or conservative kidney care. Many studies have used 3 to 4 months as a cut-off date to define a late referral but in practice it may take more than a year to prepare fully for RRT. Preparation for RRT should include planning for pre-emptive transplantation (i.e., before patients are established on dialysis). There is consensus that pre-emptive transplantation is associated with improved graft and patient survival. Retrospective and case control studies over 25 years have consistently demonstrated the detrimental effects of a late nephrology referral. These include inadequate intervention to delay the progression of renal failure, higher morbidity and mortality, poorer quality of life on dialysis, missed opportunities for pre-emptive renal transplantation and for some

patients, inappropriate dialysis treatment where conservative care might have been chosen by an informed patient/parent. Due to the lack of awareness and knowledge among medical practitioners, most referrals still come too late causing many difficulties to the transplant team and patient.

With the growing number of patients seeking renal replacement therapy, ESRD is a national health problem for developing as well as developed countries, overwhelmed by inequities in management. As for most developing countries, renal transplantation is offered selectively, mainly due to the lack of infrastructure, and survival can be compromised by the cost of immunosuppressive drugs and investigations, malnutrition and infectious diseases, in particular tuberculosis. Though factors such as social injustice and human indifference are seemingly beyond our reach, as nephrologists we can directly address some factors crucial for narrowing the disparity. Ironically, the existence of inequities in the management of ESRD provides unique, unrecognized opportunities for understanding aetiological, socio-cultural and health care system factors that can lead to improved clinical outcomes. Several recent reports have documented that structured medical care systems can reduce many chronic kidney disease related disparities and improve patient outcomes. One challenge for the nephrology community is to rethink how we might improve each element that affects long-term outcomes, without merely limiting ourselves to a procedure or protocol. It is important to inspire nephrologists to eliminate the inequities in managing ESRD and demand high-quality, structured renal care delivery systems which would minimize the unacceptable morbidity and premature mortality associated with chronic kidney disease.

Today we have our own transplant surgeon, who was trained in the UK by Dr Oswald Fernando, with another vascular surgeon assisting him. The Department of Paediatrics has recruited a lecturer who is now fully trained in paediatric nephrology, thus strengthening our force. To date 72 living related transplants have been performed with over 85% graft and patient survival over a 5 year period which is comparable to any advanced unit in the region. Moreover, we have reported the successful renal transplant of the smallest (8.5kg) and the youngest (1.5 years) child in South East Asia ²¹.

Carrying out credible research with international collaboration

Since the launch of paediatric nephrology services in 2002 at Teaching Hospital Peradeniya, a rich portfolio of research has been presented and published by the author, which is summarised below.

Invited lectures (International): 11, Publications (National & International): 20, Presentations (International): 27, Presentations (National): 28, Chapters in books: 02, Awards (Best Oral Presentations): 06.

As my research is on many aspects of paediatric nephrology, I have selected four studies which are interlinked and had a significant impact in understanding and treating childhood nephrotic syndrome, which have been cited by others more than 100 times, for presentation today.

Nephrotic syndrome is the commonest glomerular disorder in childhood, characterised by heavy proteinuria, hypoproteinaemia, oedema and hyperlipidaemia. It is a chronic distressing disorder with an annual incidence of 2-4 per 100,000 Caucasian children in the United

Kingdom. There is a racial variation in the susceptibility with a reported incidence of 9-16 per 100,000 British Asian children. Such figures are not available for Sri Lankan children but unpublished data suggests a similar incidence to that seen in British Asian children. In the pre-antibiotic era children with NS often died, usually from overwhelming infections arising as a result of immune dysfunction, which is an inherent feature of the disease, and poor nutrition. The importance of the immune system in the pathogenesis of childhood NS was first suggested by Shalhoub in 1974. Today a disturbance in the Th1 and Th2 immune mechanisms, mediated by cytokines and lymphokines, are thought to be involved in the generation of NS. These observations represent the scientific rationale for the use of cytotoxic and immunosuppressive drugs in childhood NS. With the introduction of antibiotics, and later with the use of corticosteroid therapy, the mortality of this condition has fallen dramatically.

Prednisolone was first prescribed for children with NS in 1956, when Arniel described four children who responded to a daily dose of 60mg prednisolone. Although a majority of children will respond to corticosteroid therapy, this therapy is not curative, and over 70% of children subsequently relapse. Relapses result in the administration of further courses of high dose corticosteroids that places the child at risk of a plethora of corticosteroid related side-effects. Steroid toxicity is of major concern to children with NS, and their families. In 1967 cyclophosphamide (CYC) was reported as an effective agent in maintaining sustained remission in steroid sensitive NS. However, the side effect profile of CYC has been a cause for concern, namely alopecia, bone marrow suppression leading to opportunistic infections, haemorrhagic cystitis and an unquantified long-term risk of infertility and

malignancy with obvious adverse implications for children.

In the mid 1980's the immunomodulatory drug Levamisole (LEV) and calcineurin inhibitor cyclosporin A (CSA) were added to the armamentarium of therapies with variable success rates and side effects. While the incidence of reported side effects with LEV therapy is low, its efficacy is also comparatively lower than the other agents. The side effect profile of CSA such as hirsutism, gingival hypertrophy and potential nephrotoxicity has limited its use in SSNS.

While the mechanism of a relapse is unclear, there is strong evidence that cytokines may mediate the onset of proteinuria. It is known that viral upper respiratory tract infections, bee stings and allergic reactions may trigger a relapse of the disease. However it was unclear as to why only some patients relapse with viral infections. I got the opportunity of investigating this when I came across a child presenting with a relapse of NS following the meningococcal C conjugate vaccination (MCCV). This was two months after the launch of the National Programme 1999, aimed at immunising all individuals in the UK under the age of 18 years within one year. At this point we reassured the family that it could be a coincidence. Two weeks later another child presented with a relapse of NS following the vaccination. To explore a causal relationship between the relapses and administration of MCCV, the relapse rate during the 12 month period pre and post vaccination were studied in children with steroid sensitive NS, vaccinated between November 1999 and October 2000. From a population of 224 patients who attended the NS outpatient clinic two years prior to the launching of MCCV programme, 106 patients received the MCCV during first 12 months of the campaign. The occurrence of relapses 12 months before and after MCCV

was recorded. Of the 106 children identified, 59 had no relapses while 47 (44.3%) suffered at least one relapse during the 24 month period of interest. The frequency of relapses is shown in **Figure 1**. Comparison of the number of relapses in the 12 month pre and post vaccination period is shown in **Figure 2**. It clearly indicates more relapses in the 12 months post vaccination period.

Overall 63 relapses occurred in the 12 months prior to vaccination compared to 96 in the 12 months post vaccination. Poisson regression was used to calculate the relative incidence of relapse in the post vaccination period

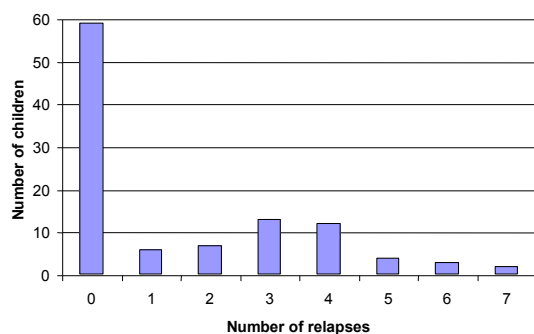


Figure 1. Frequency of relapses in vaccinated children

compared to the pre vaccination period. Using the 12 months pre-vaccination period as the background period gives a relative incidence of 1.52 (95% CI 1.10 – 2.11) in the post-vaccination period ($p=0.009$). In the 6 month post vaccination period the fraction of relapses attributable to vaccination were 26 relapses. Therefore out of 106 doses of vaccine, 26 relapses were attributable to the vaccine, which is a risk of 1 relapse for every 4 doses given to this population.

This is the first report of a series of patients where a relapse of NS was noted to cluster following administration of a vaccine.

Conjugate vaccines work by recruiting T helper cells and the cell derived cytokines to aid B cell antibody production and generating memory cells. As cytokines may play a critical role in the pathogenesis of NS, the disturbance of the cytokine milieu by the MCCV may have resulted in the observed cluster of relapses.

These results suggest a causal relationship between the administration of MCCV and relapse of NS. There could be other

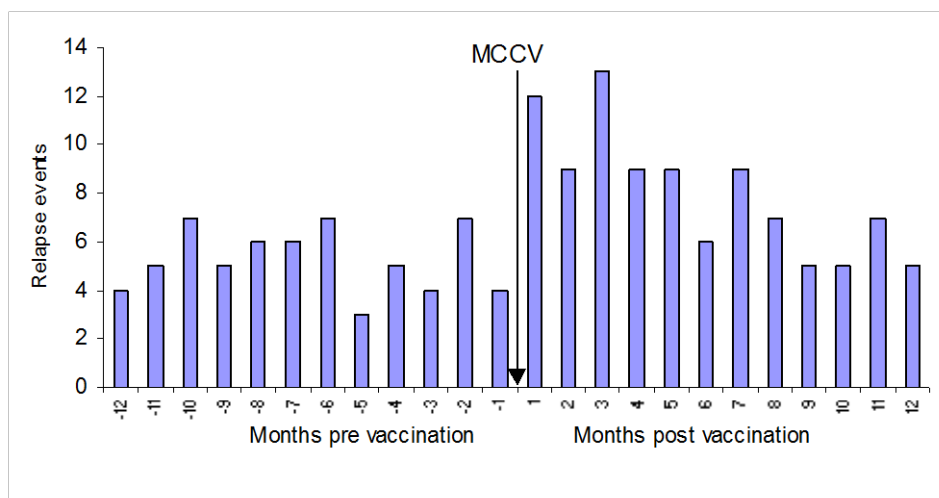


Figure 2. Distribution of relapses pre and post vaccination

immunisations which are capable of triggering a relapse of NS, and therefore paediatricians should keep close vigil on children during immunisation. Further studies on the release of cytokines following MCCV could lead to a breakthrough in understanding the mechanism of proteinuria in nephrotic syndrome.

This paper was rated as the Best Clinical Oral Presentation at the British Renal Association Spring Meeting in 2001²² and the full paper was published in the Lancet in 2004¹⁵.

From the results of this study and other studies published in the literature, it is clear that cytokine release plays a critical role in triggering a relapse. However, the question remained unanswered as to why only some get a relapse. I came up with the hypothesis that the degree of adreno-cortical suppression may impede the indigenous steroid response to stress and thereby create a cytokine storm that may trigger a relapse of the disease. However there are many unanswered questions with regard to prednisolone therapy and adrenal suppression.

- Does adrenal suppression occur with long-term alternate day prednisolone?

If so,

- What is the critical dose at which adrenal suppression is likely to occur?
- Is there an impact created by concurrent administration of Levamisole (LEV) or Cyclosporin A (CSA) with Prednisolone (PRED) on adrenal suppression?

We used the Modified synacthen test to evaluate the adrenal axis. The modified synacthen test uses a physiological dose of ACTH and has been validated against the insulin hypoglycaemia test. A cortisol response of >500ng/l was considered normal. Blood samples were collected at 10 min intervals for 1 hour for measurement of

serum cortisol concentration. Ethical approval for this study was obtained from the Institute of Child Health, University College, London, UK.

Patients and Methods

3 groups of patients were studied

1. Alternate day Prednisolone
2. Alternate day Prednisolone + Levamisole
3. Alternate day Prednisolone + Cyclosporin A

32 patients underwent evaluation- 12 on alternate day Prednisolone, 11 on alternate Prednisolone + Levamisole and 9 on alternate Prednisolone + Cyclosporin A. There was no significant difference in the mean dose of Prednisolone in the 3 groups.

Cortisol level (nmol/l)

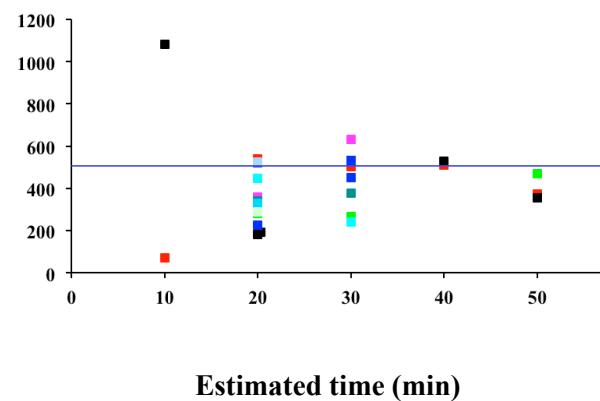


Figure 3. A significant proportion of children had a peak serum cortisol response below 500ng/l indicating adrenal suppression.

Results

In the 2 groups, PRED and PRED+LEV, over 70% had evidence of adrenal suppression. Interestingly in spite of receiving the longest duration of prednisolone, the CSA group had only in 25% of patients with evidence of adrenal suppression. These results were highly significant with a P value of 0.01.

Treatment Regimen	Cortisol response <500	Mean duration of prednisolone
PRED	72.7% (8/12)	14 (months)
PRED + LEV	81.8% (9/11)	20 (months)
PRED + CSA	25.0% (3/9)	33 (months)

Table 1. Cortisol response for different treatment regimens

During a 3 year follow up, 20 children who had a suboptimal cortisol response had a significantly greater number of relapses (95 relapses) when compared to the 12 children with a normal cortisol response with 24 relapses ($p=0.01$).

Discussion

Our data indicate that 62.5% (20/32) of children receiving alternate day prednisolone for steroid dependant NS had a suboptimal cortisol response suggesting hypothalamo-pituitary-adrenal axis suppression, and were at a greater risk of relapse.

The results of this study were presented at the Royal College of Paediatrics and Child Health Spring Meeting 2003²³, York, UK and the full paper was published in Archives of Disease in Childhood in 2007¹⁹.

In order to substantiate the findings of this study a further study was undertaken to explore the effect of increasing the dose of steroids during viral upper respiratory tract infections in reducing the risk of relapse in children with steroid dependent NS.

The study was designed to test the hypothesis that a small and short-term increase in the dose of Prednisolone during viral infections would reduce cytokine release and thereby reduce the risk of relapse in NS. Ethical approval for this study was obtained from the Institute of Child Health, University College, London, UK.

The study design was a randomised double blind placebo controlled cross over trial. In each patient the occurrence of relapse of NS was recorded for two consecutive viral upper respiratory tract infections (URTI). At the first sign of a presumed URTI parents were asked to report to the principal investigator for a clinical examination.

If the predetermined criteria to diagnose a viral URTI were met, these children were randomly allocated to take medicine A or B containing either Prednisolone or placebo with the first viral URTI and vice versa with the second viral URTI. The child was routinely reviewed on day 3 and day 7, focusing on the relapse of proteinuria and any potential adverse events due to the modest increase in the dose of prednisolone. The parents were asked to test and record the urine protein excretion each morning and the finding of 3+ proteinuria for three consecutive days was diagnostic of relapse. Relapse of NS was treated with the standard relapse regimen. The immunosuppression of these children was managed by the principal investigator in order to maintain a uniform approach. The study was carried out until 40

patients completed two episodes of viral infections.

Age at entry ranged from 1.5 to 13.2 (mean 6.4) years. There were 29 males and 11 females. The alternate day prednisolone dosage ranged from 0.1mg to 1mg/kg (mean 0.36).

The first viral infection was treated with placebo in 22 patients and with prednisolone in 18 patients and the second viral infection was treated with placebo in 18 patients and with prednisolone in 22 patients. There was a significant reduction in the number of relapses when the dose of prednisolone was increased during a viral URTI, as the 40 episodes treated with placebo were followed by 19 (47.5%) relapses while there were only 7 (17.5%) relapses in the Prednisolone treated group ($p = 0.003$ comparison of 2 proportions using Standard Error. CI 0.105 to 0.49). No significant side effects were encountered as a result of the increase in the dose of prednisolone during a viral URTI.

The results of this study confirmed the hypothesis that supplementation of glucocorticoid therapy during viral infections for children receiving alternate day prednisolone is capable of reducing the risk of relapse in NS, possibly by reducing the release of cytokines. Increasing the dose of Prednisolone during viral URTI by prescribing daily instead of alternate day Prednisolone for 7 consecutive days reduced the relapse rate by 30%. This resulted only in the administration of 3-4 extra doses of Prednisolone and was not associated with any notable side-effects.

Therefore it can be concluded that the prescription of daily Prednisolone during viral URTI in steroid dependent NS will result in a significant reduction of the number of relapses and thereby reduce the need for

cytotoxic therapy with its attendant side-effects.

The abstract was selected for presentation in a plenary session of the Royal College of Paediatrics and Child Health 9th Spring Meeting, 18-21 April 2005, University of York²⁴, UK and the full paper was published in Archives of Disease in Childhood in 2008²⁰.

(The results of this paper were cited in the section Archimedes in Arch Dis Child in 2009 titled 'Towards evidence based medicine for paediatricians' and in the Chochrane Data Base)

I also looked into the possibility of using this same strategy to reduce relapse frequency in patients with steroid sensitive NS who were off corticosteroids. In order to ascertain this, a placebo-controlled crossover trial was conducted on 48 patients with idiopathic NS who had been off corticosteroids for a minimum of three months. Patients recruited were randomized into one of two groups. Group A received 5 days of daily prednisolone at 0.5mg/kg at the onset of an URTI while group B received 5 days of placebo. Both groups were followed up for one year and the URTI induced relapse frequency was noted. A cross over was performed for the next year with group A receiving placebo and group B receiving prednisolone. The student t-test was used to compare continuous variables. The Fishers exact test was used to compare categorical variables.

Results

Of the 48 patients recruited, 33 completed the study. The mean (SD) age at baseline was 12.0 ± 2.4 years for the treatment group and 10.0 ± 2.9 years for the placebo group. In the treatment group 113 episodes of URTI led to 11 relapses, while in the control group 101

episodes of URTI led to 25 relapses. There was no significant difference between the mean number of URTIs between the treatment and control groups (3.5 ± 1.5 and 3.2 ± 1.4 , $p=0.31$). The treatment group had a significantly lesser number of relapses compared to the control group ($p=0.014$). The majority (65.6%) within the treatment group did not relapse whilst the remaining subjects had a single relapse. In contrast only 40.6% of the control group remained in remission whilst 40.6% suffered from a single relapse and 18.8% had two relapses.

Conclusion

The results of this study showed that administration of a short course of daily corticosteroids during a presumed URTI significantly reduces the frequency of URTI induced relapses in patients with steroid sensitive NS who are off corticosteroids.

The results of this study were presented at the annual scientific congress of the Sri Lanka College of Paediatricians, 2014 for which it was awarded the best paper of the congress. The research work presented and published has earned our unit international recognition as a credible research centre enabling us to collaborate with high profile research units like Dukes School of Medicine USA, Royal Manchester Children's Hospital UK, Royal Free Hospital, UK and Great Ormond Street Children's Hospital, UK. It also has given trainees an opportunity to strengthen their links with reputed medical institutions with good quality research helping them to secure good centres for training overseas and thereby add to their portfolio. Moreover I had the rare distinction of being invited as a Guest Speaker to many International Meetings such as the International Pediatric Nephrology Association 2004, British Association of Paediatric Nephrology 2006, Indian Academy of Pediatrics 2006, Indian Pediatric

Nephrology Group 2004 and 2005, International Paediatric Transplant Association 2011 and 2013, Asia Pacific Congress of Paediatrics and Asian Congress of Paediatric Infectious Disease, which is a reflection of the quality of the research published.

Gaining Recognition for Paediatric Nephrology as a Sub-speciality

The Prof. CC de Silva oration I delivered at the Sri Lanka College of Paediatricians scientific sessions based on the research I had performed in UK provided me an ideal platform to emphasise to the paediatric fraternity the importance of having sub-specialities in paediatrics. I wrote a justification to the College of Paediatricians on why paediatric nephrology should be recognised as a sub-speciality and proposed an amendment to the constitution to have a society for paediatric nephrology under the umbrella of the College of Paediatricians. At a special general meeting it was decided that the society should be formed independently, and it was formed in 2003 with participation of eminent paediatric nephrologists like Prof. Arvind Bagga (India) and Prof. Michael J. Dillon from the UK. It is now registered as a member of Asian Society of Paediatric Nephrology. Although the society did not function actively due to the small numbers, it had the desired impact. The PGIM started sub-specialty training and today we have 4 trained paediatric nephrologists and 2 are currently in training. Moreover from 2003 at almost all sessions of the College of Paediatricians, paediatric nephrology was well represented with eminent speakers attending from different parts of the world.

Future of Paediatric Nephrology in Sri Lanka

At this moment I like to make a quote from the famous human rights activist Dr. Martin Luther King, Jr. (1929–1968). “Of all of the forms of inequality, injustice in health is the most shocking and inhumane.” This is very true even in the 21st century when providing renal replacement therapy for children with ESRD in Sri Lanka. Significant proportions of patients are not offered proper renal replacement therapy due to lack of infrastructure, manpower, economic constraints social circumstances and even the distance to a transplant centre. Even today paediatric renal transplants are performed only at Peradeniya. However the ship has started to sail and Sri Lanka is now on the world map of paediatric nephrology. I firmly believe the young paediatric nephrologists will take up the challenge in further developing paediatric nephrology services in Sri Lanka to minimise the inequity and injustice in providing renal services to the paediatric population in Sri Lanka, and I firmly believe that bureaucracy and ‘red tape’ will not deter them in forging ahead.

Acknowledgement

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References

1. Jayasena L, Abeysekera CK, Abeyagunawardena AS. Levamisole in childhood nephrotic syndrome: a preliminary report. *Proceedings of Sri Lanka Association for the Advancement of Science* 1993;49:31
2. Jayasena L, Abeysekera CK, Abeyagunawardena AS. Post streptococcal glomerulonephritis in childhood. *Proceedings of the Kandy Society of Medicine* 1994;16:44-45
3. Jayasena L, Abeysekera CK, Abeyagunawardena AS. Intravenous Midazolam for sedation paediatric invasive procedures. *Proceedings of the Kandy Society of Medicine* 1994;16:44
4. Jayasena L, Abeysekera CK, Abeyagunawardena AS. Cost effectiveness of prevention of post Streptococcal glomerulonephritis. *Proceedings of the Kandy Society of Medicine* 1994;16:43
5. Abeysekera CK, Jayasena L, Abeyagunawardena AS. A study of urinary tract infections in childhood. *Proceedings of the Kandy Society of Medicine* 1995;17:1-2
6. Jayasena L, Ratnatunga N, Abeyagunawardena AS. Histopathological study of the kidneys of a selected group of children with primary nephrotic syndrome. *Proceedings of 30th Annual Scientific Congress of Sri Lanka Paediatric Association* 1995:FP10
7. Abeysekera CK, Jayasena L, Abeyagunawardena AS. Urinary tract infections in childhood. *Proceedings of 31st Annual Scientific Congress of Sri Lanka Paediatric Association* 1996:34
8. Abeyagunawardena AS, Collins S, Dillon MJ, Rees L, Van't Hoff W, Trompeter RS. Management, complications and outcome of steroid sensitive nephrotic syndrome. *Congress of the International Pediatric Nephrology Association Pediatric Nephrology* 2001; 16:C119
9. Abeyagunawardena AS, Goldblatt D, Trompeter RS. Relapse of nephrotic syndrome triggered by Meningococcal C conjugate immunisation. *Congress of the International Pediatric Nephrology Association Pediatric Nephrology* 2001; 16:C119
10. Abeyagunawardena AS, Collins S, Dillon MJ, Rees L, van't Hoff W, Trompeter RS.

Outcome of focal segmental glomerulosclerosis - 20 years experience. *Congress of the International Pediatric Nephrology Association Pediatric Nephrology* 2001; **16**:C119

11. Abeyagunawardena AS, Collins S, Dillon MJ, Rees L, van't Hoff W, Trompeter RS. Impact of cyclophosphamide therapy on renal survival in idiopathic focal segmental glomerulosclerosis. *Proceeding of British Renal Association Autumn Meeting*. 2001:21

12. Abeyagunawardena AS, Goldblatt D, Trompeter RS. Relapse of Nephrotic Syndrome following Meningococcal C conjugate vaccine. *Proceeding of British Renal Association Spring Meeting*. 2001: 37

13. Abeyagunawardena AS, Trompeter R, Adreno-cortical suppression in nephrotic syndrome. *6th International Medical Congress - Sri Lanka* 2002: 59

14. Abeyagunawardena AS, Brogan PA, Trompeter RS, Dillon MJ. Immunosuppressive therapy of childhood idiopathic nephrotic syndrome. *Expert Opinion on Pharmacotherapy* 2002; **3**(5):513-9

15. Abeyagunawardena AS, Goldblatt D, Andrews N, Trompeter RS. Risk of relapse after meningococcal C conjugate vaccine in nephrotic syndrome. *Lancet*. 2003;**362**:449-50.

16. Abeyagunawardena AS, Dillon MJ, Rees L, van't Hoff W, Trompeter RS. The use of steroid sparing agents in steroid sensitive nephrotic syndrome. *Pediatric Nephrology* 2003 **18**: 919-924

17. Abeysekera C, Abeysinghe C, Manuwickrama TD, Yasaratne BM, Abeyagunawardena AS. The validity and cost effectiveness of sulphosalysylic acid test in comparison to heat test and dipstick test in detecting proteinuria. *Sri Lanka Journal of Medicine* 2005;**14**(1):1-4

18. Abeyagunawardena AS, Sabire NJ, Risdon T, Kumarasiri PVL, Dillon MJ, Rees L, van't Hoff W, Trompeter RS. Predictors of long term outcome of children with idiopathic focal and segmental glomerulosclerosis. *Pediatric Nephrology* 2007;**22**(2):215-221

19. Abeyagunawardena AS, Hindmarsh P, Trompeter R S, Adrenocortical suppression increases the risk of relapse in nephrotic syndrome. *Arch Dis Child* 2007;**92**(7):585-588

20. Abeyagunawardena AS, Trompeter RS. Increasing the dose of Prednisolone during viral infections reduces the risk of relapse in Nephrotic Syndrome: a randomised controlled trial. *Arch Dis Child*. 2008; **93**(3):226-8

21. Ranawaka PRD, Jayaweera H, Pathmanathan T, Abeyagunewardena AS. Smallest child to undergo successful renal transplantation in Sri Lanka. *Proceedings of the 14th Annual Scientific Congress of the Sri Lanka College of Paediatricians* 2012: P-89

22. Abeyagunawardena AS, Goldblatt D, Trompeter RS. Relapse of Nephrotic Syndrome following Meningococcal C conjugate vaccine. *Proceeding of British Renal Association Spring Meeting* 2001: 37

23. Abeyagunawardena AS, Hutchinson C, Hindmarsh P, Trompeter RS. Adrenocortical suppression in nephrotic syndrome. *Proceeding of Royal College of Paediatrics and Child Health. Archives of Disease in Childhood* 2003; **88**(1): A67

24. Abeyagunawardena AS, Trompeter RS. The effect of an increased dose of prednisolone during viral infections to reduce the risk of relapse in nephrotic syndrome: a randomised double blind placebo controlled trial. *Archives of Disease in Childhood* 2005;**90**:P12