TROPICAL JOURNAL OF NEPHROLOGY

The Official Journal of the Nigerian Association of Nephrology

AIMS and SCOPE

The aims and scope include the following:

1. *To provide a medium of exchange of ideas and knowledge of nephrology in the tropics through publication of research works, clinical experiences and relevant articles.*

2. *To promote nephrology education, clinical practice and research through publication of original research works, innovative clinical experience and authoritative review articles on topical issues.*

3. *To provide an avenue for global dissemination of consensus positions on issues of concern in tropical nephrology through publication of proceedings of consensus meetings, dedicated conferences and commissioned reviews.*

4. *To serve as a scientific link between the Nigerian Association of Nephrology and other such International Organizations all over the world.*

Publication Details

The Tropical Journal of Nephrology is owned by the Nigerian Association of Nephrology and published by Samdavies Publishers, His Grace Villa, Plot 4, Adenekan-Oyejide Street, Oloruntedo Layout, Kuelu, Oloode, New Ife Road, Ibadan, P. O. Box 27411, Agodi, Ibadan, Nigeria. *Tel:* 234 02 7522086, 08023451177, 08084878480, 08054569871
E-mail: samdaviesventures@yahoo.com.

The views expressed here are solely that of the authours and do not represent that of the Association.

Subscription request should be sent to the Managing Editor. Subscription prices (2 issues) for individuals in Africa is N3, 000.00 and $50 for outside Africa. Institutional rate is N 4,500.00 for African countries and $60 for countries outside Africa.

Articles for submission should be forwarded to the The Editor-in- Chief through: The Managing Editor, Dr. B. L. Salako, Department of Medicine, University College Hospital, PMB 5116, Dugbe, Ibadan, Nigeria. E-mail: tropicaljournal_2005@yahoo.com.

ISSN 2006-49 OX

TROPICAL JOURNAL OF NEPHROLOGY

The Official Journal of the Nigerian Association of Nephrology

Founding Editorial Board

TROPICAL JOURNAL OF NEPHROLOGY

The Official Journal of the Nigerian Association of Nephrology

The Nigerian Association of Nephrology Officers 2008-2010

SECRETARIAT
THE SECRETARY GENERAL (NAN),
Renal Unit,
Department of Medicine,
Obafemi Awolowo University Teaching Hospital Complex,
P.M.B 5538, Ile-Ife,
Osun State, Nigeria.
E-mail: nephrologynigeria@hotmail.com

TABLE OF CONTENTS

TROPICAL JOURNAL OF NEPHROLOGY

Guidelines for Contributors

Manuscript should be typewritten on A4 (210 x 297) paper with double line spacing and wide margins of 4cm. the front or typeface should be "Time New Roman", 12 points and justified on both sides. The manuscript should conform to international outlays consisting of the **Title** (Use an Initial capital letter only for the first word and proper nouns. General abbreviation should be avoided in the title), **Author(s) name** with his/their address(s) and **Full address of the corresponding author, Abstract,** (not more than 250 words, Do not use sub-heading such as methods, results and conclusion in the abstracts). **Introduction, Materials and Methods, Results, Discussions, Acknowledgement, References, Tables and Figures with appropriate legends.**

Tables must be typed-double-spaced, numbered in Roman numeral I, II III and must be formatted to be read with the page in upright orientation and not sideways. All illustrations must be placed in position in the text and three copies submitted. An informed consent and approval of a well-constituted institutional ethical committee must be explicitly stated.

References should be listed in other of appearance in the text and indicated in Arabic numbers. The Authors' names should be followed by the initials, then the title of the paper, international abbreviations of the journal, year of publication, volume, number, the first to the last page must be indicated. Where authors are more than three, et al could be used for others.

Examples:

Arije A, Kadiri S, Akinkugbe O.O. The viability of haemodialysis as a treatment option for renal failure in a developing economy. Afr. J. Med Sci., 2000; 29 : 311 – 314

Kleinknecht, D. Epidemiology of acute renal failure in France today. In: Acute renal failure in the intensive therapy unit (eds Bihali, D,Neild, G) 1990;pp13-22. Springer – Verlag. New-York.

Categories of Contributions

This may be original research articles not more than 5000 words, review articles not more than 5000 words and should contain sub-headings, case reports and short communications not exceeding 3-10 pages including 2 tables, 2 illustrations and 15 references. Conference proceedings and letters to the editor may also be submitted for publication in the Tropical Journal of Nephrology.

Image Intensity

A laser printer should be used to enhance the image.

Unit of Measurement

SI (System International) unit is recommended.

The original typescript and three (3) good photocopies of the manuscript should be sent with a copy on $3^{1/2}$ inch diskette in Microsoft for Window. The final copy of an accepted article should be submitted on a floppy disk (virus screened) and two additional printout copies of the manuscript.

Condition for Publication

Manuscript submitted for publication to Tropical Journal of Nephrology must not have been submitted for consideration or published in any journal. Upon acceptance o f the submitted article, the author automatically transfers the copyright of the article to the publisher. It is advisable that the manuscript should confirm to the instruction contained there in. This would facilitate the processing of the articles

Handling Charges
A handling charge of $30 or N2, 500.00 must accompany each manuscript payable to Tropical Journal of Nephrology to defray the cost handling.

Offprint / Reprint
Orders for reprint should be addressed to the Samdavies Publishers, His Grace Villa, Plot 4, Adenekan-Oyejide Street, Oloruntedo Layout, Kuelu, Olode, New Ife Road, Ibadan, P. O. Box 27411, Agodi, Ibadan, Nigeria. *Tel:* 08023451177, 08084878480, 08054569871 *E-mail:* samdaviesventures@yahoo.com. Every order would attract a token fee.

Business Communication
Business communication should be sent to the Business Manager.

Advertisement
Advertisements are subject to editorial approval and advertising rates are available on enquiry from the business office.

Copyright

Subscription and Charges
Subscription request should be sent to the Editor / Publisher. Subscription prices in Africa are N 3, 000.00 and $50 outside Africa for individual per Volume of 2 issues. Institutional rates, N 4,500.00 for African countries and $60 for countries outside Africa.

Submission of Article
Articles completed using the above format should be submitted to the:The Editor-in-Chief through:
The Managing Editor, Prof. B.L.Salako, Department of Medicine, University College Hospital, Ibadan, PMB 5116, Dugbe, Ibadan, Nigeria. E-mail: tropicaljournal_2005@yahoo.com

Tropical Journal of Nephrology Vol.4 No2 Dec., 2009 125-128

Unilateral Shrunken Kidney in a 58 Year Old Nigerian Woman with Kidney Stone

Okafor UH[1] and Unuigbe EI[2]

[1]Renal Unit, Department of Medicine, Enugu State University Teaching Hospital, Parklane, Enugu, Nigeria.
[2]Renal Unit, Department of Medicine, University of Benin Teaching Hospital, Benin City, Nigeria.

ABSTRACT

Background Kidney stones are formed as a result of interplay between factors promoting and those inhibiting stone formation in the kidneys/urinary tracts. Kidney stones cause a lot of complications including urinary tract obstruction. Failure or delay in relieving the obstruction causes irreversible damage to the kidney and urinary tract leading to loss of function and atrophy of the kidney.

Mrs. AT was a 58 year old woman referred from a general hospital with an 8 year history of right lumbar pain. The clinical examination and investigations revealed that she had atrophy and loss of function of the right kidney secondary to nephrolithiasis.

The objective of this case study is to highlight that kidney stone can lead to unilateral kidney atrophy and loss of function.

INTRODUCTION

Renal stone is a crystal aggregate embedded in a small amount of glycoprotein matrix. The initial formation is usually at the collecting duct resulting either from super saturation of stone forming constituents or damage and dysfunction of the renal tubule. The prevalence is 36-100 per 105, increasing with age, more in whites and males [1, 2]. This variability has been attributed to various demographic, geographic and physiological factors [3,4,5,6]

The complications associated with renal stones are pyelonephritis, pyonephrosis, septicaemia, urinary fistula, ureteric scaring, stenosis and perforation. Obstruction of the urinary tracts by renal stones leads initially to enlargement/dilatation of the urinary tract (hydroureter) and kidneys (hydronephrosis), but failure/delay in relieving the obstruction leads to kidney atrophy. There is associated impairment in renal function in presence of urinary tract obstruction manifesting as acute or chronic renal failure[7].

The objective of this case report is to draw attention to the fact that kidney stones can lead to unilateral kidney atrophy and loss of function.

CASE REPORT

Mrs. AT was a 58 year old woman referred from a general hospital with an 8 year history of right lumbar pain. The pain was initially colicky but later became continuous and dull in nature, moderate to severe, radiating to the groin with no relieving or aggravating factors. The pain was recurrent with periods of remission and exacerbation, but later became non-remitant for about a year. She has had recurrent low grade fever associated with rigors but no nausea, vomiting or anorexia. She had taken a variety of analgesics for the pain but denied use of any herbal preparation.

A month prior to presentation, she noticed reduction in her urine volume. This was not associated

Correspondence: **Dr Okafor Umezurike Hughes**

Renal Unit, Department of Medicine,
Enugu State University Teaching Hospital Parklane, Enugu, Nigeria.
E-Mail: umehughes@yahoo.com

with dysuria, haematuria, nocturia or frothiness of urine.

There was no body, leg or facial swelling and no seizures or loss of consciousness. She had no cough, dyspnoea, orthopnoea or paroxysmal nocturnal dyspnoea. She was a petty trader and her diet consisted mainly of staple food in her locality.

She had been managed in various private hospitals for the abdominal pain and was diagnosed hypertensive 3 years earlier in the referral hospital and was on alpha methyl dopa and nifedipine. She is not a known diabetic. She had never used tobacco in any form and denied use of alcohol.

Clinical examination revealed middle aged anxious looking woman, who was not pale, not dehydrated and had no peripheral oedema. Her pulse rate was 84 beats/minute; blood pressure 194/90mmHg supine; JVP not raised. There was no clinical evidence of cardiomegaly or left ventricular hypertrophy. First and second heart sounds only were heard, no murmur. Chest was clinically clear on auscultation.

Abdominal examination revealed no area of tenderness, no organ palpably enlarged, no ascites and no bruit heard.

Laboratory investigations from the referral hospital revealed that the urinalysis was normal; urine microscopy showed many calcium oxalate crystals as the only abnormality, urine culture yielded no significant growth. The abdominal scan done 5 months prior to referral showed hydronephrosis of the right kidney, other viscera were normal and no ascites.

A working diagnosis of right hydronephrosis secondary to kidney stones in poorly controlled hypertension was made. Repeat laboratory investigations in our centre revealed many calcium oxalate crystals on urine microscopy, serum urea of 45mg/dl, creatinine 1.6mg/dl, sodium 135mmol/l, potassium 4.5mmol/l, bicarbonate 23mmol/l, chloride 108mmol/l, calcium 8.2mg/dl, and phosphate 4.8mg/dl and estimated glomerular filtration rate of 46ml/minute.

Abdominal ultrasound showed right kidney that was shrunken and atrophic measuring 4.5 × 2.8 cm, hyperechoic with ablation of the corticomedullary junction. The left kidney was 12.1 × 4.2 cm in size with normal echotexture and cortico medullary differentiation. The liver, adrenals and billiary tract were normal.

An intravenous urography showed radio opaque density in the right pelvis just above the right iliac bone in the scout film. There was prompt excretion of contrast by the left kidney. The left kidney was enlarged but normal in shape, position, outline and alignment. The left pelicalyceal system and ureter were grossly normal. There was no excretion of contrast by the right kidney, and the right ureter was not opacified. The bladder filled out well with regular margin and the post micturition film showed no residual urine.

The chest X ray, electrocardiography, packed cell volume and blood film was normal. A final diagnosis of acute renal failure secondary to kidney stones with unilateral kidney atrophy and poorly controlled hypertension was made.

She was placed on tablets nifedipine retard 20mg twice daily, atenolol 50mg daily, and alpha methyl dopa 250mg thrice daily, dietary counseling, and advised on liberal fluid intake. She was referred to the urologist for review and possible nephrectomy of the atrophied kidney.

She has been compliant on medications and has been regular on follow up. Her blood pressure control has been fair, and was 130/90mmHg at last visit. During her outpatient visit serum urea was 20mg/dl, creatinine 1.2mg/dl, and electrolytes were within normal. The surgeons reviewed the patient for possible nephrectomy of the atrophic kidney but she declined surgery.

DISCUSSION

The theories on the formation of stones in the kidney are the free, and the fixed particles theory. The free particle theory is that there is super saturation of the stone-forming product in the urine while the fixed theory is that there is injury or dysfunction in the renal tubules, which attracts the stone forming substances. Inhibitors and promoters of renal stone formation plays significant role. The inhibitors are Tammhorsfall protein, nephrocalcin, glycosaminoglycans, ribonucleic acid, pyrophosphate, citrate and some trace elements. The promoters include presence of calcium oxalate in urine, hypercalcaemia, hypercalciuria, uricosuria, hyperuricaemia and dehydration8. Reduction of inhibitors or elevation of promoters encourages stone formation[3]. Although this patient's urinary calcium and uric acid were not estimated she had significant calcium oxalate in the urine.

The clinical manifestation of patients with renal stone depends on the site, size, mobility, and types of stone. It also depends on the presence or absence of

concomitant infection. Patients with small stones are usually asymptomatic and may be diagnosed incidentally by abdominal imaging or passage of the stone in urine. In the moderately sized or large stone, there is usually flank abdominal pain, which may be unilateral as in our patient, or bilateral if both kidneys are affected. The pain is either colicky when the stone is in the ureter or continuous when the stone is in the kidney or completely obstructing the ureter. Pain may be mild or severe associated with nausea and vomiting, usually radiating to the groin. Other manifestations are haematuria, recurrent urinary tract infection. Post renal acute renal failure as in our patient may be the mode of presentation in patients with complete obstruction of ureter (in a solitary kidney), bladder, urethra or rarely bilateral obstruction of both ureters. Loss of affected kidneys as in our patient occurs when the obstruction is longstanding without relief [9, 10. 11, 12]. Our patient had initially recurrent colicky flank pain, which later became continuous and severe. The onset of oliguria was the only pointer to impaired renal function due to post renal urinary obstruction from stones. The renal calculi probably led to complete loss of function on the affected kidney as detected by the IVU.

Complete urinary tract obstruction lasting more than 6 weeks leads to irreversible loss of renal function [7, 13,] Sequence of events following the obstruction shows that there is vasodilatation of preglomerular blood vessels leading to increase renal blood flow thus maintaining the glomerular filtration rate (GFR) for few hours following the obstruction.

Twenty – four hours later there is increase in preglomerular vascular resistance with reduction in renal blood flow, and GFR falls to 40-50% of normal. Persistence of the obstruction leads to further fall in GFR to 30% in 6 days, 20% in 2 weeks and 12% in 8 weeks, after which the obstruction is irreversible[9].

These changes are mediated through various chemical mediators like nitric oxide, prostaglandins, angiotensin etc released by the macrophages, T-cells and juxtaglomerular cells[14].

Depending on duration of obstruction, kidneys completely obstructed by stone shows either hydronephrosis, or atrophy as in our patient. The histology varies from interstitial inflammation with cellular infiltration, tubular dilation and tubulo interstitial fibrosis[15]. The right kidney of our patient was atrophic without evidence of function on intravenous urography. It is possible that our patient may have had incomplete ureteric obstruction over the years and later became complete before presentation. The IVU detected a radiopaque object, possibly kidney stone, at the point the right ureter crosses the pelvic brim, and this we suspect to be the cause of the obstruction and subsequent atrophy of the right kidney.

Prevention of stone formation and its enlargement, with elimination of uric acid and cystine stones is achieved by avoiding dehydration, maintaining appropriate urinary flow and PH16. Patients are encouraged to take liberal fluid, to void at least 2 litres of urine daily. Urine PH is made acidic in patients with calcium oxalate stones, and alkaline in uric acid stones. Non-steroidal or narcotic analgesic is used to control pain. There were ongoing trials of steroid and nifedipine to reduce ureteric inflammation and ureteric colic respectively, but are yet to be approved [2, 17].

Various surgical interventions in nephrolithiasis are available. Indications for surgery are intractable pain, recurrent infections, and obstructions. Surgery is contraindicated in patient with active urinary tract infection, bleeding diathesis and pregnancy. The surgical procedures are extracorporal ballistic short wave lithotripsy (EBSWL), ureteroscopy with lithotripter, percutaneous nephrostolithotomy and nephrectomy which can be partial or total.[18]

In our environment, the medical management is available, and effective when diagnosis is early and patient compliant to therapy. This prevents formation of stone in 98% of patients at risk, prevents recurrence in 60%, and eliminates stones in 70% of patients[2, 18]. This can ameliorate morbidity, and prevent loss of the kidney as in our patient.

We advocate early diagnosis and prompt intervention to forestall complications such as was encountered in this case reported.

REFERENCES

1. Johnson CM, Wilson DM, O'Fallon WM *et al*. Renal stone epidemiology: a 25 years study in Rochester Minnesota. Kidney Int 1979; 16: 624 – 632.
2. Stewart C. Nephrolithiasis. Emerg med clin North Am 1988; 6: 617 - 621
3. A. Rodgers. The riddles of kidney stone disease: lessons from Africa. Uro Res 2006; 34: 92 – 95
4. Kambai A, Wahab A,Khattab A and Zaki J. urolithiasis in the Sudan. Studies on a stone

prone and a stone free population. Br J Urol 1981; 53: 7

5. Esho J. the rarity of urinary calculus in Nigeria. Trop Geogr Med 1978; 30: 86

6. Michael SJ, Michael JT, Ralph JC *et al*. demographic and geographic variability of kidney stones in the United States. Kidney Int 1994;46:893 – 899/

7. Kukreja R. Desai M and Patel SH. Nephrolithiasis is associated with renal insufficiency: factors predicting. J Endourol 2003; 34: 92 – 95

8. Scurr DS and Robertson WG. Modifiers of calcium oxalate crystallization found in urine. III studies on the role of Tammhorsfall mucoprotein and ionic strength. J Urol 1986; 136: 505 – 507

9. Klar S. Patholophysiology of obstructive nephropathy: A 1991 update. Semin Nephrol 1991; 11: 156 – 159.

10. Older RA, Libshutz HI and Kelvin FM. Post obstructive atrophy: often over looked cause of unilateral small kidney. Urol 1996; 5: 517 – 519

11. Flamm J and Felks N. Unilateral atrophy of the kidney. Wien Med Wochenschr 1986 ; 137(17): 427 – 429

12. Older RA, Libshitz HI and Kelvin FM. Post obstructive atrophy, often overlooked cause of unilateral small kidney. Urology 1976; 8(5): 517 – 518.

13. Vaughan EDJ and Gillen water JY. Recovery following complete chronic unilateral ureteral occlusion: functional, radiographic and pathologic alterations. J Urol 1971; 106: 27 – 35

14. Miyajima A, Chen J, Poppas DP, Vaughan ED and Felsen D. Role of nitric oxide in renal tubular apoptosis of unilateral ureteral obstruction. Kidney Int. 2001; 59(4): 1290-1303

15. Kellner D, Chen J, Richardson I *et al*. Angiotensin blockade decreases fibrosis and fibroblast expression in a rat model of unilateral ureteral obstruction. J Urol 2006; 176; 806 – 812

16. Olapade – Olaopa E, Agunloye A, Ogunlana D, Owoaje E and Maniho T. Chronic dehydration and symptomatic upper urinary tract stones in young adults in Ibadan Nigeria. West Afr J Med 2004; 23: 146

17. Porpiglia F, Destefanis P and Fiori C: Effectiveness of nifedipine and deflazacort in the management of distal ureter stones. Urology 2000; 56(4): 579-582

18. Cruz GNA, Garia GE, Sanz MK, Sanz MJ, Pozo MB and Lovaco CF. Partial nephrectomy in lithiasis. Arch Esp Urol 2000; 53(9): 809 – 818

19. Leslie SW. A practical approach to kidney stone prevention. Nephrolithiasis update: the role of metabolic evaluations 1996; SUNA Annual Meeting Postgraduate Course Syllabus: 12-14.

Tropical Journal of Nephrology Vol.4 No2 Dec., 2009 115-119

The Assessment of Hemodialysis Adequacy among ESRD Patients in Ilorin using Urea Reduction Ratio

Chijioke A, Aderibigbe A, Rafiu MO, Olanrewaju TO and Makusidi AM

Renal Unit, University of Ilorin Teaching Hospital, Ilorin.

ABSTRACT

Urea Reduction Ratio (URR) is a measure of adequacy of delivered dose of dialysis expressed as a percentage reduction in blood urea level after a session of dialysis which is mathematically related to Kt/V. Although Kt/V is recommended as the best measure of dialysis adequacy, URR is the most utilized because of its simplicity with both methods having similar predictive power in terms of patient outcome.

In Nigeria, there is paucity of data on adequacy of haemodialysis and few available reports show that inadequate dialysis is common. Since inadequate dialysis contributes significantly to poor patient survival, a one year retrospective appraisal of patients on maintenance haemodialysis at University of Ilorin

Teaching Hospital (UITH), Ilorin was carried out to determine the adequacy of dialysis and patient outcome.

All patients with end stage renal disease (ESRD) and were regular on at least twice weekly haemodialysis of 4 hours per session were included in the study. Data was analyzed with SPSS version 16.

Twelve out of 33 patients (36.4%) with ESRD on maintenance haemodialysis met the inclusion criteria. The mean age of the patients was 48.25 ± 17.85 with male to female ratio of 2:1. Majority were retired civil servants (33.3%), followed by serving civil servants (25.0%) and students (16.7%). The etiological factors of ESRD were Hypertensive nephrosclerosis (41.7%), CGN (33.3%), Diabetic nephropathy (25.0%) and chronic allograft dysfunction (8.3%). Mean URR was 41.83 ± 16.30% and overall mortality was 66.7%. The factors that contributed to inadequate dialysis and poor outcome were late presentation, uremic bleeding, septicemia, repeated blood transfusions and inability to sustain thrice weekly haemodialysis due to poor finances.

In conclusion, inadequate haemodialysis is common in our patients and is associated with high mortality. Major contributory factors to poor outcome were ignorance and poor socioeconomic status There is need to intensify awareness program on early diagnosis of Chronic Kidney Disease. We recommend some form of renal replacement subsidy in the current National Health Insurance Scheme of the Federal Government.

Keywords: *ESRD, Haemodialysis adequacy, Ilorin, Nigeria*

INTRODUCTION

Dialysis adequacy refers to the delivery of a dose of dialysis considered high enough to promote an optimal long term outcome [1]. An asymptomatic, physically active, well nourished, well haemoglobinized and normotensive patient are recognizing indices for assessing adequate dialysis from clinical perspective[2] [2]. Urea Reduction Ratio (URR) as a method of measuring adequate dialysis that correlate with patient outcome was first popularized by Lowrie and Lew in 1991[1]. It is a measure of adequacy of

Corresponding author : Dr. Rafiu M.O, Renal Unit, University of Ilorin Teaching Hospital, Ilorin.

delivered dose of dialysis expressed as a percentage reduction in blood urea level after a session of dialysis. It is mathematically related to Kt/V and both can be derived from each other with some amount of precision by various equations or a normogram[3].

Although Kt/V is recommended as the best measure of dialysis adequacy, URR is the most utilized because of its simplicity and the fact that it has similar predictive power to Kt/V in terms of patient outcome [4,5]. A URR of 65% which corresponds with Kt/V of 1.2 is the minimum acceptable dose in the standard thrice weekly hemodialysis if the residual kidney function is < 2ml/min/1.73m^{3}[3,6]. However, in patients with better residual renal function or those having more than thrice weekly dialysis, a lower value of URR may be acceptable[6]. The delivery of adequate dose of dialysis is an efficient way of reducing mortality of patients on maintenance hemodialysis[4]. A comparison of delivered dose with expected dose of dialysis can be used to analyze dialysis treatment, dialyzer clearance, troubleshooting and quality control activities[2].

There is no unified data system for recording and analyzing URR from various dialysis units in tropical developing countries in contracts to developed world. In Europe and America, they have European Renal Registry (ERAR) and the United State Renal Data system (USRDS) for recording, analyzing and publishing data on URR values. The few available reports showed that inadequate dialysis is common and patients' survival is very poor.[7,8] It was for this reason that a one year retrospective appraisal of patients on maintenance haemodialysis at University of Ilorin Teaching Hospital Ilorin was carried out to determine adequacy of delivered dose of dialysis and patient outcome

PATIENTS AND METHODS

All case files of patients that met the criteria for ESRD and had haemodialysis between January and December 2009 were retrieved from the records. These are patients in stage five chronic kidney disease with GFR persistently below 15mls/min/ 1.73m^{2} for three months and/or already on dialysis[9,10]. Patients that had regular 4 hourly session of dialysis for at least twice a week in two consecutive months were included in the study. Information on duration of illness before presentation, presence of uraemic bleeding, septiceamic illness, number of units of blood transfusion and socio economic status of the patients were obtained from the records. Vascular access was by femoral cannulation(66.7%), internal jugular cannulation(25%), and arterovenous fistular(8.3%).

The blood flow rate for the dialysis sessions was between 200 to 300ml/min while dialysate flow rate was 500ml for all patients. The ultrafiltration coefficient (Kuf) of dialyzers were between 7.9 to 13.7ml/hr/mmHg. The pre and post dialysis blood samples were taken at each index hemodialysis session. Predialysis blood sample was taken before commencement of each dialysis session. In patients with access catheter in-situ, 5mls of blood sample was initially taken from the arterial catheter and discarded before another 5mls syringe was used to take sample for estimation of predialysis blood urea nitrogen to avoid the dilution effect of saline and heparin.

At the end of each dialysis session, the dialysate flow is shut off for 3 minutes while the blood flow went at full tilt. The blood sample for post dialysis urea estimation was taken about 3 minutes after dialysis from the arterial sampling port to remove the effect of access recirculation. The urea reduction ratio (URR) for each index dialysis session was calculated for each patient using the formula i.e. [1- U_{post}/ U_{pre}] x 100, where $U_{pre=}$predialysis blood urea concentration and U_{post}=post dialysis blood urea concentration. The means of all the predialysis and post dialysis blood urea of the patients were calculated from which the mean URR of all the dialysis session was derived. Data was analyzed using SPSS version 16. The frequency of nominal variables and the mean ± standard deviation of numerical variable were generated.

RESULTS

Twelve out of 33 patients (36%) with ESRD met the inclusion criteria. These 12 patients had a total of 110 hemodialysis sections during the study period. The mean age of the patients was 48.25 ± 17.85 with male to female ratio of 2:1. Four (33.3%) of these patient were retired civil servants, 3 (25.0%) were serving civil servants, two (16.7%) were students, the remaining three were each, a legal practitioner, a trader and a clergy. The etiological factors of ESRD were Hypertensive nephrosclerosis in 5 (41.7%) of the patients, CGN in 4 (33.3%), Diabetic nephropathy in 2 (16.7%), and Chronic allograft dysfunction in 1 (8.3%). None of the patients was able to sustain

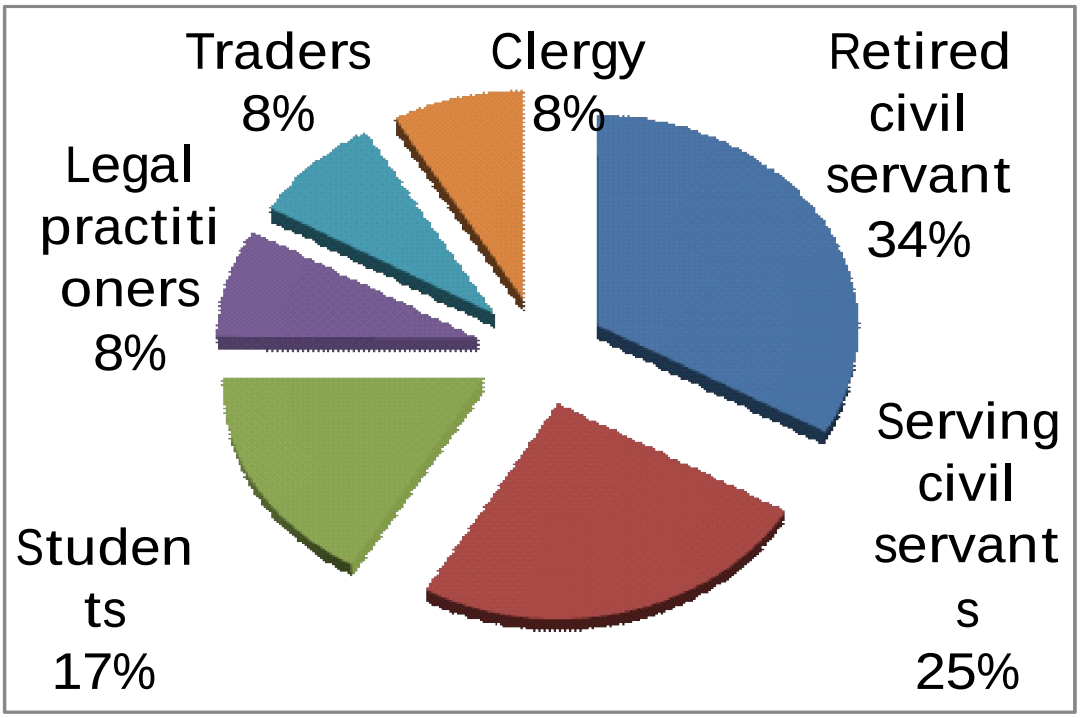

Fig 1: Occupational distribution of patients

thrice weekly hemodialysis sessions. Mean pre-dialysis and post dialysis urea were 25.29 ± 11.87 mmol/l and 14.78 ± 8.10mmol/l respectively. The mean URR was 41.83 ± 16.30% and overall mortality was 66.7%.

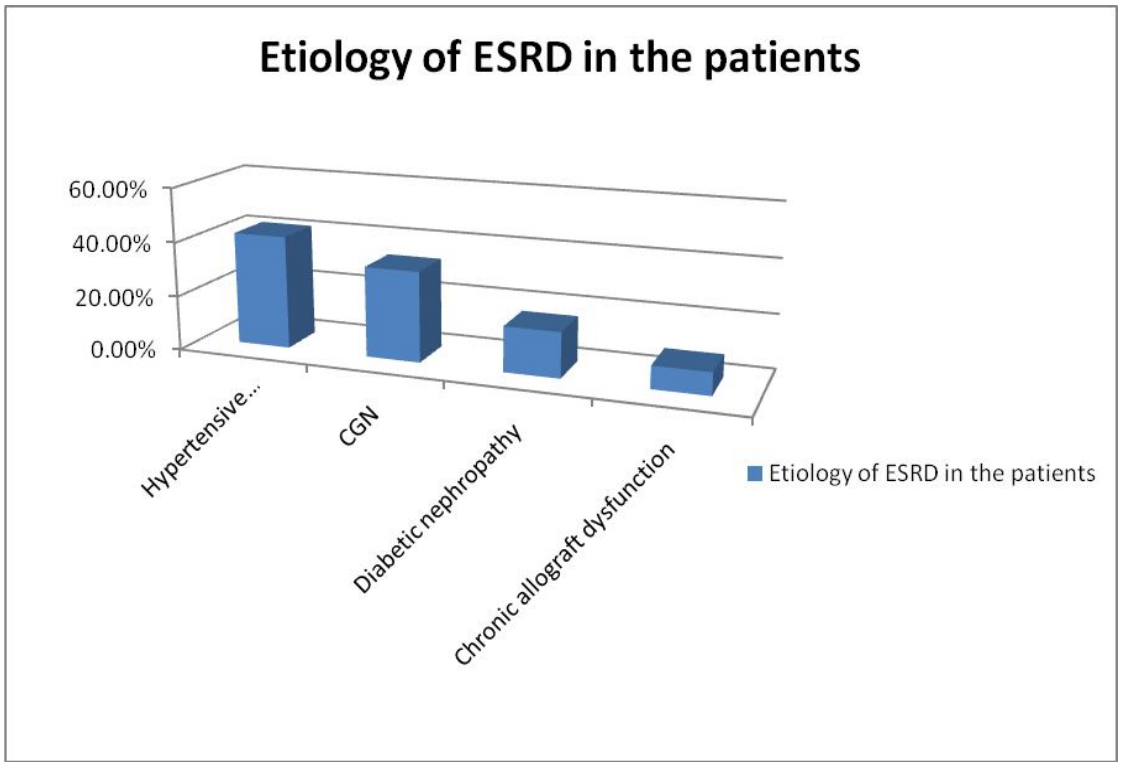

Fig 2: Etiology of ESRD in the patients

DISCUSSION

The mean URR of 41.83% in this study is clearly below the KDOQI 2006 recommendation[6]. Study from developed countries have alluded to the fact that dialysis is inadequate in most patients receiving haemodialysis[11-13]. Inadequate haemodialysis not only result in poor patient survival, but also leads to anaemia, malnutrition, functional impairment and frequent hospitalization that culminate in an increased health care cost[14-17]. The factors that appear to have contributed to inadequate dialysis and poor outcome in our patient were late presentation, uremic bleeding, septicemia, repeated blood transfusion and inability to sustain recommended thrice weekly haemodialysis due to poor finances.

Our study showed that most common cause of ESRD in patients on maintenance haemodialysis in Ilorin was systemic hypertension followed by CGN and Diabetic Nephropathy. An earlier study in this center which looked into the causes of ESRD found CGN to be the commonest cause in our environment[18]. The disparity is probably due to inclusion criteria utilized in this present study. These patients who could afford haemodialysis constituted about 20% of the general pool of ESRD in our unit.

The observed difference may also be a reflection of the fact that majority of the patients with CGN are of lower socioeconomic status and therefore could not afford maintenance haemodialysis. Majority of the patients in this study were retired civil servants, followed by serving civil servants. Retired civil servants are more likely to have financial support from their children, while those still in service may get support from their employers. This could explain why these patients were able to afford hemodialysis at least for a while. The mean age of our study subjects is similar to that of Nepalese patients undergoing maintenance haemodialysis in a cross-sectional study[19]. However, the mean URR of the patients in Nepal study was 65.3% with Kt/V of 0.99 [19]. Although the URR in the Nepal is better than our finding of 41.8%, their Kt/V of 0.99 still demonstrated inadequate dialysis. This shows that Kt/V is actually a better reflection of dialysis adequacy because of the adjustment for ultrafiltration, urea generation and urea rebound[20]. In a related study from another center in Nigeria, Agaba *et al*[7] found a mean URR of 45.3 ± 8.6% which is in accord with our mean URR value. The similarity in both studies may be due to identical vascular access, clinical features and socioeconomic characteristics of these patients. The cost of haemodialysis was borne by patients and their relatives in both studies because the National Health Insurance Scheme in Nigeria does not include cost of haemodialysis. This is particularly disturbing as most Nigerian can hardly afford the cost of dialysis. In addition to under dialysis, chronic inflammation measured by C- reactive protein and malnutrition determined by serum albumin, prealbumin and body mass index are common in Nigerian patient on chronic hemodialysis[8]. Low serum albumin concentration has been identified as a predictor of mortality in patients on maintenance hemodialysis[21]. In our study, effect of nutritional status and chronic inflammation were not assessed because most of the patients did not have the necessary parameters that could be used in this retrospective analysis. This calls for detailed prospective studies on nutritional status and chronic inflammatory changes among our chronic kidney failure patients on maintenance hemodialysis.

CONCLUSION

Our study showed that inadequate hemodialysis is common and is associated with high mortality rate. Major contributory factors to poor outcome were ignorance, late presentation and poor socioeconomic status of these patients. There is need to intensify awareness programs on early diagnosis of chronic kidney disease. We recommend incorporation of renal replacement therapy subsidy into the current National Health Insurance Scheme of the Federal Government.

REFERENCES

1. Owen WF, Lew NL, Lie Y, Lowrie EG and Lazarus JM. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. N. Engl J Med.1993; 329 (14): 1001-1006.
2. Kotanko P, Kuhlmann MK and Levin NW. Hemodialysis: technology, adequacy, and outcomes. *In:* John F, Jürgen F, Richard JJ, editors. Comprehensive clinical nephrology. 3rd ed. Philadelphia: Mosby Elsevier; 2007: 953-966.
3. Daugirdas JT. Second generation logarithmic estimates of single-pool variable volume Kt/V: an analysis of error. J Am Soc Nephrol 1993; 4: 1205-1213.

4. Philip JH, Friedrich KP, Robert AW, David CS, Caitlin EC, John TD, Wendy EB, Joel WG and Raymond MH. The dose of hemodialysis and patient mortality. Kidney Intern. 1996; 50: 550-556.

5. Robert AW, Tempie EH, Valanrie BA, Sangeetha M and Friedrich KP. Improvements in dialysis patient mortality are associated with improvements in urea reduction ratio and hematocrit, 1999 to 2002. Am. J. Kid. Dis. 2005; 45 : 127-35.

6. Kidney Disease Outcome Quality Initiative (KDOQI). Two thousand and six (2006) hemodialysis adequacy guidelines. Clinical practice recommendation. Available from: http//www.kidney.org/professionals/kdoqi/guideline.

7. Agaba EL, Lopez A, Ma I, Martinez R, Tzamaloukas RA, Vanderjagt DJ, *et al*. Chronic hemodialysis in a Nigerian teaching hospital: practice and cost. Int J Artif Organs. 2003 26: 991-995.

8. Tzamaloukas AH, Vanderjagt Dj, Agaba EL, Ma I, Lopez A, Tzamaloukas RA, *et al*. Inadequacy of dialysis, chronic inflammation, and malnutrition in Nigerian patients on chronic hemodialysis. Int J Artif Organ. 2006; 29: 1067-1073.

9. National Kidney Foundation: K/DOQI kidney disease outcome quality initiative. Am J Kidney Dis. 2002; 39: (suppl 1): S1-S266.

10. Levey AS, Eckardt KU, Tsukamotoo Y, *et al.* Definition and classification of chronic kidney disease: A position statement from Kidney Disease: Improving Global Outcome (KDIGO). Kidney Intern. 2005; 67: 2089-2100.

11. Morbidity and mortality of renal dialysis on NIH consensus statement. Consensus development conference panel. Ann Int Med. 1994; 121: 62-70.

12. Chara B, Calemand E, Ruffet M, Chazet C, Terrat JC, Vanel T, *et al.* Survival as an index of adequacy of dialysis. Kid. Intern. 1992; 41: 1286-1296.

13. Hold PJ, Blagg CR, Liska DW, Port FK, Hakim R and Levin N. The dose of haemodialysis according to dialysis prescription in Europe and United states. Kid. Intern. 1992; 38: 16-21.

14. Ifudu O, Feldman J and Friedman EA. The intensity of hemodialysis and response to erythropoietin in patients with end stage renal disease. New Engl J Med. 1996; 334: 420-425.

15. Hakim RM and Levin N. Malnutrition in hemodialysis patients. Am J Kid Dis. 1993; 21: 125-137.

16. Ifudu O, Paul H, Mayes JD, Cohen L S, Brezsnayal WF, *et al*. Pervasive failed rehabilitation in centre based maintenance hemodialysis patients. Am J Kid Dis. 1994; 23: 394-400.

17. Hakim RM, Breyer J, Ismail N and Schulman G. Effects of dose of dialysis on morbidity and mortality. Am J Kid Dis. 1994; 23: 661-669.

18. Chijioke A, Adeniyi AB. End stage renal disease: Racial differences. OJM. 2003; 15: 24-31.

19. Sultania P, Acharya PS and Sharma SK. Adequacy of hemodialysis in Nepalese patients undergoing maintenance hemodialysis. J Nepal Med Assoc. 2009; 48: 10-13.

20. Daugirda JT. Physiologic principles and urea kinetic modeling. *In:* Daugirda JT, Blake PG, Ing TS, editors. Handbook of dialysis. Philadelphia: Lippincott Williams& Wilkins; 25-58.

21. William FO, Nancy LL, Yan L, Edmund GL and Lazarus JM. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. N Engl. J Med . 1993; 329: 1001-1006.

Immunoglobulin a Nephropathy: a Critical Look at the Geographical and Racial Disparity in Reported Prevalence

Efosa Oviasu

Renal Unit, Department of Medicine,University of Benin Teaching Hospital, Beinin city, Nigeria

ABSTRACT

IgA Nephropathy (IgAN) is undoubtedly the commonest primary glomerulonephritis in the world. The apparent benign nature at presentation in most cases, diagnostic criteria and observed racial disparity in prevalence, make IgAN to occupy a unique position among other primary glomerulonephritides. Surprisingly, IgAN is relatively rare amongst blacks who are known to have a disproportionately high renal disease burden. This review provides an overview of IgAN and discusses the limitations inherent in most of the published studies which have highlighted geographical and racial disparities in its prevalence. An attempt is also made to speculate on possible outcome of prevalence studies after recognised confounding factors have been adequately addressed.

Keywords: *IgA nephropathy; African-American Blacks; Sub-Saharan African Blacks.*

INTRODUCTION

Immunoglobulin A nephropathy, which is commonly referred to as IgA nephropathy, can be said to be a relatively newly recognised form of primary GN, having been first described in 1968 by Berger and Hinglais[1]. It is now widely acclaimed to be the commonest primary GN in the world [2-7]. IgA nephropathy is an immune-complex mediated form of GN which is defined immunohistologically, following renal biopsy, by the presence of predominant mesangial IgA deposits. The mesangial IgA is predominantly of the IgA1 isotype[8]. However, other conditions with similar immunohistological findings, such as Henoch-Schonlein Purpura, Lupus nephritis and chronic liver disease, need to be excluded in the differential diagnosis of IgAN[9]. In an attempt to obviate the need for diagnostic renal biopsy a number of circulating biomarkers for IgAN, such as anti-endothelial cell antibodies(AECA), IgA rheumatoid factor, IgA immune complexes and polymeric IgA1, have been proposed, though none appears to be sufficiently disease specific[10].

The disease has a variable clinical and histological pattern[11-16] . Although initial reports regarded IgAN as a very benign condition[1], it is now known that up to 40% of cases may eventually progress to ESRD[17-19]. Interestingly, IgAN is widely reported to exhibit geographical and racial disparity in prevalence, an observation that is yet to be satisfactorily explained.

Prevalence in Diferent Geographical Regions and Racial Groups

The highest IgA nephropathy prevalence figures of 52% and 47.2% have been reported from Singapore and Japan, respectively [20, 21]. Prevalence figures between 25% and 52% have been reported from other Asian countries[22, 23]. In Europe and North America the figures are not as high as those observed in Asia but the highest prevalence figures of 35.9% and 30.1% have come from Italy and France, respectively[7, 24]. It has also been observed from comparison of studies between different time periods, that there is a general trend towards increasing

***Correspondence to* : Prof. Efosa Oviasu,**

Renal Unit, Department of Medicine, University of Benin Teaching Hospital, C/o P.O. Box 6684, Benin City, Nigeria. E-mail:efeoviasu@yahoo.com

prevalence in IgAN [22]. For example, in a UK study, the prevalence of IgAN was found to increase from 7.1% to 21.1% between two time periods of (1972-78) and (1979-86) and this was partly ascribed to the introduction of more liberal renal biopsy policy over time[25].

Reported prevalence of IgAN varies among racial groups, being most common among Orientals followed by Caucasians and rare among blacks[26]. Most reports on low prevalence of IgAN in blacks have come from studies on African Americans[27-29]. Reports from sub-Saharan African blacks have indicated even much lower prevalence rate[30]. Interestingly, the most populous black country in the world, Nigeria, had her first and only case of IgAN reported in 1992[32]. A subsequent retrospective evaluation of renal biopsies from the same Nigerian centre failed to identify any additional case of IgAN but speculated on possible missed diagnosis on account of a dearth of immunohistological evaluation facilities[33]. Undoubtedly, a multiplicity of factors could be responsible for the difficulty in determining any meaningful prevalence of IgAN in this oil rich nation, which is still nevertheless plagued by low developmental indices.

Any meaningful comparison of IgAN prevalence between different racial groups is better conducted in locations with adequate racial population mix. The United States of America and South Africa can be said to meet such conditions and findings from studies on IgAN in them have been most useful.

Reports from South Africa indicate that IgAN is not uncommon among Whites followed by Indians but very rare among blacks[31]. It is however necessary to bear in mind that these were retrospective studies conducted on renal biopsies done during the Pre-democratic era, with attendant confounding factors that were not controlled for.

Contributory Factors to Disparities in Prevalence

Any factor or group of factors that tend to influence the incidence of IgAN in a geographical area will invariably contribute to any observed disparity in prevalence when comparing studies from different regions. While a few factors may be influencing observed incidence and prevalence of IgAN in the developed countries, additional factors, such as inadequate diagnostic facilities and low level of awareness amongst patients and health care providers are invariably at play in developing countries, particularly those in sub-Saharan Africa.

While the possible contribution of traditional factors, such as level of disease awareness, access to appropriate diagnostic facilities and referral patterns to racial disparity in prevalence may not be too difficult to appreciate, the often assumed genetic basis for such disparity is yet to be confirmed.

Previous studies which have suggested that genetic factors play a role in the pathogenesis or susceptibility of IgAN have focussed on whites and orientals, due to difficulty in identifying black patients[34-35]. Limited efforts at identifying putative protective genes against IgAN in blacks, following a speculation that homozygosity for the A2m(2) allotype of IgA2 would be protective, have however proved abortive[36].

Possible Impact on Racial Disparity in Prevalence From Paediatric Studies

It is well recognised that macroscopic haematuria is far more frequent as a presenting symptom of IgAN in the paediatric age group compared to adults. Paediatric IgAN patients would therefore be more likely to attract and receive early medical attention, which could include an early referral for possible diagnostic renal biopsy. In children therefore, fewer cases of IgAN are likely to be missed, compared to adult cases. In the absence of limitations in available facilities, the privileged position enjoyed by children tends to cut across racial and ethnic barriers. This is so because of the global nature of parental love as well as the compassion that health care providers extend to children, regardless of their race or ethnicity.

In the case of IgAN in children, it follows that any possible racial disparity in prevalence would be less likely due to any racial differences in patterns of referral or biopsy selection practices. The above position is well exemplified by the study of Sehic et al[37] in which the incidence of IgAN among Caucasian children in Tennessee was found to be 3.0 per million population per year, compared with 5.7 per million per year among African-American children. These contrast very much with the very low figures recorded for adult Blacks in comparison with other races.

CONCLUSION

The prevalence of IgAN within a geographical area or racial group will be influenced by a number of factors, some of which are modifiable, such as

prevailing rate of renal biopsy, level of IgAN awareness, availability and access to appropriate diagnostic facilities. While it could be argued that successful implementation of strategies to address the above identified confounding factors in prevalent studies may help to improve true prevalence figures of IgAN in blacks, it is doubtful if such measures would be adequate to bridge the currently widely observed gap in prevalence between blacks and other races. The case for a role of susceptibility genes to IgAN appears to have been made in Oriental and Caucasian subjects [38,39]. However, until efforts at identifying any of the putative genes, believed by some investigators to be protective against IgAN in blacks bear fruit, it is perhaps premature to assume that there is a predominant genetic basis for the apparent rarity of IgAN reported so far in blacks.

REFERENCES

1. Berger J and Hinglais N. Les depots intracapillaires d'IgA-IgG. J Urol Nephrol 1968; 74: 694-695 (in Danish).

2. D'Amico G. The commonest glomerulonephritis in the world: IgA nephropathy. Q J Med 1987; 245: 709-727.

3. Julian BA, Waldo FB, Rifai A and Mestecky J. IgA nephropathy the most common glomerulonephritis worldwide: A neglected disease in the United States? Am J Med 1988; 84: 129-132.

4. Schena FP. A retrospective analysis of the natural history of primary IgA nephropathy worldwide. Am J Med. 1990; 89: 209-215.

5. Coppo R, Amore A, Hogg R and Emancipator S. Idiopathic nephropathy with IgA deposits. Pediatr Nephrol 2000; 15: 139-150.

6. Levy M and Berger J. Worldwide perspective of IgA nephropathy. Am J Kidney Dis 1988; 12: 340-347.

7. Schena FP, for the Italian Group of Renal Immunopathology. Survey of the Italian registry of renal biopsies: Frequency of renal diseases for 7 consecutive years. Nephrol Dial Transplant 1997; 12: 418-426.

8. Conley ME, Cooper MD and Michael AF. Selective deposition of Immunoglobulin A1 in immunoglobulin A nephropathy, anaphylactoid purpura nephritis and systemic lupus erythematosus. J Clin Invest 1980; 66: 1432-1436.

9. Pettersson E. IgA Nephropathy: 30 years on. J Intern Med 1997; 242: 349-353.

10. Roos A and van Kooten C. Underglycosylation of IgA in IgA nephropathy : more than a diagnostic marker? Kid Intern 2007; 71: 1089-1091.

11. Hass M. Histological subclassification of IgA nephropathy: a clinicopathological study of 244 cases. Am J Kidney Dis 1997; 29: 829-842.

12. Lee SMK, Rao VM, Franklin WA *et al*. IgA nephropathy: morphologic predictors of progressive renal disease. Hum Pathol 1982; 13: 314-322.

13. Ibels LS and Gyory AZ. IgA nephropathy: analysis of the natural history, important factors in the progression of renal disease, and a review of the literature. Medicine 1994; 73: 79-102.

14. Radford MG, Donadio JV Jr, Bergstralh EJ *et al*. Predicting renal outcome in IgA nephropathy. J Am Soc Nephrol 1997; 8:199-207.

15. Alamartine E, Sabatier JC, Guerin C *et al.* Prognostic factors in mesangial IgA glomerulonephrititis: an extensive study with univariate and multivariate analyses. Am J Kidney Dis 1991; 18: 12-19.

16. Bogenschutz O, Bohle A, Batz C *et al*. IgA nephritis: on the importance of morphological and clinical parameters in the long- term prognosis of 239 patients. Nephron 1990; 10: 137-147.

17. D'Amico G. Natural history of idiopathic IgA nephropathy: role of clinical and histological prognostic factors. Am J Kidney Dis 2000; 36: 227-237.

18. Tomino Y, Sakai H. Clinical guidelines for immunoglobulin A (IgA) nephropathy in Japan, second version. Clin Exp Nephrol 2003; 7: 93-97.

19. To KF, Choi PC, Szeto CC *et al.* Outcome of IgA nephropathy in adults graded by chronic histological lesions. Am J Kidney Dis 2000; 35: 392-400.

20. Woo KT, Edmonson RP, Wu AY, Chiang GS, Pwee HS and Lim CH. The natural history of IgA nephritis in Singapore. Clin Nephrol 1986; 25: 15-21

21. Koyama A, Igarashi M and Kobayashi M. Natural history and risk factors of immunoglobulin A nephropathy in Japan. Am J Kidney Dis 1997; 29: 526-532.
22. Chandrika BK. IgA nephropathy in Kerala, India: A retrospective study. Indian J Pathol Microbiol 2009; 52: 14-16.
23. Li LS and Liu ZH. Epidemiological data of renal diseases in from a single unit in China: analysis based on 13,519 renal biopsies. Kidney Int 2004; 66: 920-923.
24. Simon P, Ang KS, Bavay P, Cloup C, Mignard JP and Ramee MP. Immunoglobulin A glomerulonephritis: Epidemiology in a population of 250,000 inhabitants. Presse Med 1984; 13: 257-260.
25. Ballardie FW, O'Donoghue DJ and Feehally J. Increasing frequency of adult IgA nephropathy in UK? Lancet 1987; 2: 1205.
26. Crowley-Norwick PA, Julian BA, Wyatt RJ *et al.* IgA nephropathy in Blacks: Studies in IgA2 allotypes and clinical course. Kidney Int 1991; 39: 1218-1224.
27. Korbet SM, Rosangela MG, Borok R and Schwartz MM. The racial prevalence of glomerular lesions in nephritic adults. Am J Kidney Dis 1996; 27: 647-651.
28. Jennette JC, Wall SD and William AS. Low incidence of IgA nephropathy in blacks. Kidney Int 1985; 28: 944-950.
29. Galla JH, Kohaut EC, Alexander R, Mestecky J. Racial differences in the prevalence of IgA-associated nephropathies. Lancet 1984; 2: 522.
30. Seedat YK, Nathoo BC, Parag KB, Naiker IP and Ramsaroop R. IgA nephropathy in blacks and Indians of Natal. Nephron 1988; 50: 137-141.
31. Swanepoel CR, Madaus S, Cassidy MJ, *et al*. IgA nephropathy – Groote Schuur Hospital experience. Nephron 1989; 53: 61-64.
32. Oviasu E. IgA nephropathy (IgAN) presenting with the nephrotic syndrome. Trop Geogr Med 1992; 44: 365-368.
33. Oviasu E and Ojogwu LI. The rarity of IgA nephropathy in indigenous Nigerians: How real? Nigerian Postgrad Med J 1999; 6: 1-3.
34. Julian BA, Quiggins PA, Thompson JS, Woodford SY, Gleason K and Wyatt RJ. Familial IgA nephropathy: Evidence for an inherited mechanism of disease. N Engl J Med 1985; 312: 202-208.
35. Egido J, Julian BA and Wyatt RJ. Genetic factors in primary IgA nephropathy. Nephrol Dial Transplant 1987; 2: 134-142.
36. Neelakantappa K, Gallo GR and Baldwin DS. Immunoglobulin A nephropathy in blacks and homozygosity for the genetic marker A2m. Ann Intern Med 1986; 104: 287.
37. Sehic AM, Gaber LW, Roy 111 S, Miller PM, Kritchevsky SB and Wyatt RJ. Pediatric Nephrol 1997; 11: 435-437.
38. Li GS, Zhang H, Lv JC, Shen Y and Wang HY. Variants of C1GALT1 gene are associated with the genetic susceptibility to IgA nephropathy. Kidney Int 2007; 71: 448-453.
39. Pirulli D, Crovella S, Ulivi S, *et al*. Genetic variant of C1GalT1 contributes to the susceptibility to IgA nephropathy. J Nephrol 2009; 22: 152-159.

Fractured Femoral Catheter Tip in Repeated Femoral Vein Cannulation for Haemodialysis Vascular Access

Awobusuyi JO[1], Falase B[2], Johnson A[3], Ogbera AO[1] and Sanusi M[2]

Dept of Medicine, Lagos State University Teaching Hospital,[1] Dept of Surgery, Lagos State University Teaching Hospital[2] and Redington Hospital, Victoria Island, Lagos[3].

INTRODUCTION

Percutaneous insertion of haemodialysis HD catheters can be readily performed by the bedside in any of the accessible central veins, for immediate use in patients requiring dialysis. The femoral, internal jugular or subclavian veins are the favoured sites for catheter insertion.

Although the jugular and subclavian access routes are more commonly used than the femoral vein for haemodialysis because of higher incidence of thrombosis and infections seen in femoral vein cannulations, the femoral route is still considered less risky. First, there is no risk of pneumothorax and secondly, the site is directly compressible should bleeding occur. Therefore, the frequency of life-threatening complications is lower for femoral cannulation than for the other sites.

However, life-threatening complications do occur in femoral cannulations. Here we describe a case of fractured catheter tip with development of extensive deep vein thrombosis that was successfully managed in our hospital. The problems encountered in the management of the patient are highlighted.

Keywords: *Fractured femoral catheter, central venous cathetercomplication, haemodialysis*

CASE REPORT

S.O a 26yr old female student was referred to our nephrology unit on the 4th of June 2009 in view of recurrent generalized tonic – clonic seizures and reduction in urine output of 4 days duration. Her illness started about one year prior to presentation when she was diagnosed as having HIV infection and was placed on HAART therapy. Her compliance with medication was fairly regular.

Six months prior to presentation, recurrent fever and progressive leg swelling was noticed. Screening for opportunistic infections was negative. However, renal function impairment was evident, with progressive worsening over time. Patient developed tonic-clonic convulsions 4 days prior to presentation. Each episode lasting about 4-6 minutes with full recovery of consciousness in the inter-ictal period. She had six convulsions prior to her referral. Serum urea done two days prior to referral was 184mg/dl.

Physical examination at presentation showed a young woman who was conscious and alert. She was pale, anicteric, afebrile to touch and not dehydrated. She had mild pitting pedal oedema. Her vital signs at presentation were as follows: Temperature 36.1^{0}C, Pulse 88/min and a respiratory rate of 28cycles/min. Systemic examination was unremarkable except for a blood pressure of 170/ 100mmHg.

Correspondence to: **Dr. J.O. Awobusuyi**

Dept. of Medicine, Lagos State University Teaching Hospital, Ikeja. Lagos P.O. Box 5280, Festac Town, Lagos. E-mail:drjawobusuyi@yahoo.com.

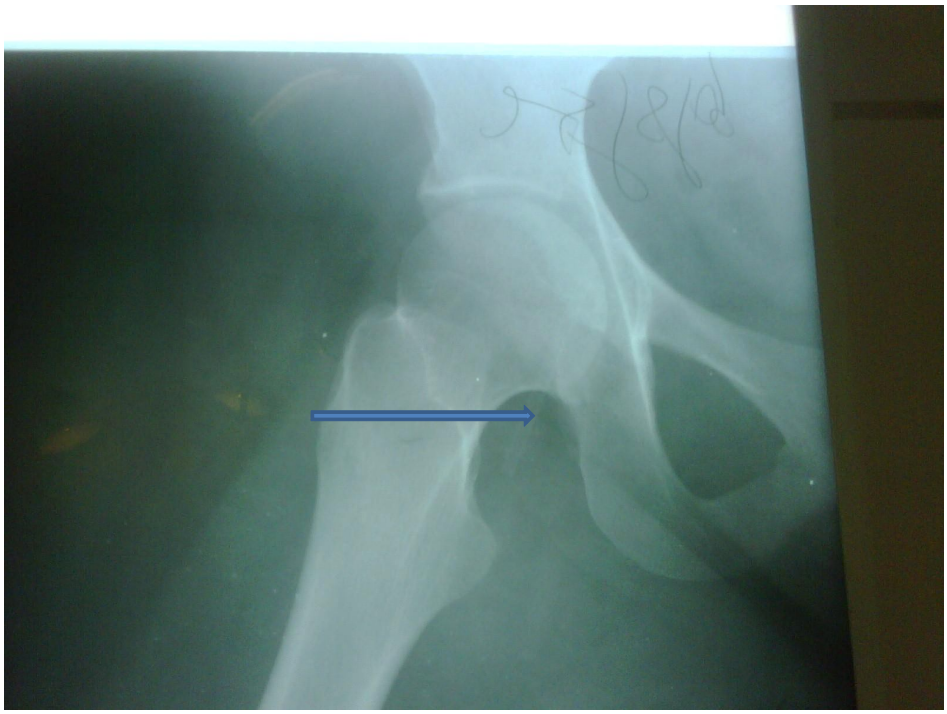

Fig. 1: Fractured catheter tip in the right femoral vein arrowed

Laboratory results are as follows: - Urea 386mg/dl, creatinine 17.0mg/dl, Na^+ 128mmol/L, K^+ 3.6mmol/L, HCO_3^- 21mmol/L, Cl^- 101mmol/L, Ca^{2+} 10.4mg/dl, PO_4^{2+} 4.0mg/dl, Cholesterol 232mg/dl, Triglyceride 125mg/dl, Total Protein 5.2mg/dl, Albumin 3.0mg/dl, PCV 18%, WBC 20,000/mm^3.

HIV Positive, HCV negative, HBsAg Negative. Renal scan revealed increased renal echogenicity bilaterally with normal renal sizes, situations where the required skills are unavailable[2].

The femoral access is still the most commonly used access route in Nigeria due to the lack of required clinical experience on internal jugular vein

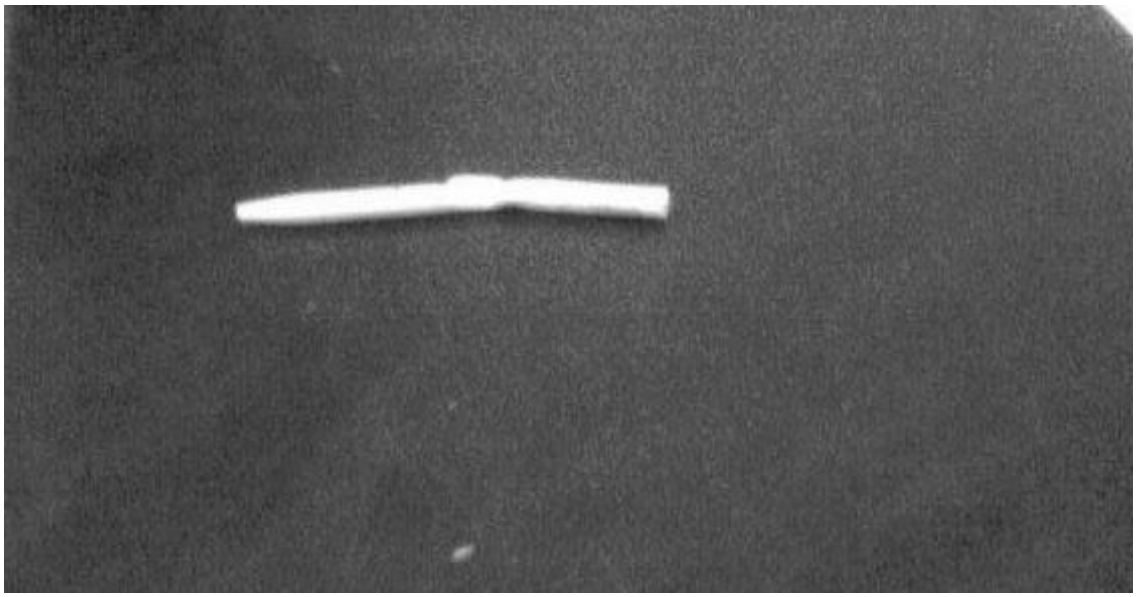

Fig. 2: Retrieved fractured catheter tip

cannulation in many centres, and the relatively high cost of catheter insertion in some centres which places an additional financial burden to the patient that is hardly coping with the cost of dialysis. For instance, the average cost of internal jugular catheter insertion in Lagos is about N40,000.00.

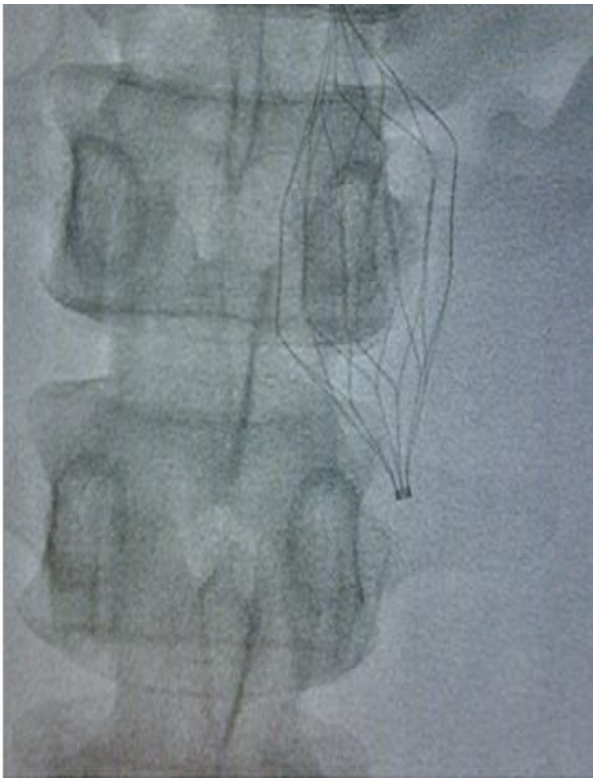

Fig. 3: Vascular filter in the inferior vena cava

Catheter fracture is one of the rare complications of venous access usage for various types of diagnostic and therapeutic management of patients. Reported cases of catheter fractures have appeared in the literature since the mid 1950s[3]. More recent publications have reported the complication to occur in 0.5% to 3% of patients with indwelling central venous catheters[4,5]. These reported cases were mainly in subclavian and internal jugular catheterizations[6,7]. The lack of report for femoral vein route is possibly related to the fact that the route is less frequently used in most developed countries for procedures such as haemodialysis. Suggested reasons for fracture occurrence include mechanical damage during insertion, manufacture defects and the 'pinch off' syndrome recognized in subclavian catheterization[6,7,8,9]. Additional reasons that may be pertinent to local practice in Nigeria is repeated use of patient's catheter many times to reduce cost to the patient and also shear and tear from friction of cannulating over a fibrosed cannulation site.

In our patient, complete catheter fracture was recognized soon after occurrence as this was noticed during catheter removal post dialysis. This is usually not the case in catheter fractures occurring at other central venous sites. Catheter fracture at these sites was usually a late complication and recognition in these circumstances was evident after catheter tip embolization to either the lungs causing pulmonary embolism[10], or the heart causing cardiac perforation, arrhythmias or atrial thrombus formation[11,12]. Partial catheter fractures have also been reported with clinical presentations attributable to extravasation of fluid and blood into the subcutaneous tissue[13,14]. Contrast radiography of the fractured catheter may reveal extravasation of the contrast medium in these instances[13].

A delay of about one month occurred between the occurrence of catheter fracture and removal in our patient. This was due to non-availability of required devices for catheter removal in the country and the need to place order for their importation abroad. During this period, the risk of catheter and/ or clot embolization and also haemorrhage from anticoagulation in a patient on regular dialysis was very high. Regional anticoagulation during dialysis was considered but our experience with this modality of anticoagulation during dialysis was limited. Hence, we opted to reduce her heparin dose to 75% of her usual heparin requirement. We recorded no incidence of extracorporeal clotting in her dialysis sessions during the period. She also had no clinically significant haemorrhage at any point of her care.

Several endovascular interventional techniques for intravascular foreign body extraction are available. The array of available devices include forceps, baskets, loop snares, moulded catheters, magnets, directable guide-wires and balloons [15,16,17,18].

These devices have been used successfully in many centres. Loop snares however appear to be the most favoured device. Advantages of these devices include minimal tissue invasion, absence of surgical scars and possible shortened hospital stay post removal. None of these devices are currently available in the country. Thus, surgical exploration and removal was performed on the patient by our cardiothoracic unit. This approach may allow better

clot removal from the thrombosed vein in addition to the fractured catheter tip removal.

Our case demonstrate some of the challenges being faced by nephrologists practicing in a developing country with inadequate facilities. More importantly, we would like to pass across the lesson we learnt that successful management through collaborative efforts, perseverance and multidisciplinary approach to patients care is achievable in face of these challenges.

REFERENCES

1. Gavin MJ, Jacqueline k, Charles DG, Vivian Y F L and Eric K H L. Deep Venous thrombosis caused by femoral venous catheters in critically ill adult patients. Chest 2000; 117:178–183
2. KDOQI Work Group. Vascular Access 2006. American Journal of Kidney Diseases. 2006; Vol 48, No 1, Suppl 1 (July): S197 – S199.
3. Turner DP and Sommers SC. Accidental passage of polyethylene catheter from cubital vein to right atrium. N Eng J Med 1954; 251: 744.
4. Klotz HP, Schopke W, Kohler A, Pestalozzi B and Largiader F. Catheter fracture: a rare complication of totally implantable venous access devices. J Surg Oncol 1996; 623: 222–555.
5. Bessoud B, de Baere T, Kuoch V, *et al*. Experience at a single institution with endovascular treatment of mechanical complications caused by implanted central venous access devices in paediatric and adult patients. AJR Am J Roentgenol 2003; 180: 527–532
6. Meester J De, Vanholder R, Roose J De and Ringoir R. Factors and complications affecting catheter and technique survival with permanent single lumen dialysis catheters. *Nephrol Dial Transplant* 1994; 6: 678-683
7. Chawla LS, Chegini S, Thomas JW and Guzman N J. Haemodialysis central venous catheter tip fracture with embolization into the pulmonary artery. AJKD. 2001; 38, 6: 1311-1315
8. Cohen SMA and Bellamy M. The stuck central venous catheter: beware of potential hazards. British Journal of Anaesthesia. 2002; 89, 4: 650-652
9. Hinke DH, Zandt-Stastny DA, Goodman LR, Quebbeman EJ, Krzywda EA and Andris DA. Pinch-off syndrome: a complication of implantable central venous access devices. Radiology 1990; 177: 353–356.
10. Weijmer MC, Kars SM and ter Wee PM. A scanning electron microscopy analysis of a spontaneous haemodialysis catheter fracture Am. J. Kid Dis. 200; 384: 858-861
11. Sattari M, Kazory A and Phillips RA. Fracture and cardiac migration of an implanted venous catheter Interact CardioVasc Thorac Surg 2003; 2: 532-533
12. Denny MA and Frank LR. Ventricular tachycardia secondary to port-acath fracture and embolization. J Emerg Med 2003; 241: 29–34.
13. Verhage AH and Van Bommel EFH. Catheter fracture- an underrecognized and serious condition in haemodialysis. Nephrol Dial Transplant. 2000; 15: 901-903
14. Venkatachalam KL and Garovic VD. Post-traumatic haemodialysis catheter fracture with bacteraemia. Nephrol Dial Transplant. 2003; 18: 618–619
15. Huang CH, Chen WJ, Ho YL, Wu CC and Lee YT. Nonsurgical transvenous retrieval of fractured implantable central venous access device. J Formos Med Assoc 1999; 98: 265–270.
16. Fisher RG and Ferreyo R. Evaluation of current techniques for nonsurgical removal of intravascular iatrogenic foreign bodies. Am J Roentgenol 1978; 130: 541-548.
17. Zaman F, Pervez A, Murphy S and. Abreo KD. Retrieval of a fractured piece of Tessio catheter with a snare using a transcutaneous transvenous approach. Seminars in Dialysis 2005; 184: 343 – 344
18. Thapa PB, Shrestha R, Singh DR and Sharma SK. Removal of central venous catheter fragment embolus in a young male. Kathmandu University Medical Journal. 2006; 43: 340-341

Tropical Journal of Nephrology Vol.4 No2 Dec., 2009 97-105

Optimisation of Blood Pressure in Stroke Patients

Mayowa Ojo Owolabi
Department of Medicine, University College Hospital, Ibadan

ABSTRACT
The management of blood pressure in stroke patients is as critical as it is controversial. There is a huge evidence gap in developed countries which is even wider in developing countries. Nevertheless, the purpose of this review is to give an overview of current evidence and propose simplified and practical recommendations for managing BP in stroke patients particularly in resource-limited settings. Lowering BP is effective for recurrent stroke prevention and the degree of BP reduction may be more important than the class of the agent used.

Further studies are required to determine specific blood pressure targets for different types of stroke, type of drugs and preferred route of administration, autoregulation, within an MAP range of 50 to 110 mmHg, cerebral blood flow is maintained at about 50ml / 100g brain tissue/min (Figure 1)[6]. This is due to variations in vascular tone which results in steady cerebral blood flow independent of the perfusion pressure [6]. However, after stroke, this mechanism is disrupted such that cerebral blood flow becomes proportional to the CPP (Figure 1) [6].

Furthermore, an acute hypertensive response occurs within 24 hours in up to 80% of patients with acute stroke[6]. This response is an increase of blood pressure above normal (i.e., 140 mm Hg systolic or 90 mm Hg diastolic) or above pre-existing levels in previously hypertensive patients[6].

Determinants of Blood Pressure in Stroke Patients

The primary cause of the hypertensive response is damage or compression of specific regions in the brain that regulate the activity of the autonomic nervous system. Pre-existing hypertension, diabetes mellitus, high concentrations of serum creatinine, and the Cushing reflex (a reactive increase in blood pressure in response to raised intracranial pressure) can all exacerbate the rise in blood pressure. Headache, pain, full bladder, nausea, urine retention, physiological response to hypoxia, infection, and stress associated with admission to hospital can lead to an imbalance in the autonomic nervous system, activate the sympathetic adrenomedullary pathway, and raise the concentrations of circulating catecholamines and inflammatory cytokines, all of which can contribute to the hypertensive response[6, 8]. In a study which correlated acute blood pressure values with other findings in the setting of acute stroke, it was found that among patients with most subtypes of ischemic stroke, elevated BP was correlated with a past history of hypertension or severity of neurological impairments[8].

Blood pressure tends to decline spontaneously without pharmacological intervention in the first few days to weeks after stroke onset [6]. The change in BP after acute stroke is also associated with the severity of the neurological deficits caused by the stroke[6]. A low to normal BP after acute stroke

Corresponding author : **Dr. Mayowa Ojo Owolabi**
Department of Medicine,
University College Hospital, Ibadan. *E-mail:* mayowaowolabi@yahoo.com

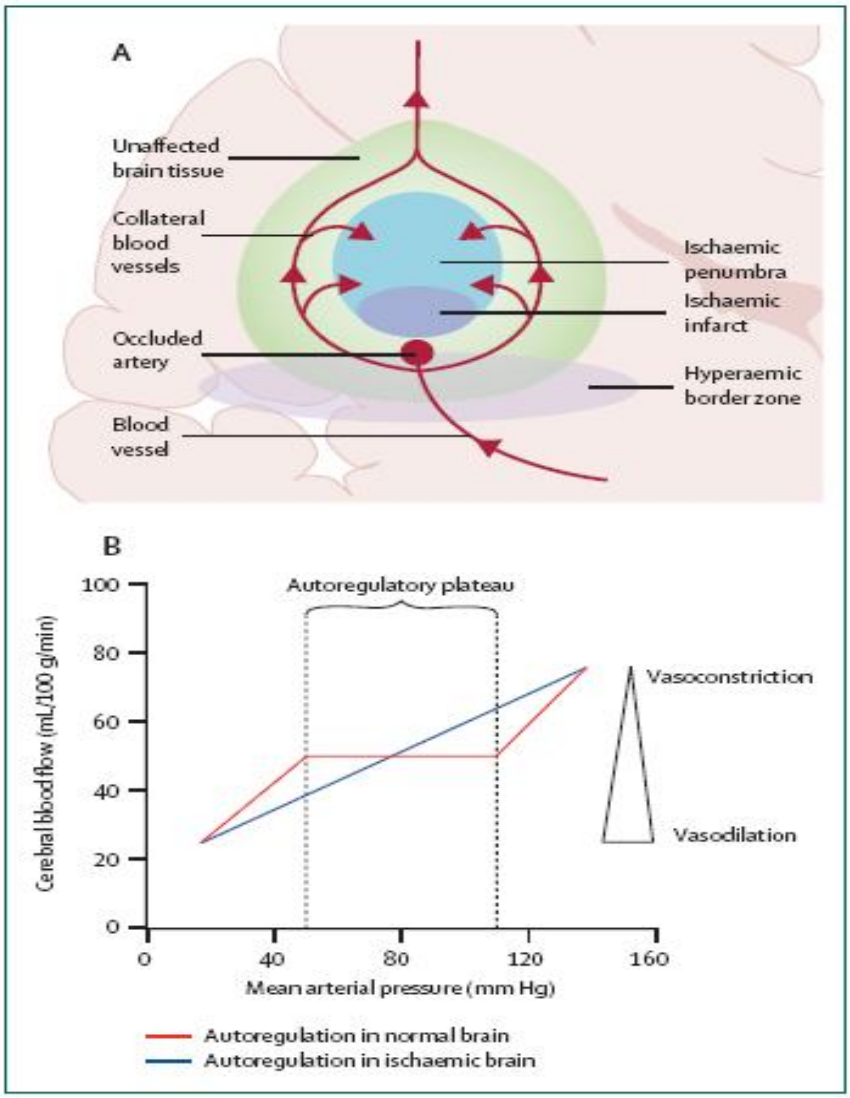

Fig 1: Blood flow in ischaemic and normal brain tissue[6]

(A) Regional blood flow surrounding an infarct. Upstream of the occluded artery, acidosis and vasoactive metabolites give rise to a hyperaemic border zone.
Downstream of the occlusion, in the ischemic penumbra, the CPP is too low for acidosis and metabolites to induce hyperaemia. The infarcted core indicates irreversibly injured brain tissue. The ischaemic penumbra consists of viable tissue that can be rescued if blood flow is restored.
(B) CBF in normal and ischaemic brain tissue. Autoregulation depends on vasoactive tone and maintains a steady blood flow through normal brain tissue independent of the CPP, whereas blood flow in ischaemic brain tissue is proportional to the CPP. [6]

Reproduced with permission from Lancet Neurology.

usually indicates extensive brain damage or concurrent coronary artery heart disease[6]. Thus, BP responses can be categorized as spontaneous decline without medication; no clear decline, or even an elevation, despite administration of antihypertensive medication; modest decline with antihypertensive medication (10% to 15% from baseline value); and intense decline with antihypertensive medication (20% from baseline value)[14].

Another important issue in management is the identification of intravascular volume depletion (dehydration) in these patients, which may result in a natural hypertensive or hypotensive response or an exaggerated hypotensive response to antihypertensive medication[14]. Early identification and appropriate fluid repletion before pharmacological intervention ensures a controlled response to treatment[14].

What is the target BP for optimal Cerebral perfusion? The hypertensive response in patients with acute stroke is an independent predictor of outcome. In both ischemic and hemorrhagic stroke, evidence from large scale studies have shown a U-shaped relationship between mortality and BP[6].

Therefore, maintaining BP within a certain range reduces mortality and assists in salvaging the ischemic penumbra in ischemic stroke and metabolic penumbra in hemorrhagic stroke by ensuring adequate CPP and cerebral blood flow (figure 1).

While the desired range remains controversial, studies have shown that for ischemic stroke, the SBP nadir appears to be 140mm Hg for those who were previously normotensive and 160mmHg for those who were previously hypertensive[6]. The best outcomes were at SBP levels ranging from about 140 to 180 mm Hg[6]. In those treated with alteplase, there is a U-shaped association with mortality and dependence at 3 months: a SBP of 141–150 mm Hg was associated with the most favourable outcomes ($p<0{\cdot}05$).[6]

In a Japanese study of hemorrhagic stroke patients, those with SBP of 150-169mmHg were more like to survive[6]. Therefore, the aim of various guidelines for different types of stroke is to improve outcome by maintaining MAP and consequently CPP and CBF within desirable range.

The aim is for a CPP of > 70mmHg[15].

Despite the high prevalence of acute hypertensive responses observed in all stroke subtypes, differences in underlying pathophysiology mandate different management strategies[14].

(a.) Regional blood flow surrounding an infarct. Upstream of the occluded artery, acidosis and vasoactive metabolites give rise to a hyperaemic border zone.

Downstream of the occlusion, in the ischemic penumbra, the CPP is too low for acidosis and metabolites to induce hyperaemia. The infarcted core indicates irreversibly injured brain tissue. The ischaemic penumbra consists of viable tissue that can be rescued if blood flow is restored.

(b.) CBF in normal and ischaemic brain tissue. Autoregulation depends on vasoactive tone and maintains a steady blood flow through normal brain tissue independent of the CPP, whereas blood flow in ischaemic brain tissue is proportional to the CPP[6]. Reproduced with permission from *Lancet Neurology.*

Management of blood pressure in ischemic stroke Management of Hypertension in Ischemic stroke[5-8,10,14].

Indications for Treatment

Theoretical reasons for lowering blood pressure include reducing the formation of brain edema, lessening the risk of hemorrhagic transformation of the infarction, preventing further vascular damage, and forestalling early recurrent stroke[7,8,16].

In addition, urgent antihypertensive therapy may be needed to treat patients with stroke who also have aortic dissection, pre-eclampsia, eclampsia, acute renal failure, acute pulmonary edema, or acute myocardial infarction[7,8,16].

Conversely, aggressive treatment of blood pressure, particularly in those with bilateral carotid diseases or hemodynamic stroke[17], may lead to neurological worsening by reducing perfusion pressure to ischemic areas of the brain [7, 8, 17].

In a majority of patients, a decline in blood pressure occurs within the first hours after stroke even without any specific medical treatment. The blood pressure often falls spontaneously when the patient is moved to a quiet room, the patient is allowed to rest, the bladder is emptied, or the pain is controlled. Hypoglycemia, hypoxia and seizures should alos be treated[8].

In addition, treatment of increased intracranial pressure may result in a decline in arterial blood pressure[8]. This can be achieved using osmotherapy with mannitol, glycerol or hypertonic saline infusion, frusemide, hyperventilation, hypothermia or barbiturate coma[7,8,15]. Euvolemia should be maintained during osmotherapy. The target levels of CO_2 for hyperventilation are 30 to 35 mm Hg and rebound increase in ICP may occur[7]. Theoretically steroids are expected to be useful in combating vasogenic oedema and raised ICP in stroke patients. However ,its effectiveness in hemorrhagic or ischemic stroke has never been shown[18,19]. Its only role is in cases where vasculitis is suspected or proven[18].Pending more data, emergency administration of antihypertensive agents should be

withheld unless the DBP is >120 mm Hg or unless the SBP is >220 mm Hg (Table 1)[5-8,10,14,16]. No data show that these values are especially dangerous and emergency treatment is needed. However, there is evidence that aggressive lowering of blood pressure among patients may cause neurological worsening, and the goal is to avoid over- treating patients with stroke until definitive data are available[5-8,10,14,16].

Table 1: Management of hypertension in acute ischemic stroke[5-8]

BP	Treatment strategy
Not eligible for thrombolytic therapy	
SBP <220 mm Hg *or* DBP <120 mm Hg	Monitor unless there is other end-organ involvement. Treat raised intracranial pressure and other clinical problems.
SBP >220 mm Hg *or* DBP <121–140 mm Hg	iv labetalol 10–20 mg over 1–2 min, may repeat or double every 10 min (maximum dose 300 mg) *or* i.v. nicardipine 5 mg/h infusion as initial dose; titrate (*with continuous BP monitoring)* to desired effect by increasing 2.5 mg/h every 5 min to maximum of 15 mg/h. Oral agent may be used to achieve target and gentle reduction. Target: 15% reduction in 24 hours.
DBP >140 mm Hg	i.v. nitroprusside 0.5 µg/kg /min infusion as initial dose *with continuous BP monitoring*.
Eligible for thrombolytic therapy :treat BP before giving thrombolytics	
SBP >185 mm Hg *or* DBP >110 mm Hg	i.v. labetalol 10–20 mg over 1–2 min; may repeat once *Or* Nitropaste 1–2 in *Or* Nicardipine drip, 5 mg/h, titrate up by 0.25 mg/h at 5- to 15-min intervals (maximum dose 15 mg/h).

Furthermore, for those who qualify for thrombolytics, it is recommended that before intravenous thrombolytic treatment, BP should be lowered if >185 mm Hg systolic or >110 mm Hg diastolic. After thrombolytic treatment, SBP should be kept <180 mm Hg and DBP <105 mm Hg (Table 1) [5-8,10,14,16]. Despite the absence of supporting evidence, these recommendations are often applied to patients receiving other forms of reperfusion therapy (eg, intra-arterial thrombolysis, clot retrieval, and so on) [5-8,10,14,16].

Rate of BP reduction

When treatment is indicated, lowering the blood pressure should be done cautiously.[5-8,10,14,16] Some strokes may be secondary to hemodynamic factors, and a declining blood pressure may lead to neurological worsening. A reasonable goal would be to lower blood pressure by 15% to 25% within the first day [8].

Any Drug of Choice?

Large studies comparing various antihypertensives are not available. Because no data support the administration of any specific antihypertensive agent in the setting of acute ischemic stroke, the treating physician should select medications for lowering blood pressure on a case-by-case basis.[5-8,10,14,16]. In the United States, labetalol, hydralazine, esmolol, nicardipine, enalapril, nitroglycerin, and nitroprusside have been recommended (Table 1) [5, 20]. Intravenous urapidil is also used in Europe [5, 20]. Sodium nitroprusside and nitroglycerin should be used with caution because these agents can potentially increase ICP.[5,20]

Intravenous or transdermal agents with rapid onset and short duration of action to allow precise titration are preferred.[6,14] BP can be monitored adequately with an inflatable cuff in most patients with acute hypertensive response, whereas intra-arterial monitoring should be considered in patients who require frequent titration with intravenous antihypertensive agents and in patients whose neurological status is deteriorating.

ICP monitoring may be necessary in patients with a suspected increased ICP, to measure and preserve cerebral perfusion pressure during systemic BP lowering.[6,14] Patients with a poor level of consciousness, midline shift, or compression of basal cisterns on computed tomographic scan may be

considered for ICP monitoring when being treated with antihypertensive agents.[6,14] Of note, CPP may overestimate regional perfusion because of its inability to measure regional pressure and autoregulatory disturbances.[6,14].

Intravenous therapy is safest with intensive BP monitoring. In resource-poor settings where this is not often feasible, oral agents may be useful. Evidence in Caucasians supports oral calcium channel blockers (including amlodipine), labetalol, lisinopril or sublingual lisinopril but not thiazides.[6,8,21,22] However because blacks have volume dependent hypertension, thiazides may also work in them. Sublingual nifedipine should never be used because of the risk of abrupt hypotension, reactive overstimulation of the sympathetic nervous system, and because short-acting nifedipine can cause myocardial infarction in patients with coronary artery disease.[6,14,17]

Management of Hypotension in Ischemic Stroke

A low or low-normal blood pressure at stroke onset is unusual, and may be the result of a large cerebral infarct, cardiac failure, ischaemia, hypovolaemia or sepsis.[7,8,17] Blood pressure can usually be raised by adequate rehydration with crystalloid (saline) solutions; patients with low cardiac output may occasionally need inotropic support.[7,8,17] However clinical trials of actively elevating a low blood pressure in acute stroke have yielded inconclusive results.[7,8,17,20]

Management of blood pressure in spontaneous intracerebral hemorrhage (SICH) Management of hypertension in SICH One third of subjects presenting with SICH continue to demonstrate hematoma expansion (with subsequent deterioration and death) in the first few hours after onset.[14,23,-26] An initial SBP >200 mm Hg is associated with hematoma expansion and increased mortality among patients with SICH. Persistently higher SBP is also associated with perihematoma brain edema formation.[14,23-26] Reducing BP may reduce the rate of hematoma expansion, although conclusive evidence of this is not available. Recent studies suggest that reduction of BP may be tolerated because of reduced metabolism (hibernation) and preserved autoregulation in the perihematoma region.[14, 23-26]

Experience in traumatic brain hemorrhage, as well as SICH, supports preservation of the CPP > 60 mm Hg.[15] Nonetheless, for SICH, little prospective evidence exists to support a specific BP threshold.

The previous recommendation was to maintain a systolic blood pressure $\leq$ 180 mm Hg and/or mean arterial pressure < 130 mm Hg.[15] The evidence to support any specific recommendation can be briefly summarized as follows: Isolated systolic blood pressure $\leq$ 210 mm Hg is not clearly related to hemorrhagic expansion or to neurological worsening.[15]

Reduction in mean arterial pressure by 15% (mean 142$\pm$10 to 119$\pm$11 mm Hg) does not result in CBF reduction in humans as measured by positron emission tomography.[15]

In one prospective observational study,[15] reduction of systolic blood pressure to a target <160/ 90 mm Hg was associated with neurological

Table 2: Management of hypertension in spontaneous intracerebral hemorrhage[15]

If SBP is >200 mm Hg or MAP is >150 mm Hg, then consider reduction of BP with continuous intravenous infusion, with continuous or frequent blood pressure monitoring every 5 minutes. eg iv labetalol 2mg/min (maximum of 300mg/day) or hydrallazine 1.5 to 5 µg / kg/ min or nicardipine 5 to 15 mg/h until target is achieved.
If SBP is >180 mm Hg or MAP is >130 mm Hg and there is evidence of or suspicion of raised ICP, then consider monitoring ICP and reducing BP using continuous or intermittent intravenous medications to keep CPP > 70 mm Hg. eg iv labetalol 5 -20mg every 15 min or iv enalapril 0.625 stat then 1.25 to 5 mg every 6 h or i.v. hydrallazine 5-20mg every 30 min
If SBP is >180 mm Hg or MAP is >130 mm Hg and there is no evidence of or suspicion of raised ICP, then consider a modest reduction of BP (eg, MAP of 110 mm Hg or target blood pressure of 160/90 mm Hg) using intermittent or continuous intravenous medications to control blood pressure, and clinically re-examine the patient every 15 minutes.
MAP = DBP + 0.4 (SBP-DBP)[12]

deterioration in 7% of patients and with hemorrhagic expansion in 9% but was associated with a trend toward improved outcome in those patients in whom systolic blood pressure was lowered within 6 hours of hemorrhage.[15]

Therefore, indications for intervention (Table 2) and recommended drugs are as shown. The general comments on choice of drugs discussed under ischemic stroke apply.[6,14,20,23-26] In addition, sodium nitroprusside is probably inappropriate for SICH because it is a potent antiplatelet drug and can raise intracranial pressure.[6,14,20,23-26]

Current Consideration for Reduction of Hematoma Expansion

A new consideration is the combination of intravenous hemostatic treatment and aggressive BP control.[6,14] In an exploratory analysis from a study of recombinant activated factor VII in ICH, initial SBP <170 mm Hg was associated with a trend toward lower hematoma expansion rates. In another study, a total of 188 patients admitted within 24 hours of symptom onset were treated with a combination of rapidly administered antifibrinolytic agents and systolic BP maintained <150 mm Hg.[6,14] Hematoma enlargement was observed in only 4.3% of patients, which supports further evaluation of this approach.[6,14].

Management of Hypertension in SAH

Given the evidence for benefit and the low risk, oral nimodipine might be indicated in patients with aneurysmal SAH.[27] Intravenous administration of calcium channel blockers, however, cannot be recommended for routine use in such patients.[27] At present, nimodipine is the only calcium channel blocker licensed to prevent vasospasm, to reduce the incidence and extent of ischaemic deficits, and to improve neurological outcomes in patients with aneurysmal subarachnoid haemorrhage.[27] Nimodipine generally is well tolerated following oral administration. Adverse effects reportedly occurred in about 11% of patients receiving oral nimodipine dosages of 0.35 mg/kg or 30–120 (principally 60) mg every 4 hours for the management of subarachnoid hemorrhage. The most common adverse effect of nimodipine is hypotension, which may be dose-related and occasionally requires discontinuance of the drug.

Nicardipine is a second-generation dihydropyridine-type CCB with high vascular selectivity and strong cerebral vasodilatory activity.[6 ,27] According to a recently published narrative review, nicardipine given intra-arterially or via prolonged-release implants might be an alternative to nimodipine. However, it reduces vasospasm but does not improve outcome significantly.[6, 27]

BP control in Primary and secondary prevention of stroke. Recurrent stroke occurs in up to 16% of Nigerian stroke patients.[4] For both recurrent and first stroke, the relationship of stroke mortality to usual BP is strong and direct at all ages, with no good evidence of a threshold at any age in the range of usual SBP above 115 mm Hg or of usual DBP above 75 mm Hg.[28-30] There is substantial evidence to support BP-lowering for prevention of a first stroke; however, few trials have focused on antihypertensive therapy for recurrent stroke prevention.[5]

While awaiting the arrival of more definitive data, the available evidence suggests that it might be reasonable to start oral antihypertensives as soon as 3 days after onset of symptoms, depending on the level of blood pressure and provided there are no contraindications such as a presumed hemodynamic mechanism of stroke.[5]

The precise target goal is not definitively known. In the PROGRESS trial, BP was lowered by approximately 10/ 5 mm Hg, and this BP target has been suggested as a reasonable one for patients according to the AHA/ASA guideline.[5] However, there is variability of absolute BP level and response to BP-lowering by the patient, especially when age is taken into account, and this must be considered before attempting to lower BP. A reasonable goal, if it can be safely achieved after ischemic stroke, is the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) target of <140/90 mm Hg for uncomplicated hypertensive patients and <130/ 80 mm Hg for those with diabetes mellitus or chronic kidney disease.[5] Persons without hypertension may also benefit from BP-lowering in relation to recurrent stroke prevention.[5]

Which Antihypertensive Drug is Most Effective?

In general, all major classes of BP-lowering agents may diminish recurrent stroke risk. Although some studies have suggested that angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may be more effective in recurrent stroke prevention

than other antihypertensive agents, this assertion has not been validated in more recent studies.[5,14,31] Thus far and based on somewhat limited data, the degree of BP-lowering may be more important than the agent used. The choice of the antihypertensive agent should probably depend more on the associated medical conditions rather than any specific cerebrovascular protective effects of a specific class of antihypertensive agents.[5] Compelling indications as stated in the JNC 7 recommendations should be followed.

Beta-blockers may have a reduced ability to protect against stroke (particularly atenolol), may favor weight gain, and cause dyslipidemia and impaired glycemic control.[5] Therefore, persons at risk for or with multiple metabolic factors may not be good candidates for beta-blocker administration unless they are vasodilator beta-blockers, which may not be associated with these latter side effects.

The fear that thiazide diuretics, which are very effective in blacks, may have dyslipidemic and diabetogenic effects when used at high doses, has been questioned by the findings of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack trial that failed to support the preference for calcium channel blockers, beta-blockers, or angiotensin-converting enzyme inhibitors compared with thiazide-type diuretics in patients with metabolic syndrome.[5] The AHA/ASA guideline recommends consideration of a diuretic in combination with an angiotensin-converting enzyme inhibitor.[5,17,32]

Lifestyle modifications are recommended as part of a comprehensive approach.[5,17,32] This include the dietary approaches to stop hypertension (DASH)[30], exercise, and smoking cessation among other recommendations.

CONCLUSIONS

The management of blood pressure in stroke patients is as critical as it is controversial. Further studies are required to determine specific blood pressure targets for different types of stroke, type of drugs and preferred route of administration, time of commencement of therapy and rate of control, as well as specific considerations in terms of race, age and comorbidities. Studies are also needed to demonstrate the clinical benefits, impact on health-related quality of life and cost-effectiveness of various therapies. Imaging modalities need to be developed that allow bedside measurement of regional cerebral blood flow and metabolism so that titration of antihypertensive treatment can be based on critical variables.[14]

At the moment, most recommendations are based on expert opinions and general principles defined by observational studies and small clinical trials. With the anticipated completion of several large clinical trials in the next 5 years, these recommendations can be established on the basis of superior levels of scientific evidence.[14]

REFERENCES

1. Lopez AD, Mathers CD, Ezzati M, Jamison DT and Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. Lancet 2006 May 27; 367(9524): 1747-1557.
2. Ogun SA, Ojini FI, Ogungbo B, Kolapo KO and Danesi MA. Stroke in south west Nigeria: a 10-year review. Stroke 2005 June;36(6): 1120-2220.
3. Komolafe MA, Ogunlade O and Komolafe EO. Stroke mortality in a teaching hospital in South Western Nigeria. Trop Doct 2007 July; 37(3): 186-188.
4. Owolabi MO, Ugoya S and Platz T. Racial disparity in stroke risk factors: the Berlin-Ibadan experience; a retrospective study. Acta Neurol Scand 2009 February; 119(2): 81-87.
5. Aiyagari V and Gorelick PB. Management of blood pressure for acute and recurrent stroke. Stroke 2009 June;40(6): 2251-2256.
6. Tikhonoff V, Zhang H, Richart T and Staessen JA. Blood pressure as a prognostic factor after acute stroke. Lancet Neurol 2009 October;8(10): 938-948.
7. Summers D, Leonard A, Wentworth D, Saver JL, Simpson J, Spilker JA, Hock N, Miller E and Mitchell PH. Comprehensive overview of nursing and interdisciplinary care of the acute ischemic stroke patient: a scientific statement from the American Heart Association. Stroke 2009 August;40(8): 2911-2944.
8. Adams HP, Jr., del ZG, Alberts MJ, Bhatt DL, Brass L, Furlan A, Grubb RL, Higashida RT, Jauch EC, Kidwell C, Lyden PD, Morgenstern LB, Qureshi AI, Rosenwasser RH, Scott PA and Wijdicks EF. Guidelines

for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. Circulation 2007 May 22; 115(20): e478-e534.

9. Vemmos KN, Tsivgoulis G, Spengos K, Zakopoulos N, Synetos A, Manios E, Konstantopoulou P and Mavrikakis M. U-shaped relationship between mortality and admission blood pressure in patients with acute stroke. J Intern Med 2004 February;255(2): 257-65.

10. Aiyagari V and Badruddin A. Management of hypertension in acute stroke. Expert Rev Cardiovasc Ther 2009 June;7(6): 637-646.

11. Jaeger M, Schuhmann MU, Soehle M, Nagel C, Meixensberger J. Continuous monitoring of cerebrovascular autoregulation after subarachnoid hemorrhage by brain tissue oxygen pressure reactivity and its relation to delayed cerebral infarction. Stroke 2007 March;38(3): 981-986.

12. Mahieu D, Kips J, Rietzschel ER, De Buyzere ML, Verbeke F, Gillebert TC, De Backer GG, De BD, Verdonck P, Van Bortel LM and Segers P. Noninvasive assessment of central and peripheral arterial pressure (waveforms): implications of calibration methods. J Hypertens 2010 February;28(2): 300-305.

13. Walters FJM. Intracranial pressure and cerebral blood flow. Update in Anaesthesia 1998; (8): 1-4.

14. Qureshi AI. Acute hypertensive response in patients with stroke: pathophysiology and management. Circulation 2008 July 8; 118(2): 176-187.

15. Broderick J, Connolly S, Feldmann E, Hanley D, Kase C, Krieger D, Mayberg M, Morgenstern L, Ogilvy CS, Vespa P and Zuccarello M. Guidelines for the management of spontaneous intracerebral hemorrhage in adults: 2007 update: a guideline from the American Heart Association/ American Stroke Association Stroke Council, High Blood Pressure Research Council, and the Quality of Care and Outcomes in Research Interdisciplinary Working Group. Circulation 2007 October 16; 116(16): e391-e413.

16. Jain AR, Bellolio MF and Stead LG. Treatment of hypertension in acute ischemic stroke. Curr Treat Options Neurol 2009 March; 11(2): 120-125.

17. Ringleb P, Schellinger PD and Hacke W. [European Stroke Organisation 2008 guidelines for managing acute cerebral infarction or transient ischemic attack. Part 1]. Nervenarzt 2008 August;79(8): 936-957.

18. Poungvarin N. Steroids have no role in stroke therapy. Stroke 2004 January;35(1): 229-230.

19. Ogun SA, Odusote KA. Effectiveness of high dose dexamethasone in the treatment of acute stroke. West Afr J Med 2001 January; 20(1): 1-6.

20. Robinson TG and Potter JF. Blood pressure in acute stroke. Age Ageing 2004 January; 33(1): 6-12.

21. Potter JF, Robinson TG, Ford GA, Mistri A, James M, Chernova J and Jagger C. Controlling hypertension and hypotension immediately post-stroke (CHHIPS): a randomised, placebo-controlled, double-blind pilot trial. Lancet Neurol 2009 January;8(1): 48-56.

22. Rodriguez-Garcia JL, Botia E, de La SA, Villanueva MA and Gonzalez-Spinola J. Significance of elevated blood pressure and its management on the short-term outcome of patients with acute ischemic stroke. Am J Hypertens 2005 March; 18(3): 379-384.

23. Steiner T and Juttler E. American guidelines for the management of spontaneous intracerebral hemorrhage in adults: European perspective. Pol Arch Med Wewn 2008 April; 118(4): 181-182.

24. Steiner T, Broderick J, Brun NC, Davis SM, Diringer MN, Mayer S and Skolnick BE. Timing is everything in intracerebral hemorrhage. Stroke 2008 July; 39(7): e117-e118.

25. Steiner T, Kaste M, Forsting M, Mendelow D, Kwiecinski H, Szikora I, Juvela S, Marchel A, Chapot R, Cognard C, Unterberg A and Hacke W. Recommendations for the management of intracranial haemorrhage - part I: spontaneous intracerebral haemorrhage. The European Stroke Initiative Writing Committee and the Writing Committee for the EUSI Executive Committee. Cerebrovasc Dis 2006; 22(4): 294-316.

26. Kulkens S, Ringleb P, Diedler J, Hacke W and Steiner T. [Recommendations of the European Stroke Initiative for the diagnosis and treatment of spontaneous intracerebral haemorrhage]. Nervenarzt 2006 August; 77(8): 970-987.

27. Bederson JB, Connolly ES, Jr., Batjer HH, Dacey RG, Dion JE, Diringer MN, Duldner JE, Jr., Harbaugh RE, Patel AB and Rosenwasser RH. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. Stroke 2009 March; 40(3): 994-1025.

28. Franco V, Oparil S and Carretero OA. Hypertensive therapy: Part II. Circulation 2004 June 29;109(25):3081-3088.

29. Franco V, Oparil S and Carretero OA. Hypertensive therapy: Part I. Circulation 2004 June 22; 109(24): 2953-2958.

30. Franco V and Oparil S. Salt sensitivity, a determinant of blood pressure, cardiovascular disease and survival. J Am Coll Nutr 2006 June; 25(3 Suppl): 247S-255S.

31. Kent DM and Thaler DE. Stroke prevention—insights from incoherence. N Engl J Med 2008 September 18; 359(12): 1287-1289.

32. Sacco RL, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Schwamm LH and Tomsick T. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. Circulation 2006 March 14; 113(10): e409-e449.

Prevalence of Anaemia and other Haematologic Derangements in End Stage Renal Disease Patients in the University of Port Harcourt Teaching Hospital

FS Wokoma and PC Emem-Chioma

Renal Unit, Department of Medicine, University of Port Harcourt Teaching Hospital, PMB 6173, Port Harcourt, Nigeria

ABSTRACT

Anaemia and other haematologic derangements are common in patients with chronic kidney disease (CKD), especially end stage renal disease (ESRD). Anaemia is an independent risk factor for cardiovascular morbidity and mortality in CKD. The prevalence of anaemia and other haematologic derangements in the population of ESRD patients at the University of Port Harcourt Teaching hospital (UPTH) is not known.The objective of the study is to determine the prevalence of anaemia and other haematologic derangements in dialysis naive end stage renal disease patients in the University of Port Harcourt Teaching Hospital. A retrospective analysis of the haematologic indices of pre-dialysis end stage kidney disease patients at the UPTH from January to December 2007 was done. There were seventy patients, 50 males, 20 females (M/F= 2.5:1), mean age of 44 $\pm$ 17.0(18-85) years and mean e-GFR of 7.1 $\pm$ 2.1(3.5-10.8)mls/min. They had a mean haematocrit of 22.8 $\pm$ 3.1(10-38) percent, mean haemoglobin concentration of 8.8 $\pm$ 3.1(3.3-16)g/dl. Others were mean ESR, 93.1 $\pm$ 45.1(7-136)mm/hr, mean peripheral total leukocyte count 7,533.5 $\pm$ 3,949.6(2,499-18,800)/mm^3 and a mean platelet count 145,000 $\pm$66,500.1 (60,000-240,000)./mm^3 . Anemia was the dominant haematologic abnormality occurring in 66(94.3%) patients. Moderate to severe anaemia occurred in 58 (82.9%) of the patients, 6 (8.6%) had haemoglobin levels within normal range. Twelve patients (17%) had leukocytosis and 2(2.9%) had leukopenia. Peripheral blood film showed evidence of iron deficiency and some abnormal cells. The e-GFR of the patients showed positive correlation with haematocrit (r= +0.2) and haemoglobin(r= +0.1) level respectively. Blood urea and serum creatinine showed negative correlation with haematocrit(r = -0.2) and haemoglobin concentration(r = -0.2) respectively. In conclusion, we found that anaemia was the dominant haematologic abnormality in dialysis naive end stage renal disease patients in the University of Port Harcourt Teaching hospital. Both haematocrit and haemoglobin levels showed positive correlation with e-GFR. The findings are consistent with previous studies. Considering that anaemia is a risk factor for morbidity and mortality in ESRD patients, there is need for increased attention to the correction of anaemia in ESRD patients in Nigeria and other resource poor countries.

Keywords: *Haematologic abnormalities, end stage renal disease, University of Port Harcourt Teaching hospital*

Corresponding author : **Dr P.C. Emem-Chioma**

Renal Unit, Department of Medicine, University of Port Harcourt Teaching Hospital, PMB 6173, Port Harcourt. E-mail:emem.chioma2008@gmail.com. Tel: 0803 310 3653

INTRODUCTION

Derangements in haematologic indices, especially anaemia, are common in patients with chronic kidney disease (CKD) and chronic kidney failure. The subject has been extensively studied globally [1-3] and to some extent, in Nigerian patients with CKD [4,5]. Whereas, the other haematologic derangements are generally minor and of less clinical importance, anaemia remains the dominant abnormality that is of significant clinical implications for the CKD patient.

The degree of anaemia worsens as the chronic kidney disease progresses. Anaemia becomes profound as the glomerular filtration rate (GFR) drops to about 30ml/min/1.73m ^{2} and worsens as CKD progresses towards end stage kidney disease [1].

Anaemia contributes significantly to the high morbidity and mortality associated with advanced CKD, especially in poor countries, where maintenance dialysis is sub-optimal and access to erythropoietin is very low [5, 6]. Anaemia is an independent risk factor for cardiovascular morbidity and mortality in CKD patients by inducing volume overload, left ventricular dilatation and left ventricular hypertrophy [7, 8].

In the University of Port Harcourt Teaching hospital, there has been no previous study of the problem of haematologic disorders in chronic kidney disease. This study therefore, seeks to determine the prevalence of anaemia and other haematologic indices of end-stage kidney disease patients before commencement of long term haemodialysis program. The results are intended to determine the magnitude of the problem in our facility, establish a base data on the subject in the hospital as well as contribute to the National data on the subject.

Aims and Objectives

To determine the prevalence and distribution of anaemia and other haematologic abnormalities in dialysis naive end stage renal disease patients at the University of Port Harcourt Teaching Hospital (UPTH).

METHODS

The study was a retrospective analysis of data of haematologic indices in CKD- 5 patients before commencement of maintenance dialysis in UPTH. The clinical case files of patients presenting between January and December 2007 were studied. The results of the first series of laboratory tests performed at first presentation before their first haemodialysis session were used for analysis.

Data extracted from the clinical case files include the bio-demographic data, date at first diagnosis of chronic kidney disease(CKD), the primary renal diagnosis, the pre-dialysis biochemical parameters namely, plasma concentrations of sodium, potassium, bicarbonate, urea, creatinine, total protein and albumin as well as the estimated glomerular filtration rate (e-GFR) . The pre-dialysis peripheral haematologic indices analyzed include , the haematocrit, the haemoglobin concentration(Hb), erythrocyte sedimentation rate(ESR), the total peripheral leukocyte count(TWBC), the percentage differential leukocyte counts, the platelet count as well as the peripheral blood film report.

National kidney foundation/kidney dialysis quality of life index (NKF/KDOQI) guidelines[9] on definition of anaema in CKD was adopted, which defines anaemia as a haematocrit level of 36% percent or less, or an haemoglobin concentration of 12g/dl or less. The degree of anaemia was categorized as mild (Hct.30- 36%; Hb.10-12/dl), moderate (Hct. 21-29.9%; Hb 7-9.9g/dl) or severe (Hct. less<21%; Hb <7g/dl) respectively. Leukocytosis was defined as a total peripheral leukocyte count of >11,000/mm^3 of blood, while leucopenia was defined as a total peripheral leukocyte count of 3000/mm^3 of blood or less. Eosinophila was defined as peripheral eosinophil percentage of 10% or higher. Thrombocytosis was defined as the total peripheral platelet count of more than 400,000/mm^3 of blood while thrombocytopenia was defined as total peripheral platelet count of less than 100,000/mm^3. Erythrocyte sedimentation rate of 20 mm/hour (Westergren) or more was taken as elevated [10].

All the tests for the haematologic and biochemical parameters were performed in the central laboratory service of the hospital.

Chronic kidney failure was defined and staged in accordance with the NKF/ KDOQI guidelines11 for the diagnosis and staging of chronic kidney disorder. The estimated GFR (e-GFR) was calculated using the Cockcroft and Gault [12] formula for estimation of GFR.

Study Population

All patients with end stage kidney disease, who commenced maintenance haemodialysis in the hospital during the study period, January to December 2007.

Exclusion

Patients with major primary haematologic disorders such as the major haemoglobinopathies, leukemia, lymphomas and other infiltrative disorders were excluded. Others include those with evidence of any other obvious major causes of anaemia, other than CKD, as well as evidence of recent blood transfusions and or recent treatment with erythropoietin. Patients with evidence of previous dialysis were also excluded.

Data Analysis

The data were analyzed using Statistical package for social sciences (SPSS- version6). Quantitave variables are presented as mean ± standard deviation. Pearson correlation coefficient(r) was used to determine the relationship between dependent variables. Student t-test was applied to determine the measures of significance between sub populations with the level of significance (p-value) set at 0.05. Tables were used as appropriate.

Study Limitations

Being a retrospective study, it was not possible to exclude patients with all other possible causes of haematologic disorders, other than those that could easily be identified from the patients' records. Similarly, more detailed haematologic indices such as mean corpuscular volume (MCV), mean haemoglobin concentration (MCHC), leukocyte function studies, iron studies and bone marrow studies were not available for study. These tests are usually not part of the routine haematologic assessment tests for pre-dialysis CKD patients in our center.

RESULTS

The data for seventy patients were suitable for analysis. They constitute 50 males and 20 females giving a male to female ratio of 2.5:1. Their ages ranged from 18 t0 85 years with a mean age of 44.2 ±17.0 years. Their e-GFR ranged from 3.50 to 10.8 ml/min with a mean of 7.1 ± 2.1ml/min. Their hematologic and biochemical profiles before commencement of first dialysis at are detailed in tables 1 and 2.Their mean haematocrit was 22.8 ± 3.1(10-38)percent , while the mean haemoglobin concentration was 8.8 ± 3.1(3.3-16) g/dl respectively. The erythrocyte sedimentation rate ranged from 7 to 136mm/hr, with a mean of 93.1 ± 45.1 mm/hr. The mean total leukocyte count was 7,533.5 ±3,949.6(2,499-18,800)/mm^3. The platelet counts ranged from 65,000 to 240,000/mm^3 with a mean of 145,000 ± 66,500.1/mm^3.

The frequencies of abnormalities of the haematologic indices are shown in table 3. Sixty eight patients (97.1%) had haematocrit levels of 36% or less, while 64(91.4%) had haemoglobin concentration levels of 12g/dl or less. Thus an aggregate of 66(94.3%) of the patients were anaemic. Twelve patients (17.1%) each had mild anaemia by haematocrit or haemoglobin estimation. Thirty-six patients (51.4%) had moderate anemia by haematocrit and 32(45.7%) by haemoglobin estimation, while severe anemia was observed in 22(31.4%) by haematocrit and 26(37.1%) by haemoglobin concentration respectively. The differences between haematocrit and haemoglobin values were not statistically significant ($p>0.05$). Six patients (8.6%) had haemoglobin and haematocrit levels that were within normal limits.

Fifty-six patients (80%) had erythrocyte sedimentation rate >20mm/hr. Leukocytosis of > 11,000/mm^3 was observed in 12(17.1%) of the patients, while leucopenia of < 3000/ml was observed in 2(2.9%). Eosinophilia of > 10% was observed in 8(11.4%) of the patients. Ten (14.3%) had

Table 1: Haematologic profiles of the patients

Haematologic parameters	Range	Mean ± sd
Haematocrit.(%)	10-38	22.8 ± 3.1
Haemoglobin conc.(g/dl)	3.3-16	8.8 ± 3.1
*ESR(mm/hr)	7-136	93.1 ± 45.1
Total white cell count.(/mm^3)	2400-18,800	7,533.5 ±3,949.6
Neutrophil %	26-96	66.1 ± 15.1
Lymphocyte%	4.0-70	29.1 ±13.1
Eosinophil%	3.0-19	5.6 ±5.1
Platelet count(/mm^3)	65,000-240,000.0	145,000 ±66,500.1

**ESR- Erythrocyte sedimentation rate (mm-hour Westergren)*

Table 2: Biochemical profiles of the patients

Biochemical parameters	Range	Mean ± sd
Sodium(mmol/l)	119-146	133.2 ± 7.0
Potassium(mmol/l)	3.3-8.0	5.3 ±1.4
Bicarbonate(mmol/l)	12-26	17.8 ± 3.3
Urea(mmol/l)	20-88.5	36.6 ± 18.7
Creatinine(umol/l)	645-2102	1110.6 ± 533.3
Total protein(g/dl)	42-87	60.7 ± 12.1
Albumin(g/dl)	12-66	31.3 ± 12.4
Fasting blood glucose(mmol/l)	2.2-24	5.7 ±4.7

thrombocytopenia and none of the patients had thrombocytosis.

Table 3: Abnormal haematologic indices

Haematologic abnormality	No.	Percentage
Haematocrit. <36%.	69	98.6
Anaemia(Hb <12g/dl)	64	91.4
High ESR(>20mm/hr)	56	80.0
Leukocytosis(>11,000/mm^3)	12	17.1
Leukopenia(<3000/mm^3)	2	2.9
Neutrophilia%(>70%)	24	34.2
Neutropenia%(<25%)	nil	0.0
Eosinophilia(>10%)	8	11.4
Thrombocytopenia(<100,000/mm^3)	nil	14.3
Thrombocytosis(>400,000.0/mm^3)	nil	0.0

The peripheral blood film showed some abnormalities (table 4). Microcytosis 12(17.1%), hypochromic red cells 8(11.4%) and microcytic-hypochromic red cells 6 (8.5%) consistent with iron deficiency anaemia were the commonest. Burr cells (crenated red cells) sometimes called renal failure cells were reported in 6(8.6%) patients , while toxic neutrophils suggestive of serious infections were reported in 4(5.7%).

Table 4: Abnormal blood film findings

Abnormal blood film.	No. of patients	Percentage
Burr cells	6	8.6
Codocytes	4	5.7
Microcytic red cells	12	17.1
Hypochromic red cells	8	11.4
4Hypochromic-microcytic	6	8.6
Poikilocytes	4	5.7
Anisocytes	8	11.4
Toxic neutrophils	4	5.7

The biochemical parameters were consistent with features of advanced kidney failure (table 2). All the patients had e-GFR values less than 15mls per minute, values consistent with end stage renal disease. The mean e-GFR was 7.1± 2.1(3.5-10.8) mls/min. The e-GFR showed positive correlation with haematocrit (r= +0.2), haemoglobin concentration (r= +0.1), platelet count(r = +0.5) and total Leukocyte count(r=+0.2) respectively.

DISCUSSION

Anaemia was the most significant haematologic abnormality occurring in 94.3% of the patients, followed by high ESR, peripheral eosinophilia and leukocytosis. The peripheral blood film showed evidence of iron deficiency anaemia and some abnormal cells such as burr cells, codocytes and toxic neutrophils.

The high prevalence of anemia as the dominant haematologic abnormality is consistent with previous studies of the haematology of CKD worldwide and in Nigeria [1, 3, 4, 5]. In terms of severity, majority of the patients (82.8 %) had moderate to severe anaemia. Six patients (8.6%) however had haemoglobin levels within normal limits. No case of polycythaemia was observed.

The findings of normal hemoglobin/haematocrit levels in six patients with stage 5 CKD was not expected, however there have been reports of polycythaemia in patients with CKD as well as among maintenance dialysis patients . Polycythaemia

have been reported in CKD due to hydronephrosis, polycystic kidney disease, dialysis patients who developed simple renal cysts and renal tumours [13-15]. Local ischaemia and eythropoetin expressing tumour cells are said to be responsible. Some post transplant CKD patients also manifest polycythaemia. Such polycythaemia is said to result from an excessive activity of the erythropoietin producing tissue in the transplant kidney in response to the pre-transplant anaemic state of the recipient [3, 16] Two of our patients had polycystic kidney disease, three had obstructive uropathy, but none of these had normal or elevated haematocrit levels.

Though the causes of anaemia in CKD patients are often multifactorial, the deficiency of the production of erythropoietin by the diseased kidneys remains dominant and most important [1]. Erythropoietin, a glycoprotein growth factor is produced by the peri- tubular fibroblasts within the renal cortex. Erythropoietin promotes the proliferation and the terminal differentiation of erythrocyte precursor cells into normoblasts and subsequently into mature erythrocytes [3]. The low erythropoietin level in CKD leads to deficiency of bone marrow erythropoiesis which results in anemia.

Several studies have demonstrated the strong relationship between the progression of chronic kidney disease and anaemia. Though the relationship is not linear, in most studies [17, 18] a positive correlation between the GFR and haemoglobin or haematocrit levels have been demonstrated in patients with CKD as was the case in this study. Similarly serum creatinine levels show negative correlation with haematocrit or haemoglobin concentration as was the case in this study. Most patients with CKD become profoundly anaemic as the e-GFR drops to 30 mls /min or below.

Anemia induces significant hypoxaemic injury to the tissues as well as a serious haemodynamic stress to the patient's cardiovascular system. Anaemia is an independent risk factor for left ventricular hypertrophy(LVH), left ventricular dilatation and death independent of hypertension in patients with CKD, thus contributes to the high cardiovascular morbidity and mortality observed in CKD patients [7, 8].

As observed in this study, moderate to severe anemia is a common presenting feature in dialysis populations in Nigeria [4, 5]. Though there are no studies linking dialysis outcomes with anemia in Nigeria, it is quite plausible that anaemia account to a large extent, for the poor clinical state at presentation for dialysis and the poor dialysis outcomes as reported from centers across Nigeria [4-6, 19-21]. Such clinical state is often characterized by the presence of moderate to severe anaemia, hypertension, haemodynamic instability, gross oedema, volume overload and pulmonary oedema. In most instances the first haemodialysis session constitute an emergency life rescue procedure as a result of haemodynamic instability. Most patients receive two to three units of blood during their first dialysis session.

The optimal control of anaemia in CKD, has been demonstrated in several studies to significantly improve the symptoms, exercise tolerance, functional ability, dialysis outcomes and the overall quality of life of CKD patients worldwide [22,23]. For this reason international guidelines have been developed for the management of anaemia in CKD patients [24, 25]. Earlier advocacy was for the normalization of haematocrit, but recent reports, however have shown that such normalization is associated with poor outcomes in patients with CKD. For this reason, NKF/KDOQI [26] in 2006 recommended the target haemoglobin levels of between 11 and 12 g/dl as optimal for CKD patients.

Recombinant human erythropoietin (r-HuEPO) is the gold standard for the management of anaemia of CKD and has demonstrated wide clinical success and acceptability globally [27, 28]. The correction of anaemia with r-HuEPO in CKD patients has contributed significantly to the better outcome and longevity of maintenance dialysis patients especially in the developed countries of the world, where ready access and optimal treatment is the norm.

Unfortunately in Nigeria, recombinant human erythropoietin is quite expensive and not within reach of majority of CKD patients. Arogundade et al [5] in a study of thirty newly diagnosed CKD patients showed that only 33.3% could afford erythropoietin therapy for three months. In our center (unpublished data) not up to ten percent receive erythropoietn, even then very irregularly. This picture is likely to be the same across the country. Erythropoietin adds extra heavy financial burden on the resource poor patients in our practice environment. The high cost of haemodialysis treatment and high cost of erythropoietin make optimal treatment of CKD patients in resource poor settings like Nigeria almost an impossible task, in the absence of any form of government or social security support. Access to

regular erythropoietin for optimal control of anaemia and access to optimal dialysis remain one of the greatest challenge facing renal care providers and CKD patients in Nigeria and other resource poor sub-Saharan African nations.

Repeated blood transfusions are not a viable alternative to erythropoietin. Blood transfusions add more nitrogenous impurities to the body of the uraemic patient. Also, blood for transfusion is increasingly becoming scarce and expensive. The risk of transmission of deadly blood borne infections is a reality in spite of pre-transfusion screening, while repeated transfusions may lead to the development of HLA antibodies [29]. From the foregoing therefore, recombinant erythropoietin remain the treatment of choice for anaemia in CKD every where in the world. Government driven intervention that will ensure the regular access to erythropoeisis stimulating agents (ESA) and dialysis in the care of patients with End stage kidney failure becomes inevitable in resource poor countries such as Nigeria and other sub-Saharan African countries.

Abnormalities in the other haematologic indices studied were few. The high rate of elevated erythrocyte sedimentation rates (ESR) could be explained by the high rate of anaemia and the evidence of possible infections in the patients. ESR values had negative correlation with both haematocrit and haemoglobin levels'(r=-0.3, and -0.4 respectively). The presence of neutrophilia (34.2%) and toxic neutrophils (5.2%) in the peripheral blood film of some of the patients is a reflection of the possible presence of pyogenic infections. With the exception of eight patients (11.4%) with leucocytosis, from whose urine organisms were cultured, there was no documented evidence of specific infections in any of the organ systems, to account for the leucocytosis. It is however possible that the patients with polycystic kidney disease and obstructive uropathy may harbour occult infections that could account for the leucocytosis.

We could not determine the exact cause of the 11% eosinophlia we found in the patients. The records could not provide any evidence of history of allergy, or intestinal and systemic parasitic infestations. It is quite possible the eosinophilia may have been due to intestinal parasitic infestations such as hook-worm infestations, which are prevalent in the tropical environment as ours. Exposure to angiotensin converting enzyme (ACE) inhibitors may be a factor as most of the patients, were on ACE-inhibitors used for their anti-hypertensive and reno-protective properties. Since the study data were pre-dialysis data, dialyser membrane (e.g. AN69) induced anaphylactic reactions was unlikely.

Though 14.3% of the patients had thrombocytopenia with platelet counts of less than 100,000.0/mm^3, none of the patients manifested clinical features of haemorrhagic diathesis. There was no record of excessive bleeding during haemodialyis sessions in spite of heparin dialysis. The absence of spontaneous bleeding in these patients may be because none of them had thrombocytopenia below 50,000.0/mm^3. Some studies have demonstrated that functional platelet abnormalities tend to predominate in uraemic patients[30, 31] .

The peripheral blood film of our patients showed some abnormal cells (table4). The presence of microcytes, hypochromia and microcytic-hypochromia were indicative of iron deficiency, which is common in CKD patients [28, 31]. Causes of iron deficiency in CKD patients are multi-factorial and include poor dietary iron intake, chronic gastrointestinal blood loss, intestinal infestations, as well as blood loss from dialysis. Iron studies and bone marrow iron staining were however not done to confirm iron deficiency state in these patients. The presence of iron deficiency is however of significant relevance for effective treatment of the anaemia of CKD with erythropoietin. In the absence of iron, recombinant human erythropoietin will not be effective, as haem would not be incorporated into the haemoglobin molecule. For optimal response to erythropoietin therapy the iron deficit in renal anemia must be determined and corrected with parenteral iron to replenish the iron stores during erythropoietin therapy. There are international guidelines [26] for iron therapy in CKD patients. Burr cells and codocytes are commonly found in the peripheral blood film of chronic renal patients and are sometimes called renal failure cells, but they are not pathognomonic of chronic renal failure[31].

CONCLUSION

This study as in previous local and international studies confirm anaemia as the dominant and most important haematologic derangement in patients with end stage renal disease. Moderate to severe anaemia is most prevalent in our patients. The role of anemia as a major risk factor for poor outcomes in CKD patients in Nigeria and similar resource poor settings are

discussed. The central role of optimal erythropoietin therapy in reversing the deleterious effects of anaemia, and improving outcomes in CKD patients is well established. Poor access to optimal erythropoietin therapy and optimal dialysis remains one of the most important challenges facing renal care in Nigeria.

REFERENCES

1. Eschbach JW. The anaemia of chronic renal failure: Pathophysiology and effects of recombinant erythropoietin. Kidney Int 1989; 35: 134-148.

2. Lewis SL and Van Epps DF. Neutrophil and monocyte alterations in chronic dialysis patients. Am J Kidney Dis 1987; 9: 381-395.

3. Himmelfarb J. Haematologic manifestations of renal failure. In: Greenberg A, Cheung AK, Falk RJ, Coffman TM, Jennifer J(eds) PRIMER ON KIDNEY DISEASES . Academic Press Ltd. Canada 1988: 465-491.

4. Akinsola A, Durosinmi MA and Akinola NO. Haematologic profile in Nigerians with chronic renal failure Afr J Med Sci 2009; 29: 13-16.

5. Arogundade FA, Bappa A, Sanusi AA, Akinola OO, Adediran I A and Akinsola A. Haematologic indices and response to erythropoietin therapy in chronic renal failure. Trop J Nephrol 2006;1:13-20.

6. Arije A. Problems of haemodialysis in the management of chronic renal failure in Ibadan. Arch Ibadan Med 2001;2(1):14-15.

7. Eschbach JW and Adamson JW. Anaemia of end stage renal disease. Kidney Int. 1985; 28(1) :1-5.

8. Foley RN, Parfrey PS, Harnett JD, Kent GM, Murray DC , Barre PE. The impact of anaemia on cardiomyopathy, morbidity and mortality in end stage renal disease. Am J Kidney Dis 1966; 28(1): 53-61.

9. National Kidney Foundation. K/DOQI clinical practice guidelines for anaemia of chronic kidney disease 2000. Am J Kidney Dis 2001; (suppl.1)37: S182-S238.

10. Mosby Diagnostic Laboratory Test Reference (7th.ed) Pagara KD, Pagara TJ (eds) 2005. ELSERVER MOSBY. UNITED STATES OF AMERICA.

11. National Kidney Foundation. K/DOQI Clinical practice Guidelines for definition, classification of stages of chronic kidney disease. Am J Kidney Dis 2002; 39(suppl 1): S1-S266.

12. Cockcroft DW and Gault MH. Prediction of creatinine clearance from serum creatinine .Nephron 1976; 16(1): 31-41.

13. Simone S, Winkelman B, Kluthe C , Roigas J, Querfeld U and Muller D. Polycythaemia and increased erythropoietin in a patient with chronic kidney disease(case report). Nature Clin Pract Nephrol 2007; 3(4): 222-226.

14. Feustel A, Bellmann H and Hefftler U. Renal polycythaemia as a facultative leading symptom on kidney tumour, hydronephrosis and cystic kidney. Z Urol Nephrol 1970; 63: 705-714.

15. Lutzeyer W and Teichman HH. Kidney tumour and polycythaemia. Arzti Wolchensch 1960; 15: 253-257.

16. Donati RM, Lange RD and Gallagherin NI. Nephrogenic erythrocytosis. Arch Int Med 1963; 112: 960-965.

17. Harris K. Assessment of chronic kidney disease. In : Chronic kidney Disease (selected materials from the Oxford Desk Reference Nephrology). Barrett J, Harris K, Topham P (eds).OXFORD UNIVERSITY PRESS 2009; 3-9.

18. McClellan W, Aronoff SL, Bolton WK, Hood S, Lorber DL, Tang KL, Tse TF, Wasserman B and Leiserowitz M. The prevalence of anaemia in patients with chronic kidney disease. Curr Med Res Opin 2004; 20: 991-996.

19. Arogudade FA, Sanusi AA and Akinsola A. Epidemiology, clinical characteristics and out comes in ESRD patients in Nigeria: Is there a changing trend?.Tropical Journal Of Nephrology 2006; 1(1)41-42.

20. Wokoma FS and Okafor UH. Spectrum of patients presenting for dialysis in a new dialysis facility at the University of Port Harcourt Teaching Hospital Jan-

Dec,2007.(Abstract). Tropical Journal Of Nephrology 2006;1(1)52-53.

21. Menakaya NC, Adewumi AJ, Braimoh RV and Mabayoje MO. End stage renal disease at the Lagos University Teaching Hospital Nigeria, a ten year update review. Trop J Nephrol 2006,1(1)42-43.

22. Ross SD, Fahrbach K and Frame D. The effect of anaemia treatment on selected health related quality of life domains: a systematic review. Clin. Ther. 2003; 25: 1786-1805.

23. Leaf DE and Goldfarb DS. Interpretation and review of health related quality of life data in chronic kidney disease patients receiving treatment for anaemia. Kidney Int 2009; 75: 15-24.

24. Eschbach J, Deoreo P, Adamson J, Berms J, Biddle G, Comstock T *et al*. NKF-DOQI clinical guidelines for treatment of anaemia in chronic renal failure. Am J Kidney Dis 1997; 30(suppl 4): S192-S240.

25. Working Party for European Best Practices Guidelines for management of anaemia in patients with chronic renal failure. European Best Practices Guidelines for the management of anaemia in patients with chronic renal failure. Nephrol Dial Transplant 1999;14(9) suppl 5:2071-A356.

26. NKF/KDOQI. KDOQI National kidney foundation KDOQI-clinical practice Guidelines and clinical practice recommendations for anaemia in chronic kidney disease. Am J kidney Dis 2006;47:S11-S145.

27. Eschbach JW, Abdulhadi MH, Browne JK *et al*. Recombinant human erythropoietin in anaemic patients with end stage renal disease. Ann Intern Med 1989;111:992-1000.

28. Lopez JM, Gomez R, Jofre I, and Valderrabano F. Use of epoetin in pre-dialysis patients; A review article. ERYTHROPOESIS :NEW DIMENSIONS IN THE TREATMENT OF ANAEMIA 2000; 10:3-109.

29. Festentien H, Sach JA, Rugum GD, Pari, AMI and Morehead JF. Influence of HLA matching and blood transfusions on outcome of 502 London Transplant Group and renal graft recipients. Lancet 1976;1:157-161.

30. Stewart JH. Platelet numbers and life span in acute and chronic renal failure. Thromb Diath Haemorrh 1967; 17:532

31. .Erslev AJ. Anaemia of renal failure. In: William JW, Beautler E, Erslev AJ, Rundles RW.(eds) HEMATOLOGY (2 nd. ed.)McGRAW HILL BOOK COMPANY.New York 1977: 288-295.

Errata

In Volume 3, No. 2 (December) 2008, pages 103-109 in the article "*A Two Year Review of Patients with Chronic Kidney Failure undergoing Heamodialysis in a New Dialysis Centre in Nigeria: Any New Lesson?"* The name of one of the authors was mistakenly written as Okunlola OO instead of **Okunola OO.**

The initials of one of the authors of the article *"Urinary Abnormalities, Blood Pressure and Anthropometric Profiles among Students in a Nigerian University"* (pages 21-29) in Volume 4 No. 1 (June 2009) was mistakenly written as PO Ogunro instead of **PS Ogunro.**

We regret the errors

Editor