KIDNEY KOLUMNS

Freely filtered from the ISN

Inside

Dear Readers,

We are pleased to bring to you the latest issue of Kidney Kolumns. This time we have focussed on the constantly evolving subject of Diabetic Kidney Disease (DKD). In this edition, we delve into the latest research, management strategies, and preventive measures for this growing health concern which every practising nephrologist faces on a day to day basis . As always, our goal is to provide valuable insights for clinicians, researchers, and students, keeping you informed on the advances in DKD.

On a somber note, we stand in complete solidarity with the young doctors of Kolkata who are bravely protesting the horrific incident at R.G. Kar Medical College and Hospital. The incident has shaken up not only the entire medical fraternity but also the nation.The entire Kidney Kolumns team echoes their call for justice, safety, and accountability within the healthcare system. We hope their voices are heard, and steps are taken to ensure that such tragedies never happen again. Our thoughts and support are with all those fighting for a safer and a conducive environment for healthcare professionals across the country.

Sincerely,

Editors - in-Chief

KIDNEY KOLUMNS

COVER IMAGE : "Revolution is the Celebration"

In the context of celebrating Durgapuja when the goddess, an embodiment of women power is not only worshipped as the holy mother and but also as a daughter returning home, the barbaric events against a daughter and the ensuing controversies force us to turn to the Goddess who will defend the defenceless, armed with the scales which represent justice, brooms to represent cleansing the corrupt system, brain representing the conscience & the stethoscope representing the Durgas amongst us, the doctors.

As people from all sects of society, weaponise the Divine Goddess with the quivers of justice...the longing Mother slays the demon but still remains helpless for her daughter's unserved justice. She reminds us, "Biplob-i utshob" (That for the oppressed, Revolt is the Festival)

Image Credits Roumyajit Hazra (UG, 3rd Prof Part 2), IPGMER & SSKM Hospital Kolkatta

Hon. Secretary's Message

Dear Friends,
Greetings from the Indian SN secretariat!
I hope that all of you are getting regular emails and other information regarding the activities of ISN through various channels, such as emails and the social media team. I congratulate our young team on the Indian SN newsletter, which provides updates about recent advances and important clinical issues in nephrology. In this issue of the newsletter, our team has started a separate column on statistics for the benefit of young faculty.
I will take this opportunity to highlight some of the important activities done in the last quarter and update you about plans by Indian SN:

1. **World Congress of Nephrology**- You might get messages from the secretariat regarding WCN 2025 to be held in India from 6th-9th February in Yashobhoomi Convention Centre Dwarka. I want to congratulate our members who actively submitted their abstracts for WCN, and the number of abstracts is approximately 50% (750/1500) of total abstracts in WCN25.

2. **Registration** is now open for WCN 2025, and I am delighted to share with you that a unique discount code for WCN '25 individual registrations from the Indian Society of Nephrology was made available. This discount gave a 35% reduction on the published fees. The Indian Society Members will pay $250 USD (plus GST)! Instead of published rates of USD 385 (plus GST) **Code: WCN35IND.** This discount was valid until 6 November. After this, standard, published rates will apply. Register online via the WCN'25 Registration portal. Link at https://www.theisn.org/wcn/registration/-. In case of questions, please get in touch with **registrationswcn@theisn.org**

3. **Membership of Indian SN-**I would request everyone again to become a member of Indian SN if you are not. Indian SN is actively collaborating with many important societies like ISN, ASN, ERA and TTS, and our members will get the benefits in meetings and memberships. The online membership of Indian SN is available at www.isn-india.org. If you are not getting messages from the secretariat despite being a member, kindly check your spam mail or mail me at **drshyambansal@isn-india.org**.

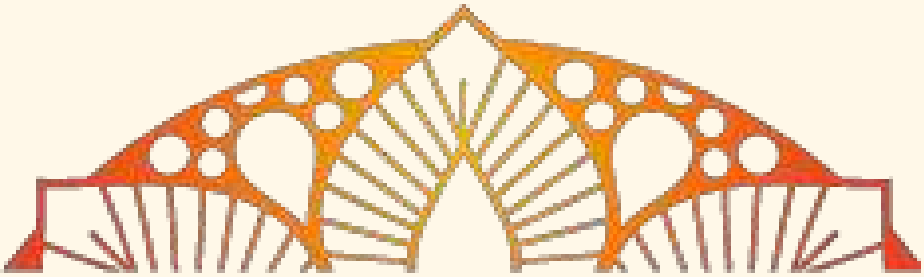
4. **The Educational activities**- Apart from regular journal clubs and social media activities of Indian SN, the society conducts regular webinars with international societies and experts. In the last quarter, we conducted two webinars- one in **collaboration with TTS on a very common problem of -post-transplant pyelonephritis** on 22nd August, which was attended by more than 500 delegates across the World. Subsequently, we conducted a webinar on -**atypical HUS in** collaboration with PCRRT Iconic, which was again attended by more than 300 delegates from all over the World. Additionally, we also conducted a Nephrology Update with Abbott Pharmaceuticals on 15th September, which was attended by > 400 nephrologists from India.

5. **Kidney Konversations**- This is the new initiative by the #SoMe team of Indian SN led by Dr Arvind Canchi, where a member of the team interviews pioneers and achievers related to Nephrology, whether they are doctors, social workers, NGOs, bureaucrats or politicians. This new initiative by our social media team is being greatly appreciated by everyone.

With that, I hope everyone had a Safe and Prosperous Deepawali. I also take this opportunity to wish everyone a very happy New Year - 2025.

Dr Shyam Bihari Bansal
Hon. Secretary Indian Society of Nephrology

WCN'25 is Coming to India in February and You Can Join Us for Less!



Get your special 35% discount

Join us at the World Congress of Nephrology 2025 (WCN'25) in New Delhi, India, from February 06-09, 2025.

Register for WCN'25 by November 6 to take advantage of special rates for the premier global kidney event of 2025. Delegates from the Indian Society of Nephrology and the South Asia Region are eligible for an **additional 35% discount on published fees**. **Early bird rates and this exclusive discount are available only until November 6.**

Get the 35% special discount for WCN'25

Don't miss this incredible chance to connect with global experts and immerse yourself in an unforgettable WCN experience!

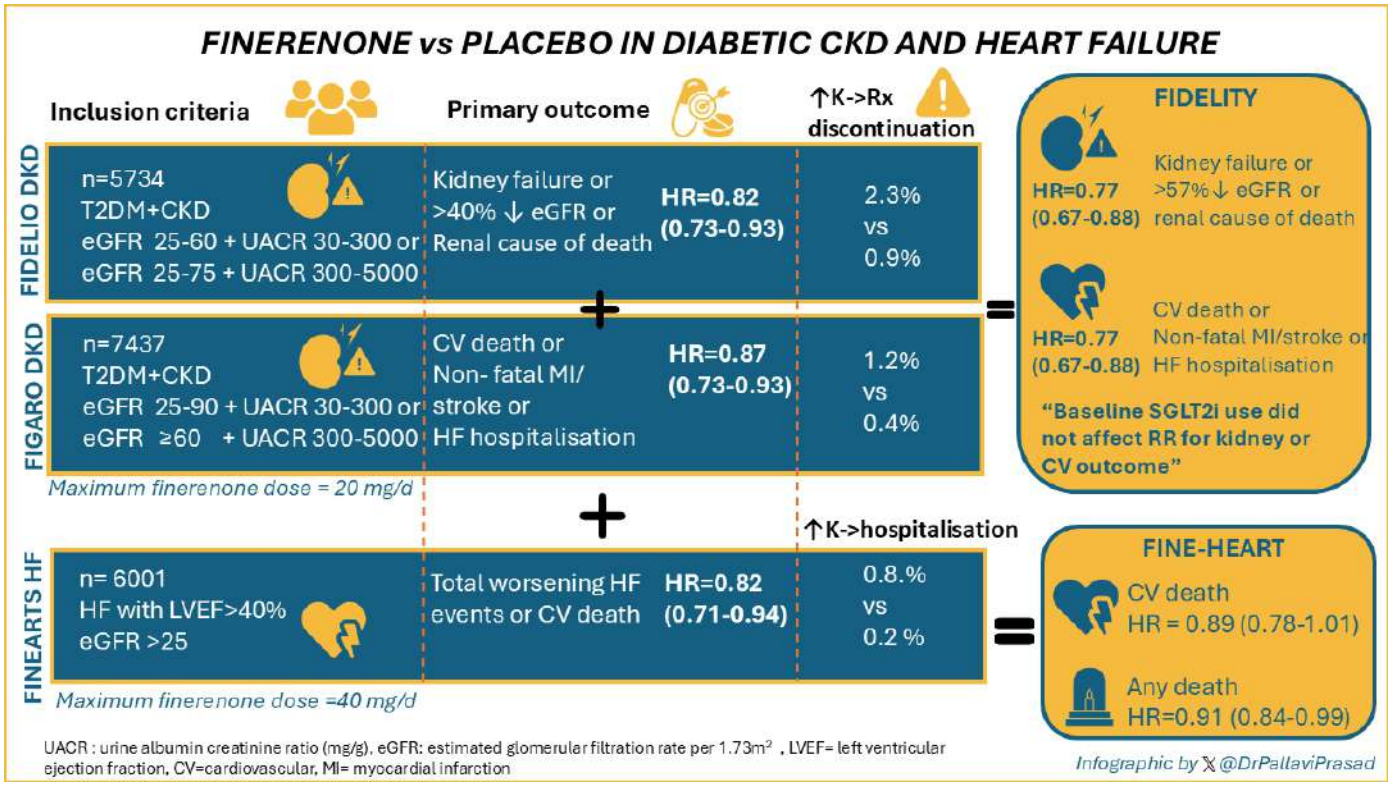
WE CAN'T WAIT TO SEE YOU!

Fine Tuning Outcomes-Unpacking insights from the FIDELITY analysis

A commentary on 'Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis' *and* 'Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes by Sodium-Glucose Cotransporter 2 Inhibitor Treatment: The FIDELITY Analysis.'

Diabetic nephropathy is the most common cause of end-stage renal disease and is significantly associated with cardiovascular (CV) deaths. Despite maximal therapy with Renin Angiotensin system inhibitors (RASi), some 'residual risk' remains, suggesting shifting from RASi to Renin angiotensin aldosterone system inhibition (RAASi). The steroidal MR antagonists (MRAs), spironolactone, and eplenerone are associated with significant steroidal side effects and hyperkalemia, necessitating novel non-steroidal MRAs. Finerenone has a higher affinity for the MR and no steroidal side effects, with a balanced tissue distribution between the heart and kidney (1:1 compared to 1:6 with spironolactone).

FIDELIO-DKD and FIGARO-DKD showed the beneficial effects of finerenone on renal and cardiovascular outcomes, respectively, in diabetic CKD. FIGARO-DKD provides data on early CKD, and FIDELIO-DKD provides data on the later stages of CKD. FIDELITY is the prespecified pooled analysis from both trials, making it one of the largest trials and providing data across the CKD spectrum. It included 13,026 patients with a mean follow-up of 3 years. Finerenone caused a significant reduction in composite CV outcome (CV death, non-fatal myocardial infarction or stroke, hospitalization for heart failure - HHF) and the composite kidney outcome (sustained ³ 57% decline in eGFR or renal death) by 14% and 23%, respectively. The overall safety profile was comparable to that of the placebo, but the development of hyperkalemia needing permanent drug discontinuation was higher with finerenone (1.7% vs 0.6%).



In FIDELITY, patients with symptomatic heart failure were excluded. Still, a considerable relative risk reduction (22%) was seen in the number of heart failure episodes, which was more significant in patients with LVH at baseline. Also, new-onset atrial fibrillation was reduced by 29% with finerenone (p=0.016). The efficacy and safety of finerenone in symptomatic heart failure with mildly reduced or preserved ejection fraction

(EF>40%) is shown in the FINEARTS-HF trial, which also showed a 25% reduction in the incidence of new-onset diabetes mellitus with finerenone.

Rossing et al. conducted a pre-specified pooled analysis on the combination of Finerenone with SGLT2i in FIDELITY. Of the 13,026 patients, 6.7% received SGLT2i at baseline, and 8.5% were initiated during the trial. The reduction in composite CV and kidney outcomes between SGLT2i users and non-users was 33% vs 13% (p=0.46) and 78% vs 20% (p=0.29), respectively. The benefits of finerenone were independent of SGLT2i use. The combination of SGLT2i and finerenone is being evaluated in the CONFIDENCE and FLAMINGO trials, while CONFIRMATION-HF evaluates their use in patients admitted with heart failure.

Finerenone use is expanding to non-diabetic CKD (FIND-CKD), IgA, primary membranous nephropathy, etc. The EFFEKTOR trial is evaluating its effect on proteinuria, cortical perfusion, and fibrosis in renal transplant recipients. The ReFineDR /DeFineDR studies hypothesized that finerenone reduced the progression of diabetic retinopathy.

These studies were the first to test whether the antiproteinuric effect of aldosterone blockade safely prevents kidney and CV disease progression. Also, the associated studies have shown the beneficial effects of finerenone in the spectrum of diabetes-related complications. This has led to the establishment of the four pillars of DN therapy: RASi, SGLT2i, GLP1 receptor agonists, and Finerenone.

Dr. Varun Kumar Bandi
Professor, Dept of Nephrology,
Dr. Pinnamaneni SIMS & RF, Andhra Pradesh

Dr. Harsha NNSS
Assistant Professor, Dept of General Medicine,
Dr. Pinnamaneni SIMS & RF, Andhra Pradesh

Renin-Angiotensin inhibitor use in advanced CKD : Learnings from STOP-ACEi TRIAL - Looming fear with the use of RASi in advanced renal failure

ACE inhibitors and ARBs have been the backbone of CKD management for the last 20 years, with several trials [RENAAL-NEJM 2001, IDNT-NEJM 2001] demonstrating that using RAS inhibitors slows CKD progression and reduces proteinuria. It is a common practice among nephrologists to discontinue RASi in advanced renal failure [CKD IV and V] as there is a fear of hyperkalemia and worsening renal function associated with the use of these drugs. In this competition-driven world, an unreported fear is the fear of losing patients on follow-up because these drugs are associated with some early decline in GFR, which is difficult for the patient to understand. Hence, prescription usage of these drugs is suboptimal, as reported in a study by Prasad et al., RAS blocker use was seen only in 47.9% of patients with mild to moderate renal failure.

The discontinuation of RASi in advanced CKD was supported by a single centre, open labelled, cohort study of 52 patients in the UK [Ahmed et al 2010]. In this study after discontinuation of RASi, authors demonstrated a delay in the onset of renal replacement therapy.

STOP-ACEi-The trial :

This trial was designed to assess if discontinuation of RAS inhibitors in patients with stage-4 and 5 CKD would slow down CKD progression. It was a multicentre, randomized, open-labelled trial conducted across 39 centres in the United Kingdom. The trial included adults (≥18 years) with stage 4 or 5 CKD who had not started dialysis or had not undergone kidney transplantation. All eligible patients were required to have had a decrease of more than 2 ml/min per 1.73 m2 of GFR during the previous 2 years and should have been receiving RASi for more than 6 months.

Both the groups were allowed to have any guideline-recommended antihypertensives added to their regimen to meet the study blood pressure target of < 140/85 mm Hg including Mineralocorticoid receptor antagonist (which also inhibits RAS). Results of the study showed, that of the 411 patients randomised into 2 groups, at 3 years the least mean squares GFR in the

continuation group was comparable to the discontinuation group (12.6 ± 0.7 vs 13.3±0.6) as was the composite outcome of ESRD, KRT or a decrease in eGFR of > 50%. There were numerically higher cardiovascular events in the discontinuation group but it was statistically insignificant.

Learning from the STOPACEi trial:

This trial did not find any benefit from stopping ACEi or ARB's, indeed the discontinuation arm had a 6% numerically higher risk of RRT and numerically higher CV events, which did not translate into statistical significance. These results are in contrast to the study by Ahmed et al in the UK cohort.

STOP ACEi trial was a well-designed RCT which had included CKD patients of all aetiologies; however, the open-label nature of the study and predominance of white participants make the results less generalisable. Also, the study did not provide the dosing information for RAS inhibitors and other antihypertensives that were used.

Renin-Angiotensin Inhibitors: Benefits beyond kidneys:

KDIGO-CKD guidelines-2024 recommend against the discontinuation of RASi with an eGFR of less than 30 ml per minute. The cardioprotective benefits of RAS inhibitors in advanced CKD have been demonstrated in large observational studies (Fu et al-JASN 2020, Qiao et al-JAMA Intern Med 2020). Fu et al had reported a notably higher risk of mortality and MACE after discontinuation of RAS inhibitors. Similar findings were reported Qiao et al in patients with advanced renal failure. These drugs have a proven benefit in patients with heart failure with reduced ejection fraction which is frequently seen in patients with advanced renal failure. Hence discontinuation would not be recommended in this subset, provided monitoring of the eGFR and serum potassium at regular intervals.

Dr. Mudit Khurana
M.D. (Medicine), D.M. (Nephrology)
Associate professor, Nephrology
Sarojini Naidu Medical College,
Agra Uttar Pradesh

IgA nephropathy

slowly progressive; 25%-30% pts become ESKD in 20-25 years;2nd-3rd decade.

A. Etio-pathogenesis

4 HIT PROCESS;

1.Increased circulating levels of Gd-IgA1.
2.Production of Anti-IgA1 abs(IgA/IgG).
3a. Immune complex form in the circulation.
3b. Immune complex form in situ.
4.Immune complex form in the mesangium cause local immune activation & injury.

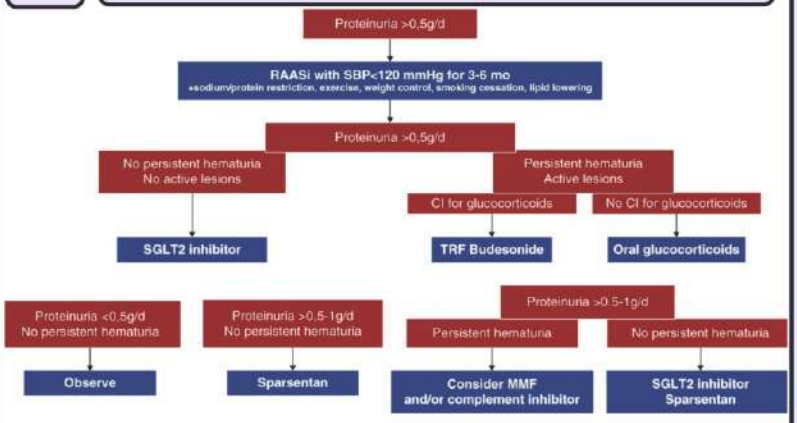
B. Clinical features

- Episodic macroscopic hematuria(40%-50%)(>20-<40yrs).
- Asymptomatic microscopic hematuria(30%-40%) & proteinuria(<2gm/day).
- Nephrotic syndrome(<5%)(MesPGN).
- AKI(<5%)(>67YRS)(Cresentic IgAN)

C. Diagnosis

- >=1 episode of gross hematuria with/without URTI.
- persistent microscopic hematuria with? without proteinuria.
- slowly progressive kidney function impairment.

D. How to approach IgAN patient(1)



Proposal for an individualized treatment approach in patients with IgA nephropathy. CI, contraindication; MMF, mycophenolate mofetil; TRF, targeted-release formulation; SGLT2, sodium–glucose transporter 2.

ACEi/ARB	Initial dose(mg/day)	Max dose(mg/day)
• Azilsartan	20	80
• Candesartan	16	32
• Irbesartan	150	300
• Losartan	50	100
• Olmesartan	20	40
• Telmisartan	40	80
• Valsartan	80-160	320
Non DHP CCB		
• Diltiazem	180-240	480
• Verapamil	120-360	480
ETAR-B/ARB		
• Sparsentan	200	400
SGLT2 inhibitor		
• Dapagliflozin	5	10
TRF budesonide	8	16

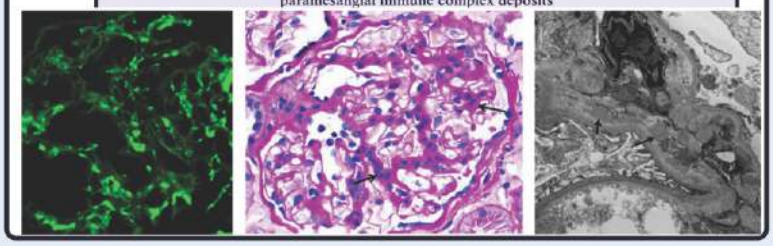
Lifestyle Interventions:
Healthy diet, Na+ <2gm/day,Regular exercise,Weight control,Smoking cessation,Address lipids.

Prognostic markers at presentation in IgAN

CLINICAL:
Poor prognosis-
-HTN,renal impairment, severity of proteinuria, smoking,hyperuricemia,gross obesity,increasing age.
Good prognosis-
Recurrent macroscopic hematuria
No impact on prognosis-
Gender,serum IgA level
HISTOPATHOLOGIC:
Poor prognosis- MEST-C,capillary loop IgA deposits
No impact on prognosis-Intensity of IgA deposits

E.

Immunofluorescence staining for IgA in a kidney biopsy specimen from a patient with IgAN showing mesangial staining. (B) Periodic acid–Schiff staining of a kidney biopsy specimen from a patient with IgAN. Arrows indicate mesangial expansion and hypercellularity. (C) Electron micrograph of kidney biopsy.electron-dense material representative of mesangial and paramesangial immune complex deposits



F. Associated diseases

- Rheumatic/autoimmune;
- A.spondylitis,R.arthritis,Reiter synd.
- GI disease-Celiac disease
- Hepatic- ALD,Nonalcoholic cirrhosis
- Lung disease-sarcoid
- skin-Dermatitis herpetiformis
- Infection-HIV,Hep.B

A 6–9-month course of oral glucocorticoids as immunosuppressive therapy. The moderate dose glucocorticoid regimen used in TESTING (0.4 mg/kg per day, maximum 32 mg/d, weaning by 4 mg/d per month).

(1)Proposal for an individualized treatment approach in patients with IgA nephropathy
El Karoui, Khalil1; Fervenza, Fernando C.2; De Vriese, An S.3,4. Treatment of IgA Nephropathy: A Rapidly Evolving Field. Journal of the American Society of Nephrology 35(1):p 103-116, January 2024. | DOI: 10.1681/ASN.0000000000000242

Dr. Tanmay Vagh
3rd year, DM Nephrology from MGM Jaipur

Semaglutide and Tirzepatide: The next frontier in CKD and obesity? Insights from FLOW and SURMOUNT

As obesity rates rise around the world, the spotlight has been placed on the critical link between obesity and chronic kidney disease. Epidemiological studies have shown an independent association between obesity and chronic kidney disease (CKD). An increasing BMI is associated with the development of proteinuria, a lower estimated glomerular filtration rate (eGFR), and a higher incidence of end-stage renal disease (ESRD).

Renal disease due to obesity has been defined as a distinct entity called obesity-related glomerulopathy (ORG). ORG is characterised by proteinuria, commonly in subnephrotic range, and progressive decline in renal function. Glomerulomegaly and focal segmental glomerulosclerosis (FSGS), usually the perihilar subtype, are noted to be pathological hallmarks of ORG. Multiple mechanisms have been postulated as the cause for renal lipotoxicity in ORG. Lipid accumulation in visceral organs can cause release of adipokines which exert pro-inflammatory and pro-fibrotic effects. Hemodynamic alterations causing glomerular hyperfiltration and Renin-Angiotensin-Aldosterone system (RAAS) activation lead to podocyte injury which is the driving force for ORG progression. Insulin resistance and hyperinsulinemia, reduced nephron mass and genetic factors may also play a role. Renin–angiotensin system (RAS) inhibitors, sodium–glucose cotransporter 2 (SGLT2) inhibitors, and finerenone have been shown to have nephroprotective and antiproteinuric effects as well as reduce the risk of adverse cardiovascular outcomes in patients with obesity.

GLP-1 receptor agonists are incretin based therapies which have been shown to promote natriuresis by inhibiting proximal tubular Na/H exchanger 3, reduce the activation of RAAS and also have direct anti-inflammatory and anti-fibrotic effects on the kidney. GLP-1 RAs are also associated with relevant and sustained weight loss, both in subjects with (REWIND) and without T2DM (STEP 1), thereby making these drugs very attractive for the treatment of ORG. SUSTAIN-6 study showed the reduction of cardiovascular (CV) outcomes in diabetic patients with high CV risk. Meta-analyses have shown benefit in secondary renal outcomes particularly a reduced risk of persistent macroalbuminuria.

The FLOW (Evaluate Renal Function with Semaglutide Once Weekly) trial was a dedicated study done to determine the effect of semaglutide on renal outcomes. It was a double-blind, randomized, placebo-controlled trial conducted across 28 countries and included 6.5% of participants at baseline from India.

Adults with type 2 diabetes (glycated hemoglobin level, ≤10%) with high-risk chronic kidney disease on RAS inhibitors were included. High risk CKD was defined as estimated glomerular filtration rate (eGFR) of ≥50 to ≤75 ml/min/1.73 m2 (calculated by CKD-EPI 2009 formula) and urinary albumin-to-creatinine ratio (UACR) of >300mg/g and <5000mg/g or eGFR ≥25 and <50 ml/min/1.73 m2 with UACR >100mg/g and <5000mg/g. Patients with NYHA class IV heart failure and uncontrolled proliferative diabetic retinopathy were excluded. Eligible participants were randomly assigned in a 1:1 ratio to receive semaglutide or matching placebo. The use of SGLT2 inhibitors and mineralocorticoid-receptor antagonists (MRAs) was permitted.

An 8-week dose-escalation regimen for semaglutide was used, with dose escalation (as long as unacceptable side effects did not occur) from 0.25 mg per week as subcutaneous injection for 4 weeks to 0.5 mg per week for another 4 weeks, followed by a maintenance dose of 1.0 mg per week throughout the remainder of the treatment period.

The primary outcome was major kidney disease events, a composite of onset of kidney failure (initiation of long-term dialysis, kidney transplantation,

or a reduction in the eGFR to <15 ml/min/1.73 m2 sustained for ≥28 days), a sustained (for ≥28 days) ≥50% reduction in eGFR from baseline, or death from kidney-related or cardiovascular causes. Total eGFR slope and major cardiovascular events (a composite of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes) and death from any cause were the secondary outcomes studied.

From 5581 patients screened, 3533 patients underwent randomization. Mean age was 66 years in both groups. Mean eGFR was 46.9ml/min/1.73m2 in the semaglutide arm compared to 47.1 in the placebo arm. More than two-thirds of the study group in both arms were in the A3 category of albuminuria. >90% of patients were on ACEI or ARB. Over a median follow-up of 3.4 years, there was a 24% lower relative risk of the primary-outcome events in the semaglutide group compared to the placebo group (331 events vs 410 events; HR = 0.76, CI = 0.66-0.88, p = 0.0003)

Benefits were observed for the three confirmatory secondary outcomes. The annual decline of eGFR was slower in the semaglutide group than in the placebo group (−2.19 vs. −3.36 m/min/1.73 m2/year, p<0.0001). The risk of MACE and death from any cause were also 18% and 20% lower respectively in the semaglutide group in comparison to the placebo group.

The other notable findings were improvement in urinary albumin-to-creatinine ratio, glycated hemoglobin level and systolic blood pressure in semaglutide arm. Eye disorders reported as serious adverse events were more common among participants who received semaglutide than among those who received placebo (3% vs 1.7%), whereas the numbers of diabetic retinopathy events were similar in the two groups.

Hence the trial concluded that in patients with type 2 diabetes and high risk CKD, semaglutide significantly reduced the risk of major kidney disease events by 24%. Semaglutide also reduced the risk of major cardiovascular events and death from any cause while slowing the annual loss of kidney function by a mean of 1.16 m/min/1.73 m2. Average weight loss in the semaglutide arm was 4.1kg. The cardiovascular and survival benefits of semaglutide in such patients are particularly important, since they are among the populations at highest risk for cardiovascular disease and death.

In addition to Semaglutide, twincretins are therapeutic peptides that mimic the effects of gut hormones secreted after a meal. They can help control blood glucose levels and reduce weight. Tirzepatide, a dual agonist of GLP1 and glucose-dependent insulinotropic polypeptide (GIP) and GLP-1, was studied in the SURMOUNT trials.

SURMOUNT-1 study was an international, phase 3, double-blind, randomized, placebo-controlled trial which examined the efficacy and safety of tirzepatide in adults with obesity or overweight who did not have diabetes. 2539 adults with a body-mass index of ≥30 or ≥27 with at least one weight-related complication, were assigned to once-weekly subcutaneous tirzepatide at one of three doses (5, 10 and 15mg) or placebo, in addition to lifestyle intervention. The co-primary endpoints, both the percentage change in weight and the percentage of participants with at least 5% weight reduction were significantly greater with all three doses of tirzepatide than with placebo. In the SURMOUNT-3 trial, tirzepatide demonstrated clinically meaningful additional body weight reductions in adults with overweight or obesity following initial weight loss with intensive lifestyle intervention.

In SURMOUNT-4, after achieving clinically meaningful weight reduction during a 36-week tirzepatide lead-in treatment period, adults with obesity or overweight who continued treatment with maximum tolerated dose tirzepatide for an additional 52 weeks demonstrated superior weight maintenance and continued weight reduction compared to those who switched to placebo. It showed beneficial effects on glycemic and blood pressure control. Renal outcomes with tirzepatide have not been studied in a dedicated trial. Post-hoc analysis of the SURPASS-4 trial demonstrated

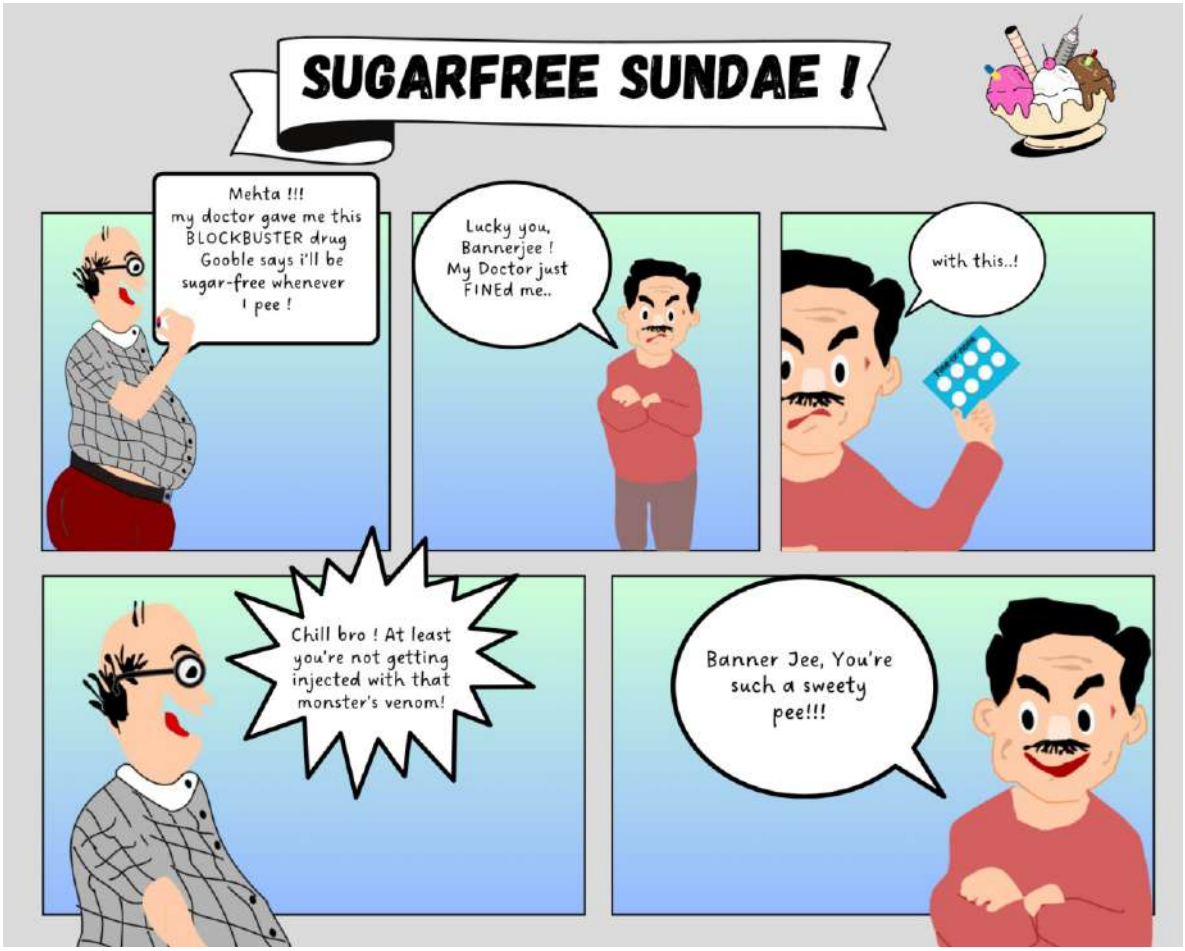
lowering of UACR and slowing of rate of eGFR decline in the tirzepatide arm.

The results of the FLOW study have established GLP1RAs among the pillars of management of diabetic patients with CKD to reduce incidence of renal adverse outcomes. As the diabesity epidemic rages on, the combination of body weight and blood pressure reduction with various pleiotropic effects of the incretin based medications and twincretins would lead to greater use of these drugs to reduce progression of kidney disease in obese patients. Further kidney-focussed trials on renal safety and efficacy of tirzepatide are required.

Dr. Padmini S
Asst. Professor, Dept of Nephrology,
MGM medical college and superspecialty hospitals, Indore

Dr. Sandhya Suresh
Asst. Professor, SRIHER, Chennai

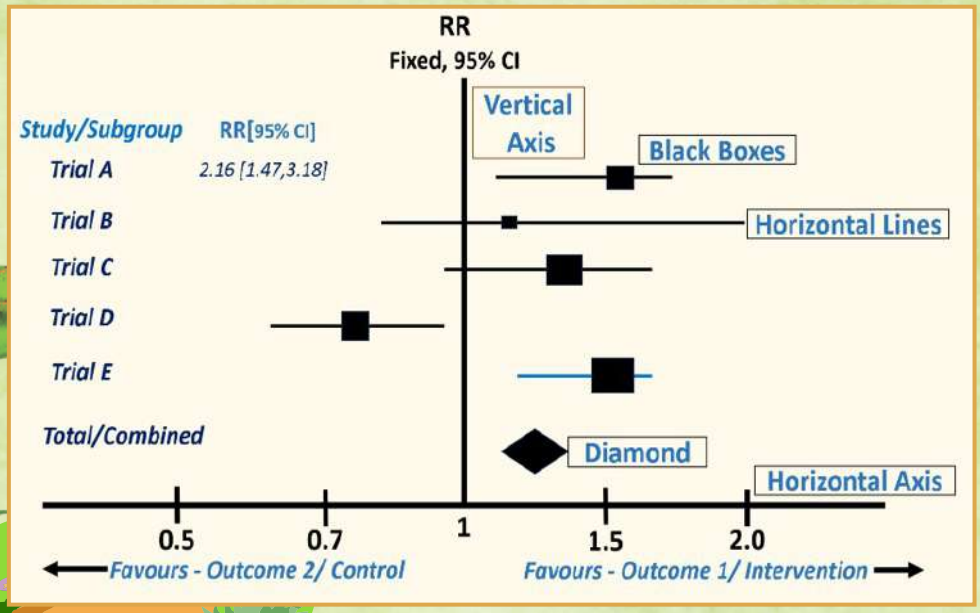
Stay Tooned !

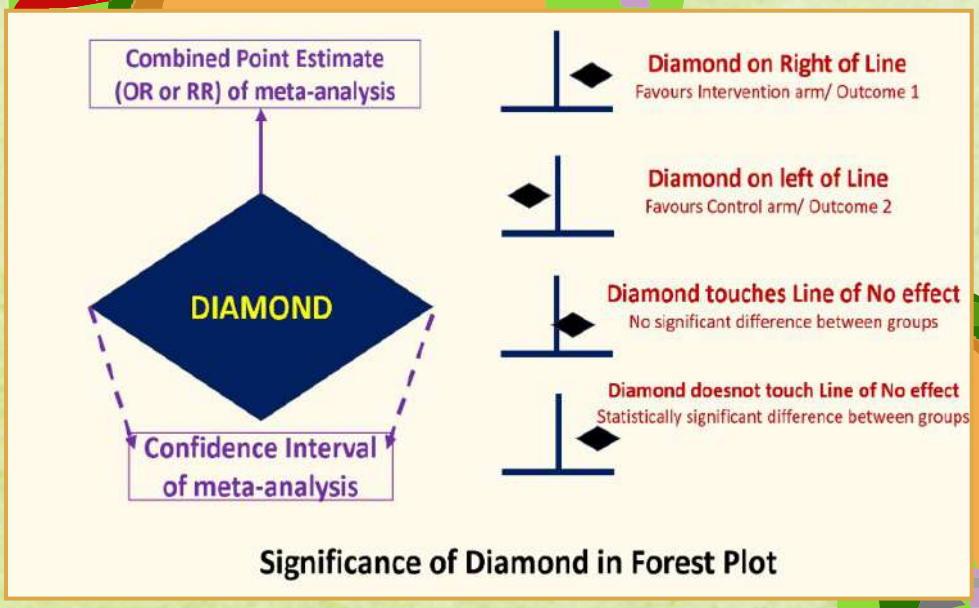


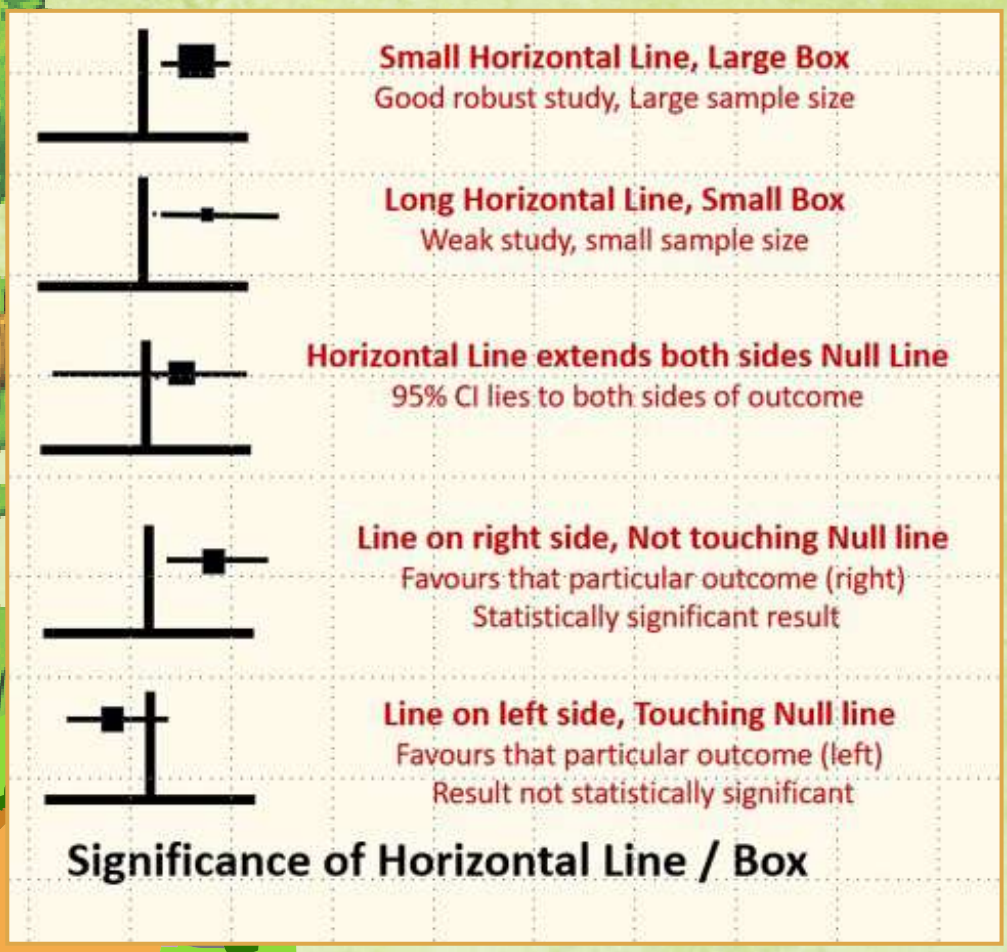
by Dr Anand Chellappan

The views and opinions expressed in this cartoon are those of the creator and not that of his/her employer. The content is fictional and any resemblance to actual persons or events is purely coincidental.

Fathoming the FOREST PLOT with Ambily & Vineet...







Character	Interpretation
Vertical Axis	Line of Null effect (RR or OR = 1) (Relative statistic: 1, Absolute statistic :0)
Horizontal Axis	Statistic of interest [Relative (OR, RR) or absolute (eg. absolute risk reduction, standardized mean difference)
Each Horizontal Line	Individual study included in meta-analysis
Length horizontal line	95% confidence intervals (CI) of the point estimate
Black box	Point estimates (Result of study)
Size - Black Squares	Weight of each trial in meta-analysis
Diamond	Overall treatment effect
Diamond - Centre/Tips	Combined treatment effect/95% CI

KNOW YOUR SEMAGLUTIDE !!!!!

Question 1: What is the mechanism of action of semaglutide ?
A) Insulin secretion stimulation
B) Glucagon-like peptide-1 (GLP-1) receptor agonism
C) Dipeptidyl peptidase-4 (DPP-4) inhibition
D) Sodium-glucose cotransporter 2 (SGLT2) inhibition

Question 2: What is the primary mechanism by which semaglutide improves glycemic control?
A) Increasing insulin secretion
B) Enhancing glucagon suppression
C) Delaying gastric emptying
D) All of the above

Question 3: What is a potential benefit of semaglutide beyond glycemic control ?
A) Weight loss
B) Blood pressure reduction
C) Cardiovascular risk reduction
D) All of the above

Question 4: What is the incidence of hypoglycemia with semaglutide in clinical trials ?
A) <1%
B) 1-5%
C) 5-10%
D) 10-20%

Question 5 : What is a common side effect of semaglutide ?
A) Hypoglycemia
B) Nausea and vomiting
C) Increased urination
D) Headaches

Question 6 : Which of the following is a contraindication for semaglutide ?
A) Type 2 diabetes
B) Pancreatitis
C) Hypertension
D) Hyperlipidemia

Question 7 : Semaglutide has been linked to an increased risk of :
A) Gallbladder disease
B) Cholecystitis
C) Medullary thyroid cancer
D) All of the above

Question 8 : What is the primary site of action for semaglutide's weight loss effects ?
A) Brain
B) Pancreas
C) Liver
D) Gut

Question 9 : Semaglutide's weight-reducing effects are primarily mediated through :
A) Decreased appetite
B) Increased satiety
C) Enhanced fat oxidation
D) Improved insulin sensitivity

Question 10 : What is the average weight loss observed in clinical trials with semaglutide ?
A) 2-5% body weight
B) 5-10% body weight
C) 10-15% body weight
D) 15-20% body weight

Question 11 : What is the recommended initial dose of oral semaglutide ?
A) 3 mg once daily
B) 7 mg once daily
C) 14 mg once daily
D) 28 mg once daily

Question 12 : What is the recommended initial dose of semaglutide for type 2 diabetes ?
A) 0.5 mg once weekly
B) 1.0 mg once weekly
C) 2.5 mg once daily
D) 5.0 mg once weekly

Question 13 : Question 19 : What was the percentage reduction in urinary albumin-to-creatinine ratio (UACR) with semaglutide (in the SUSTAIN-6 trial)

A) 10-20%
B) 20-30%
C) 30-40%
D) 40-50%

Question 14 : What is the potential mechanism how semaglutide exerts renoprotective effects ?

A) Reduced inflammation
B) Improved insulin sensitivity
C) Decreased glomerular pressure
D) All of the above

Question 15 : What is the dose for semaglutide use in patients with eGFR<30 or or dialysis ?

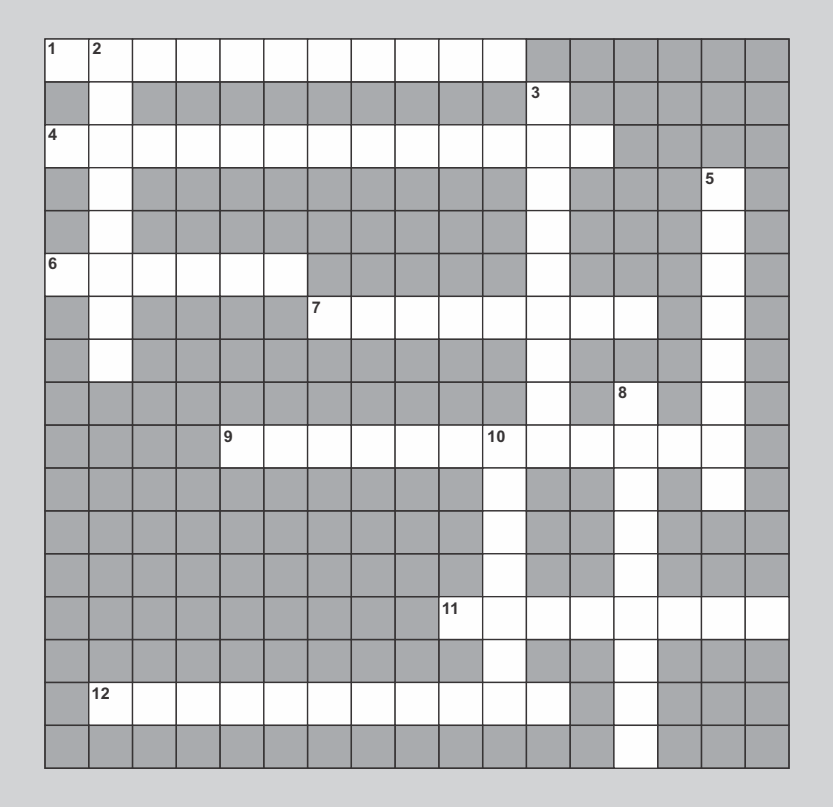
A) Use with caution, monitor renal function
B) Reduce dose by 50%
C) Reduce dose by 25%
D) Not recommended

R K Yadav
Vineet Behera

ANSWERS : 1-B, 2-D, 3-D,4-B, 5-B, 6-B, 7-D, 8-A, 9-A, 10-B, 11-B, 12-A, 13-C, 14-D, 15- D

Diabetic Dilemmas

By Dr Ambily K, Dr Sandhya Suresh, Dr M Subashri & Dr Pallavi Prasad



Please follow the link to access the crossword

Across

1. An observational study describing benefits of dapagliflozin treatment for CKD without Diabetes across different albuminuria categories
4. A novel dual sodium-glucose cotransporter-1 and -2 (SGLT-1/2) inhibitor approved by FDA in 2023 in T2DM patients with CKD and those with heart failure, irrespective of diabetic status or ejection fraction.
6. Meta-analysis of efficacy of Flozins with or without GLP-1 receptor agonists
7. This classification published in 1983 described 5 stages of diabetic nephropathy with emphasis on the incipient stage
9. This tongue-twister GLP-1RA was studied in the ELIXA trial and also as a therapeutic agent in Parkinson's disease in the LIXIPARK study
11. A post-hoc analysis of that trial showed that anti EPOR antibodies in patients with type 2 diabetes and chronic kidney disease were associated with adverse kidney and cardiovascular outcomes and mortality.
12. This drug improves eGFR in DKD by activating the keap1/Nrf2 system that plays a role in defense response against oxidative stress.

Down

2. Renal gluconeogenesis occurs in this part of the tubule
3. The first Pancreas transplant was done in 1966 by Dr William Kelly and Richard Lillehei in this University
5. This landmark trial was one of the studies on dual ARB/ACEI blockade and had 3 arms including Telmisartan, Ramipril and the combination
8. Pooled analysis of finerenone in 3 prospective RCTs of patients with cardio-kidney-metabolic syndrome.
10. Angiotensin-II causes tyrosine dephosphorylation of this podocyte protein leading to its interaction with β-arrestin and endocytosis thus causing its downregulation

Answers to the Crossword are available on page 24

Dialysis versus conservative care in elderly patients with end stage kidney disease : The jury is still out !

Comprehensive conservative care (CCC) focuses on providing kidney supportive care (KSC) without including renal replacement therapies. Kidney supportive care (KSC) includes approaches to improve the quality of life of patients with kidney disease, with early identification and optimal management of their physical, psychosocial and/ or spiritual problems. CCC may be appropriate for elderly patients who have a limited life expectancy or significant comorbidities. The estimation of survival rates for CCC is complex because, unlike dialysis, there is no distinct initiation point. Of the several studies examining the mortality rates of elderly patients with end stage kidney disease (ESKD) who undergo dialysis or choose CCC, most of them compare HD with PD, or either with CCC, rather than all the three together. Additionally, research investigating the mortality in patients who receive CCC is vulnerable to lead-time bias, while analyses focusing on a specific point of GFR in dialysis patients may be susceptible to immortal time bias.

This article reviews a recent study from Thailand that sought to compare the mortality rates among elderly ESKD patients who underwent HD, PD, or comprehensive conservative management using a propensity score analysis. In this retrospective cohort from Chiang Mai, Thailand, eligible ESKD patients aged ≥70 years who opted for HD, PD or CCC between January 2008 and December 2018 were included. Those opting for CCC were provided with medical treatment and counselling, including advance care planning and were monitored by the treating nephrologist, nurses, and dietitians at regular intervals. The outcome of interest in this study was the time to all-cause mortality which was determined through medical records and national vital statistics. Patients were followed from the entry date until they died, changed treatment method, or the study terminated. Entry date was considered as the date of dialysis initiation for those who chose either HD or PD, and as the first date with estimated GFR (eGFR) <15mL/min/1.73m^2 for those who chose CCC.

The final cohort comprised 719 ESKD patients of whom 317 (44.0%) chose HD, 352 (49.0%) chose PD, and 50 (7.0%) chose CCC. There were significant baseline differences between the three groups in terms of age, body-mass index (BMI), Charlson Comorbidity Index (CCI) score, eGFR and serum albumin. The authors then performed propensity score weighting with the inverse probability treatment weighting (IPTW) technique using three parameters: age, CCI score, and eGFR. The IPTW cohort included 535 patients [233 (43.6%) in the HD group, 280 (52.3%) in the PD group and 22 (4.1%) in the CCC group] and was still not well-balanced, with a standardized mean difference of >0.1 for age and CCI across the three groups. A flexible parametric survival analysis was performed to estimate hazard ratios, due to violation of the proportional hazards assumption. The following four models were evaluated: Model 1: univariable analysis, Model 2: Model 1 + adjustment with age, sex, and Charlson comorbidity index score, Model 3: Model 2 + adjustment with dialysis center, hemoglobin levels, and body mass index, Model 4: Model 3 + adjustment with serum albumin levels.

Over a median follow-up period of 22.1 months, 432 (60.1%) patients died. The authors found that CCC in elderly ESKD patients resulted in lower survival compared to HD or PD, both before and after IPTW in all four models. The authors also found that the survival advantage persisted even in patients over the age of 80 years. Although PD appeared to have a greater mortality rate than HD on univariable analysis, this difference was no longer evident in the fully adjusted model (Model 4). These results were in line with another retrospective study, which found that dialysis treatment was associated with longer survival in patients over 65 years of age. However, this study contradicts other previous studies (again retrospective) in that it shows survival advantage of dialysis over CCC even in patients aged > 80 years. A 2022 systematic review of 22 studies (of which 10 were prospective) had similar results with lower mortality for patients choosing dialysis compared with CCC (HR 0.47; 95% confidence interval: 0.39–0.57), even in those with older age and severe comorbidities. This systematic review showed considerable heterogeneity and a high risk of selection bias and residual confounding in most of the included studies.

In addition to the retrospective nature of the study, other limitations to the present analysis include residual confounding – sicker patients being chosen for CCC leading to excess mortality in the first month, non-inclusion of other confounders such as functional status,

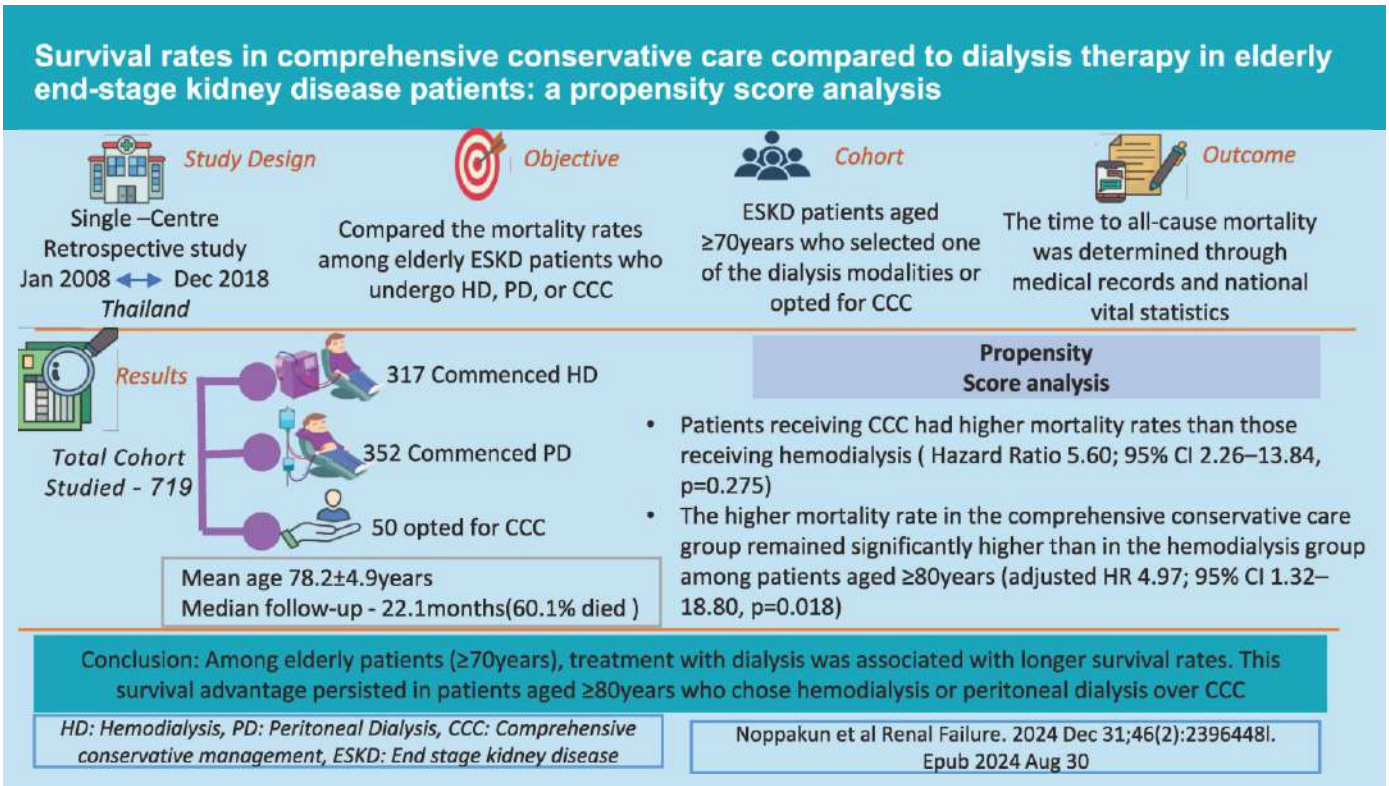
economic status and extent of family and caregiver support. The sample size was rather small, especially in the CCC group (only 22 patients in the IPTW group), > 1/3rd study population had missing data for variables such as BMI, hemoglobin and serum albumin, there was disproportionately higher attrition in the CCC group, and the inability to achieve matching despite the propensity scoring. Finally, the study population belonged to one ethnicity, which could limit the generalizability of the findings.

It is pertinent to stress that the decision to initiate dialysis in elderly ESKD patients should not be based solely on survival advantages. Factors such as frailty, quality of life, cost of dialysis, treatment burden and patient/ family beliefs and preferences are very important considerations when it comes to KSC and CCC. Also, we have evidence that initiating dialysis in elderly patients causes a significant and sustained deterioration in the functional capacities.

(https://pubmed.ncbi.nlm.nih.gov/19828531/) Unfortunately, the present study did not consider quality of life (and/or other patient/family reported outcome measures) which is the primary focus of CCC, rather than merely prolonging survival.

To conclude, with the available literature including the present study, the jury is still out regarding preferring dialysis over conservative care in the elderly. While this study guns for the survival advantages of dialysis in this population, conservative care should continue to be discussed by nephrology stakeholders till future prospective studies can bring home conclusive evidence in either direction.

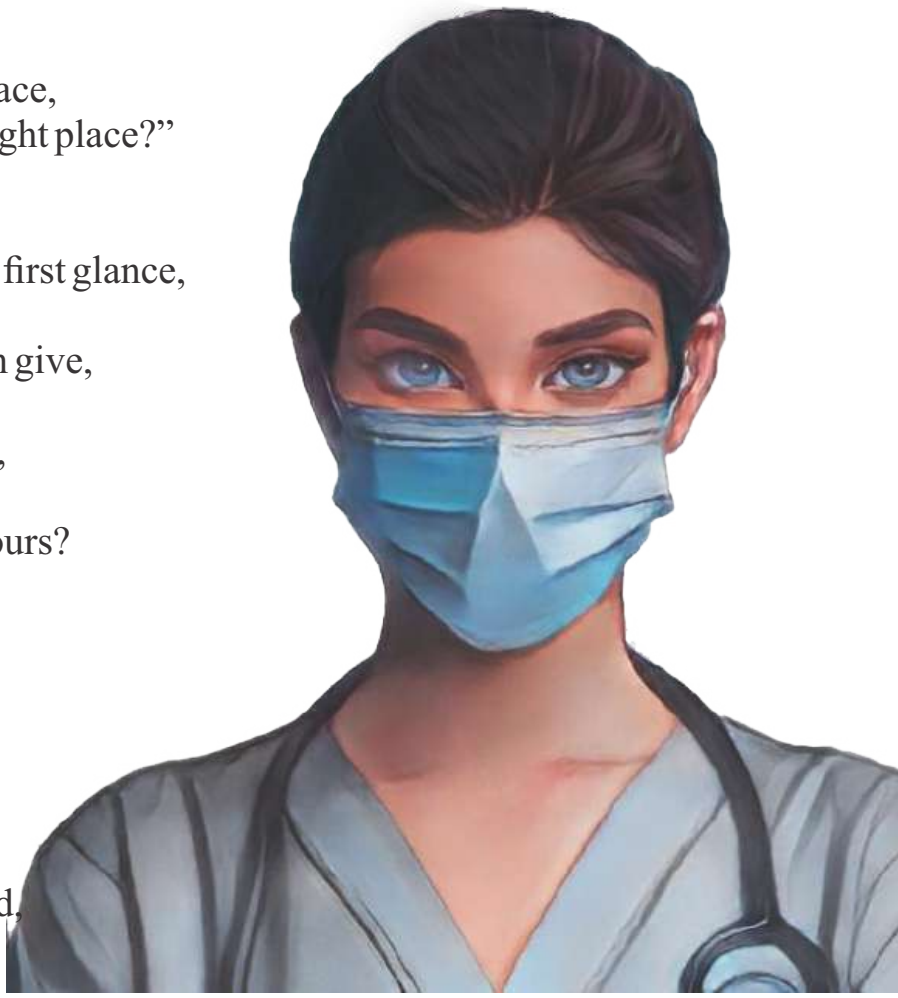
Shilna Muttickal Swaminathan,
Indu Ramachandra Rao,
Shankar Prasad Nagaraju
Department of Nephrology,
Kasturba Medical College,
Manipal, MAHE, Manipal, India



Guarding Lives, Risking Their Own : Female Doctors in Unsafe Spaces

- Dr. Urvashi Khan

In scrubs of blue, we walk these halls,
But beneath it all, our spirit calls.
Not for the medicine we've learned to give,
But for the right to truly live.
We wear this coat, we hold this chart,
Yet something tears inside our hearts.
They see the doctor, but still the doubt,
In whispered words, they shut us out.
We've studied hard, we've earned our place,
But still, we stand in this endless race.
For every step, we are questioned more,
While others pass with open doors.
Our hands are steady, our minds are clear,
But they reduce us to the roles we fear.
Not a healer, not a guide,
But someone they cast easily aside.
We've bled and worked to reach this space,
Yet still we are asked, "Are you in the right place?"
Is it because we are polite or small?
Is that why they built these walls?
We are more than the gender they see at first glance,
More than a woman seeking a chance.
We are a doctor, resident with all we can give,
But in this struggle, we barely live.
The burden's heavy, the nights are long,
We wonder when we'll truly belong.
We mend their wounds, but who heals ours?
In this world, where is the line to ours?
Yet still we stand, still we rise,
With every failure, with every sigh.
For one day, we hope they'll see,
A doctor's a doctor, no matter her plea.
But today, our heart is sore,
As we fight this battle, just like before.
To be seen, to be heard, to be understood,
In this world where equality should.



Residents' Corner

The Kolkata horror and its aftermath : an on-ground report from resident nephrologists

On 9th August 2024, in a government hospital and medical college of Kolkata, a heinous crime took place that shook not only the medical fraternity but the whole nation. The brutal incident of physical assault and murder of a young lady doctor rekindled the issue of workplace safety and security of doctors, especially of resident doctors. Immediately after news of the murder broke, the whole fraternity erupted in protest, one that is still going on in Kolkata and other medical colleges of West Bengal. The residents who are the driving force behind the protest, have mainly demanded justice for their colleague who lost her life, and steps to prevent similar offences in the future, including the institution of stringent security measures and strong punitive action against those who brazenly commit such crimes.

A narrative is doing the rounds, that the hospitals have stopped all services due to the strike by resident doctors. However, as we report from the ground that this is not so. The senior doctors and medical officers are working beyond their usual working hours and taking care of all the out and in-patient department case loads, while aligning with residents in their quest for justice and security. Though patient footfall to hospitals initially dipped, these are returning to normal as well.

Like all other departments, the nephrology residents here are also an integral part of the protests. While the number of interventions such as biopsies and catheter placements seem to have decreased due to the call to strike, hemodialysis, peritoneal dialysis and emergency procedures are being carried out seamlessly with the help of technologists and nursing staff guided by the senior faculties of the hospitals and medical colleges.

The residents are unified in their decision that unless the proper justice is served and the security of the hospitals is taken care of, there is no point in and no question of getting back to work. Lastly, we are hopeful that these demands are acceded to, that the medical fraternity and the civilized society achieve normalcy and we never have to wake up to such horrific news again.

Gopambuj Singh Rathod
Pallavi Mahato
Bibek Maulik
Senior Residents, Department of Nephrology, IPGMER and SSKM Hospital, Kolkata

Doctors image created with the assistance of AI from Craiyon.com

Eradicating "Bhaya" from the dark alleys of our hospitals

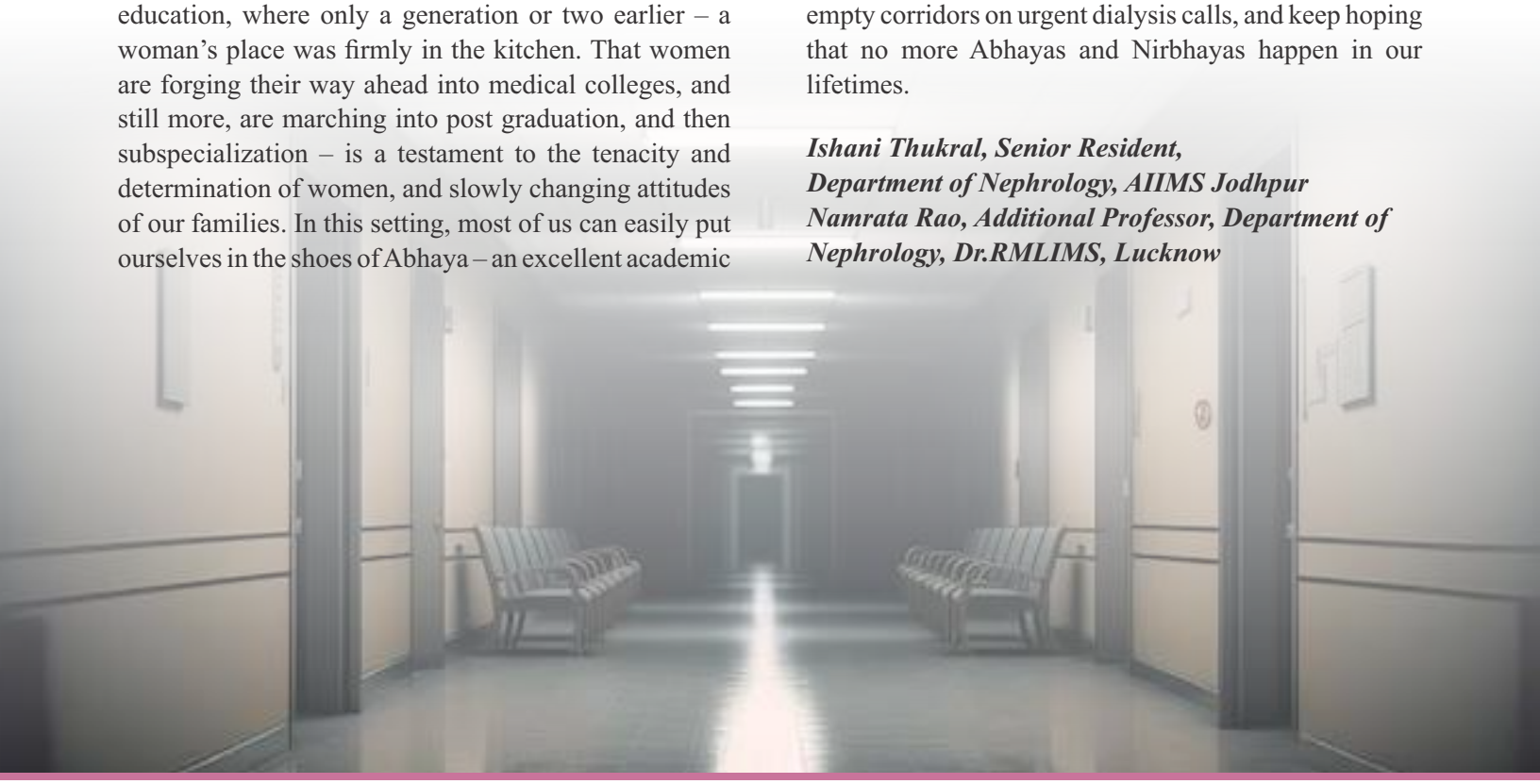
The brutal and terrifying incident that snuffed the life of a lady resident doctor in Kolkata on 9th August 2024 has shaken us to the core. In fact, this literally took us back to the infamous Nirbhaya case of Delhi in December 2012, where fear and paranoia gripped every girl and her family, whenever girls had to venture "out" in the dark. This paranoia still reappears as flashbacks occasionally, when we pass warily through empty corridors.

But this time, it has hit us much closer, much like a sucker-punch when least expected. Ensuring a safe environment for healthcare workers is the most important prerogative – so they can dedicate themselves to the art and practice of healing, and not have to keep looking over their shoulders. All the resident and faculty associations, in addition to all the representative societies, including our Indian Society of Nephrology, concur that healthcare worker safety, irrespective of their gender, hierarchical order and position within the healthcare system – remains the paramount goal of the protests and the demands to the Government.

Beyond the issue of safety, we wish to highlight the special struggles of being a woman, and pursuing post graduation in India. Women still struggle to convince their families to "allow" them to pursue higher education, where only a generation or two earlier – a woman's place was firmly in the kitchen. That women are forging their way ahead into medical colleges, and still more, are marching into post graduation, and then subspecialization – is a testament to the tenacity and determination of women, and slowly changing attitudes of our families. In this setting, most of us can easily put ourselves in the shoes of Abhaya – an excellent academic record, a gruelling work schedule, and a hospital that does not boast of CCTV surveillance at all places – we shudder to think of her last moments and the unending misery of her parents. We marvel at the kind of "assurances" we protesting doctors are demanding – safe duty rooms, presence of thoroughly-vetted security personnel, fast-track justice to deter such dastardly attacks in the future - shouldn't these systems be in place already in a country that boasts of the highest number of medical colleges? Do we need to protest to get our basic issues sorted? Did Abhaya have to die? Can there be reparations to a wonderful life lost ?

That the entire medical fraternity in India, and many from across the world, are rallying behind our cause is noteworthy. We wish that the general public understands our angst, like they did in the Nirbhaya saga, and not get swayed by misinformation and mistrust against the medical community. Our hopes have risen with the staunch public support that the protesting doctors are receiving daily in Kolkata. We hope that governments all across, wake up and ensure the safety of healthcare workers, in our place of work and beyond, by stringent legislative measures. Till then, sadly, we will have to hone some defensive techniques, keep packing the pepper spray along with our stethoscopes, pray along empty corridors on urgent dialysis calls, and keep hoping that no more Abhayas and Nirbhayas happen in our lifetimes.

Ishani Thukral, Senior Resident,
Department of Nephrology, AIIMS Jodhpur
Namrata Rao, Additional Professor, Department of Nephrology, Dr.RMLIMS, Lucknow



CASE REPORT
Fibrillary glomerulonephritis : A rare presentation of an underlying biliary tract malignancy

Introduction

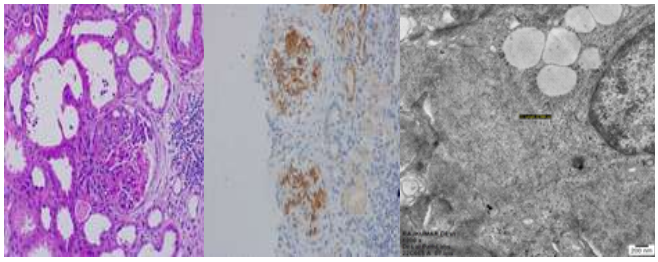
Case report

The index patient was a 47-year-old female from eastern Uttar Pradesh who presented to us with decreased urine output for 15 days and anasarca for 10 days. She also complained of vomiting for 5 days with nausea and decreased appetite. There was no history of hematuria and lower urinary tract symptoms. At presentation the patient was normotensive (BP 110/70mmHg) and pulse rate was 110/min. Patient was afebrile.

On investigation the patient was found to have advanced renal failure with creatinine of 7.8mg/dl. Her urine examination showed 4+ proteinuria with plenty of RBCs, mostly dysmorphic. 24hr urinary protein was 1.2gm/day (with urinary volume 200ml).

Her immunological profile (including ANA, dsDNA, MPO-ANCA, PR3-ANCA, and Anti-GBM Ab titres) was negative and serum complement levels were within normal limits. Myeloma profile (SPEP, IFE, Free light chain assay) was within normal range.

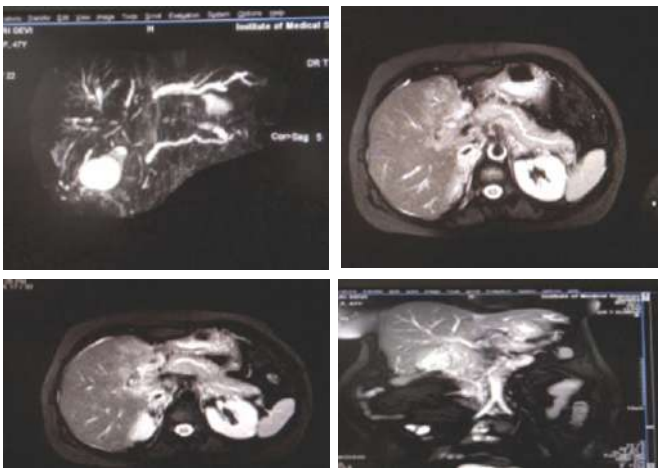
A renal biopsy was done which revealed Fibrillary Glomerulonephritis.



(1) Light Microscopy H and E stain
(2) Immunohistochemistry: DNAJB9 stain
(3) EM: randomly distributed fibrillary structure, 22-25 nm

Light Microscopy showed 19 glomeruli, out of which 3 were globally sclerosed. Rest showed variable mesangial expansion which was PAS positive, and non-congophilic. There were 4 crescents (3 cellular,1 fibro cellular). On DIF IgG: 3+ polyclonal (kappa, lambda both positive) C3: 3+, on IHC for DNAJB9 showed positivity in mesangial areas. Electron microscopy revealed randomly oriented, non-branching fibrillary structures in mesangial areas having 16-23 nm diameter.
The patient was diagnosed as a case of fibrillary glomerulopathy and dialysis access was obtained. He remained oliguric throughout the hospital stay and needed regular Hemodialysis and was discharged with advice to continue thrice a week hemodialysis.

The patient visited us after 15 days with jaundice, bilious vomiting and right upper quadrant pain. On investigation, we got direct hyperbilirubinemia with raised alkaline phosphatase and GGT. The patient underwent MRCP on gastroenterology advice which revealed a mass of size 4.1 x 3.4 x 1.5 cm in hepatic hilum contiguous with circumferential thickening of CBD extending till ampulla with associated moderate left lobar IHBRD and main pancreatic duct dilatation also, Gallbladder lumen show few calculi of average size 1.5cm is seen. However, there was no gallbladder wall thickening or mass lesion. MRCP revealed a probable diagnosis of Cholangiocarcinoma.



MRCP Images.

She underwent regular HD, but during her hospital stay, she developed septic shock. The patient was shifted to ICU and was put on CRRT, but unfortunately, the patient succumbed.

DISCUSSION

FIBRILLARY GN is a rare form of glomerulonephritis that was first described in 1977 and is defined by the ultrastructural finding of organized, randomly oriented, nonbranching fibrils with a mean diameter of 20 nm (range 15–25 nm).

The diagnosis of FGN can only be established by renal biopsy, and the incidence of FGN in native renal biopsies is less than 1%

Clinical characteristics in FGN

Table 1. Clinical characteristics of patients with FGN in the 3 largest cohorts

	Columbia (n = 61)	Mayo Clinic (n = 84)	UNC (n = 42)	Weighted average
Age, yr	57	59	54	57
White race, %	92	NA	71	83
Female, %	61	74	60	66
Creatinine, mg/dl	3.1	2.5	3.2	2.9
Renal insufficiency, %	69	71	NA	70
Proteinuria, g/d	6.4	5.1	5.7	5.7
Full nephrotic syndrome, %	52	25	NA	36
Hematuria, %	60	90	97	82
Hepatitis C, %	17 (6/34 patients)	7	27 (7/26 patients)	13
Autoimmune disease, %	5	14	13	11
Diabetes mellitus	20	24	28	24
Malignancy, %	7	10	12	9
Dysproteinemia, %	15 (7/46 patients)	4	42 (8/19 patients)	13

FGN, Fibrillary glomerulonephritis; UNC, University of North Carolina.

Among patients with FGN, autoimmune disease was seen in 11% of patients, diabetes mellitus in 24%, and malignancy in 9%. The most common malignancy associated with FGN is Plasma cell dyscrasias. FGN has been reported secondary to malignancy of Thyroid, hepatocellular, breast, uterine, prostate, colon, renal cell carcinoma, and melanoma

Autoimmune conditions documented to cause secondary FGN are Crohn's disease, SLE, Graves' disease, ITP, primary biliary cirrhosis, ankylosing spondylitis and Sjögren's syndrome.

The fibrils that characterize FGN are predominantly confined to glomeruli and stain intensely by IF for IgG, C3, kappa and lambda strongly suggesting that the fibrils are composed of a complex of antibodies and antigens.

The pathogenesis of FGN is largely unknown. FGN is thought to represent an immune-complex type glomerulonephritis in which the IgG deposits are polymerized into fibrils. A novel proteomic tissue biomarker for FGN, namely, DNAJB9, was first reported to be highly specific for FGN in a research article published in 2017. DNAJB9 was found to have a sensitivity of 98% and specificity of 99% for the diagnosis in 84 patients of FGN. DNAJB9 functions as a co-chaperone to heat-shock protein family members, assisting in protein folding and the degradation of misfolded proteins. Hence it is up-regulated in response to Endoplasmic reticulum stress. DNAJB9 was shown to co-localize with IgG and components of the classic complement pathway in glomeruli. These suggest that DNAJB9 may act as an autoantigen in FGN.

The prognosis for patients with FGN remains poor, with limited data to suggest optimal therapy. The median time to reach ESRD is 2 years (strongest predictor- serum creatinine at presentation). Steroids, cyclophosphamide and Rituximab have been tried in various studies, but no agent has shown efficacy. Following renal transplant, histological recurrence of FGN is around 21% at 10 years. But, Outcomes for transplantation in FGN were similar to the overall transplant population concerning 10-year patient and renal allograft survival. Hence, renal transplantation is a viable option for patients with FGN, but the risk of recurrence is not negligible.

CONCLUSION

Fibrillary GN is a rare cause of RPGN, but when suspected, the patient should be investigated for viral diseases, autoimmune diseases, dysproteinemia and malignancy. EM and IHC for DNAJB9 are essential for the diagnosis of Fibrillary GN. Definite treatment for idiopathic FGN has not been defined, Renal transplant is an option for patients with ESRD due to FGN.

Nikhil Chaudhary, Shivendra Singh,
Akshay Zalavadiya, Mohit Mishra,
Uttam Kumar Singh
Senior residents, Nephrology,
IMS BHU Varanasi, UP

ISN CROSSWORD ANSWERS

1. OPTIMISE-CKD : OPTIMISE-CKD is an observational study describing dapagliflozin treatment for CKD. Adult patients with CKD without type 2 diabetes were included in the primary analysis. 1480 patients had low (n = 796) and high (n = 684) UACR. After dapagliflozin initiation, an acute eGFR dip of 3 mL/min/1.73 m2 was observed, followed by a flat development in both groups. The eGFR slope [95% confidence interval (CI)] for patients with low UACR was 0.79 mL/min/1.73 m2 per year (–0.59, 2.56), and similar to patients with high UACR [0.40 mL/min/1.73 m2 per year (–0.46, 1.38)]. Risks of cardiorenal complications and all-cause mortality were similar, with adjusted hazard ratios of 0.89 (95% CI 0.66, 1.19) and 1.10 (95% CI 0.63, 1.92), respectively. Analogous results were found in those with normal/mildly elevated UACR.

2. PROXIMAL : The kidney accounts for 40% of endogenous gluconeogenesis, predominantly in the proximal tubule. The process is regulated by insulin, cellular glucose levels, acidosis and stress hormones

3. MINNESOTA : The first human pancreas transplant was performed in 1966 by William Kelly and Richard Lillehei at the University of Minnesota. A duct-ligated segmental pancreatic allograft and a deceased donor kidney were transplanted into a 28-year-old diabetic woman with ESKD. Post-transplantation immunosuppression was azathioprine and prednisone. A pancreatic fistula complicated the patient's postoperative course and both the kidney and pancreas were removed about 2 months later.

4. SOTAGLIFLOZIN : Sotagliflozin is a novel dual sodium-glucose cotransporter-1 and -2 (SGLT-1/2) inhibitor that was developed by Lexicon Pharmaceuticals. Clinical trials have demonstrated its efficacy in reducing cardiovascular death, heart failure hospitalizations, and urgent visits, particularly in T2DM patients with chronic kidney disease (CKD). The drug was approved in 2023 by the Food and Drug Administration for reducing cardiovascular death and heart failure in T2DM patients with CKD and those with heart failure, irrespective of diabetic status or ejection fraction.

5. ONTARGET - The study showed that, in patients with vascular disease or high-risk diabetes, Telmisartan was equivalent to Ramipril while the combination was associated with more adverse events without additional benefit

6. SMART-C : This was a collaborative meta-analysis of 12 randomised, double-blind, placebo-controlled trials.. 3065 of 73 238 participants with diabetes were using GLP-1 receptor agonists at baseline. SGLT2 inhibitors reduced the risk of major adverse cardiovascular events, hospitalisation for heart failure , cardiovascular death and CKD progression regardless of GLP-1 receptor agonist use at baseline.

7. MOGENSON : The original paper describing the 5 stages applicable to diabetic nephropathy in type 1 diabetes was thought to be useful for clinical work and research activities and described the stage of incipient DN as a forerunner of overt DN

8. FINE-HEART : This was a pooled analysis of FIDELIO-DKD, FIGARO-DKD and FINEARTS-HF trials including 18,991 trial participants.There was no significant benefit of finerenone in the primary outcome of cardiovascular death (HR 0.89 ,CI= 0.78-1.01, p=0.076) but it was seen to significantly reduce secondary outcomes of all cause mortality, hospitalisation for heart failure and composite kidney outcome.

9. LIXISENATIDE : The ELIXA study showed that addition of this drug to usual care in diabetics with recent ACS did not alter the rate of MACE. It has shown neuroprotective benefits in Parkinson's disease.

10. NEPHRIN - Nephrin tyrosine dephosphorylation is required for interaction with -arrestin leading to internal trafficking of nephrin in podocytes and is stimulated by Ang-II. The Ang II enhanced binding to nephrin and subsequent nephrin endocytosis provides a novel molecular mechanism to explain the anti-albuminuric moiety of Ang II inhibition beyond hemodynamic effects.

11. CREDENCE : Anti EPO Receptor antibodies were associated with disease progression in diabetic kidney disease. Post hoc analysis of the CREDENCE trial assessed the association of these antibodies with composite kidney and cardiac events, and mortality in patients with T2DM and CKD.

12. BARDOXOLONE : Inhibition of inflow of calcium into mesangial cells and the resulting suppression of mesangial cell contraction and improved nitric oxide biovailability leading to maintenance of vascular endothelial function are observed with it which leads to increased GFR.