Dear Readers...

We present to you yet another edition of the Kidney Kolumns in which we have tried to focus on the theme of 'Critical Care Nephrology'. From the ever-confusing debate of choice of fluids to the magic of 'POCUS', we have tried to simplify a part of this aspect of Nephrology.

Since Diversity, Equity and Inclusion is a current hot button topic in medicine, we also have an interesting debate about 'Manels' which our editors have succinctly yet playfully argued out the pros and cons of. We are sure you will enjoy this debate along with the brain wracking Critical Kidney conundrums-The Crossword.

We hope you enjoy reading all this customised material in Nephrology as much as we enjoyed putting it all together.

We would love to hear your comments, criticisms or compliments because that is what helps us going. Do write to us at education@isn-india.org

Editors-in-Chief

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KIDNEY KOLUMNS

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COVER IMAGES:

Left : Atypical large lymphoid cells fill the lumina of the glomerular capillaries and peritubular capillaries. The interlobular artery is spared. (H&E X400)
Center : Glomerular capillaries are engorged and filled with neoplastic cells (PAS, Jones silver X400)
Right : Lymphoid cells negative for CD3 and positive for CD20

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Mentorship: The Cool Way of Learning

The word “Mentor” has its historical origin in Greek mythology. Ulysses entrusted his son Telemachus to the care of his trusted friend named Mentor before his epic voyage. Mentor guided Telemachus through his pursuits, and this is where we get the word “Mentor” today. Mentoring has also been an age old tradition in Indian culture, with the concept of ancient Gurukuls, Buddhist monasteries, or Zen schools; that thrived on the “Guru-Shishya Parampara” of imparting life’s lessons, which sculpted an individual into a fine human being. Leapfrog to 2023, “Mentoring, Mentee and Mentor” – are frequently talked about buzzwords today. Let us look at the nuts and bolts of Mentorship, which I am sure each one of us has experienced in a small or big way in our life. A Mentor is someone who shares his knowledge, skills and experience to help another person to progress in his area of need which could be personal, professional or on any aspect of life. Mentors provide guidance, advice, feedback, and support to the mentee; serving different roles as an advisor, role model, teacher, counselor, sponsor, advocate, and ally, depending on the prespecified objectives and goals of the relationship.

Functioning of Mentor - The Mentor can start off by establishing together the explicit objectives and goals for the relationship with the mentee, and can commit towards it for a specified time frame. He meets the mentee regularly, listens to the mentee, provides honest and constructive feedback, respects the limits of mentee and delineates his own limits. He reviews his goals and objectives regularly, and works around them empathetically.

Selecting a suitable Mentor by mentee - A Mentor should be a good listener who can extract the core problem faced by the mentee. Mentor should have clarity of thoughts and vision, which a regular teacher may not be able to see. A mentor may be younger in age to mentee, as age and gender have nothing to do with mentorship. A good mentor for someone may not be equally good for others. The choice varies with your needs and specific requirements. A mentor may not be the best in his field, most famous, or a hero; he could be ordinary person who can impart extra-ordinary advise. It is always wise to invest one’s efforts and time in looking for a good mentor, suited to one’s needs.

Nephrology Mentorship in India - This is an idea whose time has come and I believe that the Indian society of Nephrology should take the initiative to set up a formal structured mentorship program matching the mentors with the mentees. This will go a long way in fulfilling the unmet needs of the early career Nephrologists as they need a bit of hand holding and personalized guidance to meander through their journey in the initial days of practice. Agreed there is a surfeit of online teaching and training programs including FOAMED resources yet I believe there is a need for focused and personalized discussions especially on career related topics. To test this hypothesis, A nationwide survey was done amongst all young nephrons (doing DM/DNB or completed nephrology within last two years) spanning most nephrology institutes of major government and private hospitals or colleges or the country. The common areas which need mentorship are shown in Figure below.

This survey confirmed my belief that mood is overwhelmingly in favor of having some form of a mentorship program, I suggest a multipronged approach which includes selection of key topics or areas which require mentorship, create short 30 min video modules for important topics and distribute them directly to nephrologist or through social media, and have a face to face meeting/Group Discussions/Panel Discussions conference in which young nephrologists can interact with senior Nephrologists, willing to be mentors. I am reasonably sure a lot of Nephrologists would be more than willing to join hands in this endeavor to guide the young Nephrons. Happy Mentoring !!!

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Continuous kidney replacement therapy (CKRT) is a commonly used treatment modality in critically ill patients with severe acute kidney injury (AKI). Anticoagulation is necessary during CKRT to prevent clotting within the extracorporeal circuit. Two commonly used anticoagulation strategies are regional citrate anticoagulation (RCA) and heparin. The 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines suggest using RCA rather than heparin in patients who do not have contraindications for citrate; and suggest using either unfractionated or low-molecular-weight heparin as the alternative choice. RCA works by chelating ionized calcium in the extracorporeal circuit, thereby inhibiting the coagulation cascade. Since it is a regional anticoagulation, the risk of bleeding complications is minimal. Heparin binds to and activates antithrombin III, thereby inactivates thrombin, factor Xa and other proteases.

Multiple randomized trials and meta-analyses have shown that RCA is better than heparin at preserving filter patency and has a lower risk of adverse events, including bleeding. In a large randomized trial by Oudemans et al., 200 patients treated with postdilution CVVH were randomized to citrate or the low-molecular-weight heparin, nadroparin. Safety signals were significantly better in the citrate group with only two patients requiring a change in anticoagulation regimen vs. twenty patients in the nadroparin group. Circuit survival did not significantly differ. Rather surprisingly, improved renal recovery and an improved hospital survival was noted in the citrate group.

The largest meta-analysis (11 randomized trials, 992 patients) by Bai et al., compared RCA with either systemic (nine trials) or regional (two trials) heparin, also showed that the risk of circuit loss was lower with RCA when compared with regional heparin (hazard ratio [HR] 0.52, 95% CI 0.35-0.77) and systemic heparin (HR 0.76, 95% CI 0.59-0.98). The risk of bleeding was lower with RCA compared with systemic heparin (relative risk [RR] 0.36, 95% CI 0.21-0.60) and similar between RCA and regional heparin. There was no difference in survival between groups. The above evidences led to the KDIGO recommending RCA as the anticoagulant modality of choice for CKRT in the absence of any contraindications. Despite these advances, heparin continues to be the predominant choice in most Indian hospitals, largely due to the perceived risk of metabolic complications and additional complexities with the use of citrate protocol. Although several western studies have demonstrated the effectiveness of RCA, data from India is scarce. In the recently published first Indian study, comparing the efficacy and safety of RCA versus heparin in CKRT, Senthilkumar et al. found no significant difference in filter lifespan or risk of metabolic derangements. In this single center, prospective, open label, nonrandomized comparative study, adult patients admitted to ICU over one year period with renal insufficiency and requiring CVVHDF were included, with 25 patients each being allotted to the heparin and citrate groups. Primary outcome studied was the filter life span and secondary outcomes included metabolic derangements, bleeding episodes, and patient survival. The mean estimated filter lifespan was 46.94 h for the citrate group and 40.05 h for the heparin group (p value = 0.29). No significant metabolic derangements or bleeding episodes were noted in either group. Overall patient survival was higher in the citrate group at 52% versus 32% in the heparin group (p value = 0.15). A lower dose of citrate (2.0-2.5 mmol/L) which was used in the study may be enough, especially in the Indian context and helps to bolster the safety profile of the RCA protocol.

The choice between RCA and heparin anticoagulation in CRRT depends on various factors such as patient characteristics, comorbidities (coagulation status, bleeding risk, liver function), and institutional experience. RCA provides effective anticoagulation, with minimal risk of circuit clotting, and lower risk of bleeding complications compared to heparin. Citrate has been shown to have potential benefits in modulating the inflammatory response and improving filter lifespan. However, the main concerns with citrate anticoagulation are the risks of metabolic complications, particularly in patients with liver dysfunction or impaired citrate metabolism. Citrate can lead to a decrease in ionized calcium levels, which can result in hypocalcemia and manifest as cardiac arrhythmias, muscle spasms, and neurologic symptoms. Both the anticoagulant options have their benefits and challenges, and the decision should be made on a case-by-case basis, considering the individual patient's needs and circumstances. RCA is particularly advantageous in patients with increased bleeding risk, but with careful monitoring of electrolytes and acid-base status. Heparin remains a viable option, especially when there are concerns regarding citrate metabolism. Overall, the available trial evidence suggests that RCA is a safe and effective alternative to heparin for CRRT. RCA is associated with longer filter life span and fewer
bleeding complications, and there is no clear difference in mortality between the two groups.

**Dr Praveen Kumar Etta**
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**Choice of fluids in the ICU-And the battle continues !**

From the time of the cholera epidemic in London, UK (c. 1832), intravenous (IV) fluids have been in clinical use and are considered life-saving therapy. “Normal” saline or 0.9% saline was the first fluid used worldwide as a physiological replacement of depleted bodily fluids. This was followed by various “balanced” fluids, containing other electrolytes, in addition to sodium and chloride alone. It is important to choose the optimum fluid for the resuscitation of patients in the intensive care unit (ICU). This topic was covered very elegantly in a recent review published in the Nephrology, Dialysis, Transplantation Journal (2022:0:1-10; doi:10.1093/ndt/gfac279).

In states of intravascular fluid depletion, IV fluid administration improves the venous return to the heart and this increase in preload results in increased cardiac output in keeping with Starling laws. The increased cardiac output results in improved perfusion of organs and oxygen delivery. Conditions of hypovolemic shock require immediate fluid resuscitation to substitute for fluid losses. The effect of immediate fluid replacement continues only until the flat part of the Frank–Starling curve is reached, after which there is no improvement in cardiac output with further fluid administration.

Loss of the endothelial glycocalyx of the vessel wall in conditions like sepsis and trauma causes albumin to leak into the extravascular space. Further fluid administration at this stage is more counterproductive with the risk of fluid overload. While the exact amount of fluid needed for resuscitation is debatable, it has been observed that <30ml/kg in the first 3 hours leads to higher mortality and is the reason for this dose being recommended. Lower values have the advantage of improved weaning from mechanical ventilation, albeit at the risk of increased acute kidney injury and renal
replacement therapy requirement.

**Crystalloids**

Crystalloids are the most commonly used IV resuscitation fluids and both observational and experimental data seem to suggest that fluids that are “balanced” i.e., having approximately the same electrolytes and in similar concentration as plasma, are superior to the erstwhile used 0.9% (“normal”) saline, which may predispose to hyperchloremic metabolic acidosis and possibly major adverse effects including death. The latter was shown in the (Isotonic Solutions and Major Adverse Renal Events Trial, ) as well as the (Saline Against Lactated Ringer’s or Plasma-Lyte in the Emergency Department), both of which were published in the same issue of the New England Journal of Medicine in 2018.

The findings were negated by two subsequent trials. However, in the latter trials, patients were “contaminated” i.e., had received IV fluids prior to enrolment in the study. The post hoc analysis showed that the use of a balanced solution improved the 90 days mortality. Secondary analysis of the SMART trial also had similar conclusions. Metanalysis of the high-quality trial data concluded that there is 90% chance that 0.9% saline is associated with increased mortality in adult patients in the ICU.

As important exception is patients with traumatic brain injury in whom it has been incontrovertibly seen that 0.9% saline is the ideal resuscitation fluid. Patients with prolonged vomiting, excessive loss of gastric fluid and patients who are hyponatremic as well as hypochloremic may also benefit from IV 0.9% saline resuscitation.

The recently conducted BEST-Fluid trial showed lesser incidence of delayed graft function (DGF) with balanced crystalloid solution fluid therapy compared to normal saline in deceased donor kidney transplant recipients.

**Colloids**

Colloids are intravenous fluids with high molecular weight substances suspended in crystalloid solution. The attractiveness of colloid usage lies in their ability to remain in the intravenous space longer and the macromolecules in solution would generate greater osmotic pressure intravascularly. Intravascular filling volume requirement is theoretically only a third of that required by crystalloids. This advantage is lost when the endothelial glycocalyx is damaged. There is no evidence of benefit in using colloids for initial volume resuscitation.

Of the colloids, the semi-synthetic hydroxyethyl starch (used worldwide for several years) has been shown in multiple studies to be nephrotoxic and has gone out of clinical use. The other semi-synthetic ones – gelatin and dextrin are fraught with adverse effects including coagulopathy, acute kidney injury and allergic reactions.

The natural colloid albumin is a relatively safe, (though more expensive) alternative for volume resuscitation in the ICU. Albumin has anti-oxidant, anti-inflammatory and anti-apoptotic properties. For conditions such as septic shock, and in patients with cirrhosis of the liver, where large volumes of intravascular fluid administration are required, albumin is a good option for fluid resuscitation. Hence, when large volume paracentesis of the ascitic fluid is planned or in conditions of hepatorenal syndrome and spontaneous bacterial peritonitis in cirrhosis, IV administration of albumin is beneficial. Both 5% (iso-oncotic) and 20% (hyper-osmotic) albumin infusions are beneficial but 4% (hypo-oncotic) has detrimental effects. Use of 20% albumin to maintain serum albumin levels >3gm/dl reduces 90-day mortality in patients with septic shock compared to crystalloids alone.

**Conclusion**

The choice of IV fluid used for the resuscitation of patients in the ICU is an important one to make apriori. Except in patients with traumatic brain injury or pronounced hypochloremia (who should receive 0.9% saline), balanced crystalloids are the fluids of choice. In conditions where large volumes of replacement fluid are required, 20% albumin may be used preferentially, especially in patients with sepsis and septic shock.

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Dear Friends,

First of all, I would like to congratulate our young and enthusiastic team of the Young Nephrology Forum and editorial team for the very successful and much appreciated first edition of our newsletter `Kidney Kolumns`. The first edition of the Kidney Kolumns is being greatly appreciated due to its novelty, inclusion and variety. The Kidney Kolumns will work not only as a source of the latest development in the field of Nephrology but would also act as the mouthpiece of society and important announcements and activities of ISN would be shared through this.

To highlight some of the important activities of ISN in the previous quarter-

We conducted a very successful webinar on Onconephrology on 12th May in association with the American Society of Onconephrology, which was greatly appreciated by members. The link to the recording is available on our website www.isn-india.org. In May itself, we started a new initiative of the ISN Journal club, spearheaded by our two young nephrology colleagues, Dr Arun Kumar from AIIMS Delhi and Dr Dharshan Rangaswami from Manipal Hospital, Banglore. The first ISN JC on 24th May was well attended by approximately 200 Nephrologists. Prof Vinay Sakhuja and Prof. Sanjeev Gulati provided their guidance as faculty. The ISN JC would be done every 3rd Wednesday of the month and a PG student from a different zone and two faculty will discuss. I am sure this initiative would provide a much-needed academic resource for our students and practising Nephrologists.

In the month of June, ISN did a very useful webinar on Practical aspects of Ig A Nephropathy with two international faculty and eminent Indian panellists including Prof. Narayan Prasad, Prof. Soumita Bagchi and Prof Suceena Alexander. There was discussion about the Indian experience and use of Budenoside in IgA Nephropathy.

ISN also conducted a mock exam on 9th-10th June in association with Mumbai kidney foundation at Madras Medical Mission Hospital Chennai, which was attended by approximately 100 students from all over the India and greatly appreciated by students and faculty.
I am happy to announce that much-needed online registration to become a member of Indian SN has been activated on our website. Please click on this membership registration link [https://isn-india.org/register] on our website and pay through the QR code provided on our website and you will get the acknowledgement of provisional membership within 24 hours.

About ISNCON 2023 Kolkata, an exciting program is being prepared by the scientific committee of ISN. This year, the scientific committee has decided to do workshops on day 1 of the conference. The workshops are on- Genetics, Histopathology, Critical care nephrology, Acid-base disturbances, intervention Nephrology and on scientific writings. The workshop on scientific writing would also have international faculty Dr Amit Garg, Dr Camille Kotton and Dr Dorry Segev. We will also have the president of the American Society of Nephrology Dr Michelle Josephson and the President of the International Society of Nephrology Prof. Mamosi Nangaku as our guest speakers among others. I am sure, the members would have an academic feast. Kindly register for ISNCON 2023 by clicking this link [www.isncon2023.com] and get early bird benefits. I would encourage everyone to submit the abstract on ISN website www.isn-India.org.

Dr Shyam Bihari Bansal
Hon. Secretary
Indian Society of Nephrology
Managing septic shock with either fluids or vasopressors is a grey zone and robust data to support either of these is still lacking. In sepsis, vasodilation leads to intravascular volume depletion. Hence, many clinicians administer intravenous (IV) fluids for initial resuscitation of patients with septic shock. While additional fluids may help some patients, excessive use can cause fluid overload, prolonged ventilation, progression of AKI and increased mortality. On the other end of the spectrum are the vasopressors which induce vasoconstriction thereby increasing cardiac contractility. However the perils of vasoconstriction with these agents include tissue ischemia, increased cardiac workload and arrhythmias.

The recently published Crystalloid Liberal or Vasopressors Early Resuscitation in Sepsis (CLOVERS) trial compared the effects of a restrictive fluid strategy (with early use of vasopressors) to a liberal fluid strategy for sepsis-induced hypotension. Investigators hypothesised that a restrictive fluid strategy used during the first 24 hours of resuscitation would lead to lower mortality before discharge home by day 90.

This multicenter, randomised, unblinded superiority trial included adult patients with a suspected or confirmed infection and sepsis-induced hypotension with SBP<100 mm Hg after the administration of ≥1000 ml of IV fluids. Exclusion criteria were lapse of more than 24 hours since presentation, previous receipt of >3000 ml of IV fluid, presence of fluid overload, and severe volume depletion from non-sepsis causes. The primary outcome was death from any cause before discharge home by day 90. Secondary outcomes included 28-day measures of the number of days free from ventilator use, days free from renal-replacement therapy, days free from vasopressor use, days out of the ICU, and days out of the hospital.

From March 7, 2018 to January 31, 2022, 1563 patients at 60 U.S. centres were enrolled with 782 patients assigned to the restrictive fluid group and 781 to the liberal fluid group. The trial was halted for futility at planned interim review. Before randomization, patients in both the restrictive and liberal fluid groups had received similar volumes of intravenous (IV) fluid (median, 2050 ml). However, there were differences in the volume of IV fluid administered during the first 6 days.

**Does early restrictive fluid management lead to lower mortality than liberal fluids in sepsis-induced hypotension?**

<table>
<thead>
<tr>
<th>STUDY DESIGN</th>
<th>TREATMENT GROUPS</th>
<th>PRIMARY OUTCOME</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multicentric</td>
<td>LIBERAL FLUID STRATEGY: (N = 781)</td>
<td>Death before discharge home by day 90</td>
<td>Extravasation in 3 patients</td>
</tr>
<tr>
<td>Open label</td>
<td>• 2000ml fluid at randomization</td>
<td>14.0% (11.6 to 16.4)</td>
<td>310 (39.7%)</td>
</tr>
<tr>
<td>Randomized</td>
<td>• 500ml bolus as per criteria</td>
<td>190 (24.4%)</td>
<td></td>
</tr>
<tr>
<td>Superiority</td>
<td>• “Rescue vasopressors” if severe hypotension/volume overload/ &gt;5 litters IV fluid/ Lactate &gt;4 mmol/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trial</td>
<td>RESTRICTIVE FLUID STRATEGY: (N = 782)</td>
<td>Estimated difference</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Halt bolus, maintenance fluids</td>
<td>-0.9 (-4.4 to 2.6%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Start norepinephrine to achieve</td>
<td>14.9% (12.4 to 17.4)</td>
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<tr>
<td></td>
<td>• MAP ≥ 65 mm Hg</td>
<td>190 (24.4%)</td>
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</tr>
<tr>
<td></td>
<td>• “Rescue fluids” if severe refractory hypotension/hypovolemia/ ↑ lactate/ clinical team decision</td>
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</table>

Conclusion: In sepsis-induced hypotension, the early restrictive fluid strategy used in this trial did not result in significantly lower (or higher) mortality before discharge home by day 90 than the liberal fluid strategy.
hours with the restrictive group receiving a median of 500 ml vs 2300ml in the liberal group. In terms of vasopressor usage, the restrictive group had a higher proportion of patients receiving vasopressors compared to the liberal group (59% vs. 37%). Moreover, vasopressor administration was initiated on average 1.4 hours earlier (95% CI -2.0 to -0.8) in the restrictive group and continued for 4.2 hours longer (95% CI 3.3 to 5.2) compared to the liberal group. Despite this separation between the two groups, the trial showed no significant difference in mortality before discharge home by day 90 which occurred in 109 patients (14.0%) in the restrictive fluid group and in 116 patients (14.9%) in the liberal fluid group (estimated difference, −0.9 percentage points; 95% CI, −4.4 to 2.6; P = 0.61). These results are in conjunction with the recently published CLASSIC trial.

The number of reported serious adverse events were similar in both groups. No significant differences in secondary outcomes were noted among both groups. 24 patients (3.3%) in both arms required renal replacement therapy. One interesting finding from this trial is the excellent safety outcome reporting for peripheral administration of vasoconstrictors. 500 patients, in both arms, received vasopressors through peripheral venous catheters. Only three complications were noted due to extravasation which resolved without any intervention and leaving no clinical consequences.

The study does have multiple limitations. The unblinded nature of study may have influenced adverse event reporting. Approval from treating clinician was required for enrollment in the study leading to a possible selection bias. Effects may have been diluted by allowing alternative therapies in both groups. The usage of study-specific pre-specified hemodynamic parameters to guide protocolized vasopressor and fluid administration while newer studies have adopted use of POCUS (Point of care ultrasound)-guided fluid administration is another limitation. The fluid administration regimes were not defined by the patient's weight.

So will the CLOVERS trial change clinical practice? One change that may come from this trial is the use of peripheral access for infusion of pressors which may allow for earlier administration. But for the types of patients with septic shock enrolled in this trial who were neither overtly volume overloaded nor volume depleted, either a vasopressor predominant or fluid-predominant approach resulted in similar outcomes. The heterogeneous nature of septic shock indicates that fluid or pressor strategies should be tailored for individual patients with use of dynamic measures of fluid responsiveness.

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All roads lead back to creatinine!!

The never-ending search for something faster and more accurate for the management of acute kidney injury never stops. Rise in serum creatinine although a cheap and convenient diagnostic modality, has a considerable time lag in AKI which several new biomarkers have tried to fill. The use of these biomarkers is however mostly restricted to research, since they are costly and often their place, in the heterogenous spectrum of AKI, is in contention. In this original research paper Ralib et al, recruited 70 patients with sepsis and evaluated the ability two different ways of using creatinine to predict development and recovery from AKI. The first being, the use of the E/G (excretion/ estimated generation) ratio, the second the use of kinetic eGFR. Of the 70 patients they recruited, 49 went on to develop AKI and their analysis showed that the KeGFR was useful in the early diagnosis of AKI while the E/G Ratio was predictive of renal recovery.

Kinetic GFR (KeGFR) was developed by Chen as a good method to detect AKI early, since it looks at rapid changes in serum creatinine over time, creatinine production and volume of distribution. Olivera Marques et al found KeGFR to have a good association with long term outcomes such as mortality, 1 year survival and need for KRT (kidney replacement therapy). Rather than replace the existing AKI classification, it seemed to complement the classification by adding prognostic relevance. In the paper by Ralib et al, KeGFR, incorporating both cystatin and creatinine, was noted to have the best AUC for early diagnosis of AKI on Day 1, however KeGFR was not found to be predictive of death or dialysis. Despite these shortcomings, kinetic GFR is here to stay and rapidly expanding its portfolio to include different categories of AKI such as pancreatitis and drug dosage strategies in AKI of different etiologies.

E/G ratio was made popular by John Pickering et al. The concept was that in steady state creatinine production and excretion are equal. When production exceeds the excretion, it means that excretion is impaired i.e., in the setting of an AKI. When the excretion exceeds production, it means the AKI is recovering. In their paper they found that the E/G) ratios of > 1.55 had a 90% sensitivity for diagnosing recovery from AKI. Ralib et al explore the use of E/G ratio for diagnosis of AKI where it falls short of other methods for early diagnosis with an AUC of 0.69; however, when it comes to recovery from AKI, E/G ratio had the highest AUC of 0.81 of all the methods compared. The E/G ratio has also been studied by Endre et al in the setting of delayed graft function where it was found to have a good predictive performance with an AUC of 0.87.

The strengths of this study are its practical relevance and ease of application. The limitations of the study are its strict inclusion criteria of procalcitonin in addition to the sepsis definition and the use of back-calculation by MDRD to estimate baseline creatinine. Definitions for renal recovery have been controversial and this study also proffers its own definition of renal recovery. The last word is that E/G ratio and kinetic GFR are here to stay in the armamentarium of AKI diagnosis and recovery. When it comes to generalizing information for AKI recovery to all types, more research with larger patient numbers and standardization will be required.

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&
Dr. Vinoi George
Professor and Head Nephrology CMC Vellore
Medical conferences and CME events have always served as important platforms for furthering research & education, providing avenues for networking and professional development. We all make the time and effort to go and listen to a panel of grizzled and wise looking experts in the field. And until recently, no one really voiced any concern that somehow these experts were almost always all men. A growing chorus against what has come to be known as “manels” has resulted in varying degrees of voluble opposition from organizers, behind the scenes snide commentary and some begrudging change across specialties. Nephrology is no different. In this article, I intend to argue for more change and, to use a loaded phrase, a dismantling of the patriarchy.

While it is true that the medical field has historically been male-dominated, conferences should strive to foster inclusivity and represent the diversity within our community. These manels no longer reflect the demography in Nephrology in India and either deliberately or inadvertently exclude the valuable perspectives and expertise of our female colleagues. There is today, a growing and increasingly vocal, community of accomplished female nephrologists to choose from for our conferences. Providing them with well-deserved platforms would act as catalysts of change.

An often-heard argument is that “manels are a reflection of merit”. But this overlooks the historic and systematic biases that exist within the medical profession and society at large. These biases contribute to the under-representation of women in leadership positions. Relying solely on "merit" perpetuates this cycle and hinders progress. Surely it cannot be anyone’s case that our female colleagues are inherently less meritorious than us. Conference organizers that actively seek to include women as faculty do not just promote the community of accomplished female nephrologists to choose from for our conferences. Providing them with well-deserved platforms would act as catalysts of change.

Then there are the purists who argue that they focus on the science, not the speakers’ gender. While the scientific content of conferences is undoubtedly paramount, it is naive to assume that gender has no influence on research or its interpretation. Systemic and academic biases have resulted in underrepresentation of women across the board and have also skewed the gender representation of published academic research against women. Acknowledging this and seeking to diversify voices can only lead to new insights and innovations.

Conference organizers also argue that it is difficult to find qualified female speakers. While this argument is unironically an acknowledgement of the systemic biases against women, it also reflects a lack of effort to address the underrepresentation of women in our specialty. Conferences must proactively identify and reach out to talented female speakers, encouraging their participation and providing opportunities for growth. The recent formation of women only organizations and conferences dedicated to highlighting women in nephrology demonstrates that there are indeed highly qualified women who can contribute meaningfully to our conferences. Left unacknowledged and unaddressed, this can also result in an unnecessary schism in what is an otherwise healthy and respectful nephrology community.

None of this is an argument for tokenism. While it is important to have a balanced representation of experts on panels at medical conferences, regardless of gender, it is also not helpful to have women on a faculty list simply because they are women. All efforts must be made by conference organizers to include women who are fully qualified to deal with the topic at hand and do not merely fill a checkbox. Making conferences more inclusive overall for women should be a welcome objective. This can be done by providing childcare, flexible scheduling, and other accommodations that make it easier for women to attend conferences, both as delegates and faculty.

A transparent process of faculty selection in medical conferences that is also gender equitable is a necessary step toward creating a fair and representative nephrology community. By embracing diversity, inclusivity, and representation, our conferences have the potential to foster an environment that celebrates and benefits from the contributions of all nephrologists. To borrow a cliche from Ravi Shastri, by dismantling manels we ensure that, in the end, Nephrology is the WINner (the pun was intended).

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An oft-visible sight these days on social media, is a lady scientist posting a random picture of a podium full of well-dressed men in a conference, followed by a “you can do better” sign-off. It is a well-intentioned trigger, on most counts. Because, after all, the lady scientist posting it, is a legitimate mid-to-senior level academician, who has worked hard to get where she is, and from her vantage point, she truly wishes to make it better for her beleaguered junior female colleagues in this big, bad, unfair world, and is therefore, fighting to get female representation on the podium. At the outset, can anyone blame her for fighting this crusade of sorts? The answer for me, is a ‘NO’. I agree that we need the powerful women leaders in science/ medicine/ nephrology fighting to get early career professionals their due place, but what I disagree with, is the compulsory female inclusivity in conference scientific programs. Let me take you through my reasons and I am sure, even my WINner seniors and friends (rational, lovely women, all of them) will vouch for my side of the debate (and not the least because I am a woman).

Expertise and passion, and not one’s gender to ensure a place at the table: Scientific committee members, virtually perform ballets of sorts to ensure that speakers with area of expertise are balanced with the inclusion game (zone, seniority, Bhaichara, et cetera). With this newfound fear of being labelled as “manels”, the organizers usually introduce the “tadka” of an added female panellist. We ought to sympathize with scientific committee members for these balancing acts. We also ought to empathize with the intended panellists if they were (God forbid!) all male, as these men will get pictured in the social media for being men and frankly not anything more. Finally, we must understand the discomfiture of the added female panellist(s) outside their area of work, included just because of the inclusivity bitter-pill that the conference organizers swallowed. All these “Manels Must Go” banners would be unnecessary if the inclusion game were not played at all. Too much conference-utopia, readers?

Build up overall Winners, not “Womanels”: We all will agree that women in science/ nephrology tend to rise professionally, later in careers than their male counterparts, as biology plays an unfair obstacle course in the 20s to 40s for many women. To alleviate these, we need constructive morale-building activities with active WIN sidelines and booths at pertinent conferences with specialized meet-and-greet, networking with women in allied/other specialties, and mentorship opportunities with hybrid options. Tokenism with “Womanels” is an ego-booster at best, and can give a false sense of complacency to the women in question, that they have indeed won their place in this niche community. Also, the recent advent of hybrid conferences, has augmented participation of early career women — generally a restricted-mobility class. This is a healthier alternative to creating panels with inclusivity as a sole criterion.

Giving men their due – moving from “Manels” to “Men”torship: All of us, in nephrology owe our place in this world to our wonderful teachers, of both sexes, who gave us the necessary impetus to land us in our orbits. We need to impart these values, morals and principles to our juniors and students of both sexes. Whether it’s the Bhaichara culture or forced sisterhood (both being gender-specific attitudes), looking for only “acceptable/ideologically comfortable” mentees rather than the “right” ones, will never make for truly successful mentorship programs. In short, women teachers need to give men, their due, in terms of equal growth and opportunities, so that we do not breed an environment of jealousy and one-upmanship. Eventually, the place at the table, will go to the ones who rightly deserve it, whether male or female.

Gender-based inclusivity for faculty at conferences is a dangerous trend, hinders representation of experts in the field, and fosters complacency, which has no place in scientific discourse. That said, only transparent competency-based selection of speakers and panellists, would improve scientific exchanges, and can hope to solve the problem of underrepresentation of women at conferences.

Bibliography:
WIN: Women in Nephrology — a popular acronym; WIN India is a recently established and rapidly growing society for women nephrologists in our country
Manels: Men-only panels in scientific conferences
Womanels: You guessed it right – the XX version of the manel abomination
Bhaichara: literally meaning brotherhood in Hindi, but also used to convey a prevalent buddy system common to men in many professions

Dr Namrata Rao
Associate Professor, Nephrology,
Dr RMLIMS, Lucknow
1. A 54-year-old woman with end-stage renal disease on irregular hemodialysis presents with shortness of breath and anasarca. You encounter this finding while performing POCUS-assisted physical examination. Transducer is in the right mid-axillary plane, approximately at the level of xiphoid process. Identify the finding?

2. A 70-year-old man on regular hemodialysis, a case of tubercular right pleural effusion (on antitubercular therapy), severe left ventricular dysfunction (EF 25%), is admitted to the hospital with fever, dry cough, progressively worsening dyspnea for 5 days duration. Clinical examination shows tachypnea, edema and bilateral crackles. A quick lung ultrasound examination was done. What do the following images demonstrate?

3. A patient of acute gastroenteritis with moderate dehydration was treated with aggressive intravenous fluids for 2 days. He developed oliguric acute kidney injury with azotemia (creatinine 6.5mg/dL) with urine output of 200 ml over 24 hours. You are performing POCUS examination to assess the status of inferior vena cava status and right atrial pressure. Based on the following image obtained from the subxiphoid window, what is hydration status and the estimated right atrial pressure?
4. A 65-year-old man presents with an elevated serum creatinine of 3.4 mg/dL. Four years ago, it was 1.2 mg/dL, and no labs are available in between. Images from nephrologist-performed kidney ultrasound are shown below, which shows right kidney of 9.2cm and left kidney of 8.9 cm. What is the finding seen in relation to kidneys and can we comment on type of kidney disease?

5. A 42-year-old man is admitted to the intensive care unit for septic shock secondary to pneumonia and developed oliguric acute kidney injury. He is intubated and sedated. A Foley’s catheter is placed for monitoring urine output. The nurse calls you and informs that the patient did not pass any urine for 12 hours after the placement of catheter. You perform a POCUS of the urinary bladder, findings of which are shown below.

**Answers**

1. **Right pleural effusion.**

Fluid appears anechoic (black) on ultrasound and this anechoic area is suggestive of right pleural effusion. Atelectatic lung is seen as a mobile echogenic structure within the effusion (Whale Tail Sign). Spine shadows are not seen normal state, i.e., when the lung is filled with air because air scatters on ultrasound. But fluid is a good transmitter of ultrasound and hence the beam is able to hit the thoracic vertebrae in pleural effusion (Spine sign).

2. **B-lines in the lateral (dependent) lung zones suggestive of pulmonary congestion.**

Air scatters the ultrasound beam and air-filled lung tissue cannot be seen on ultrasound unless consolidated / atelectatic. Normal lung demonstrates horizontal hyperechoic artifacts placed equidistantly called the A-lines that are created by ultrasound reverberation from the pleural interface. Vertical hyperechoic artifacts called the B-lines represent interlobular septal thickening. B-lines arise from the pleural line, extend to the bottom of the screen without fading, and move synchronously with breathing. Pleural line appears as a bright linear structure with a shimmer (rhythmic to-and-fro movement) that represents pleural sliding. In lobar consolidation, lung appears similar to that of liver in echotexture (hepatization).
3. **IVC collapsibility/right atrial pressure cannot be estimated because the vessel shown here is the aorta, not inferior vena cava.**

The size and collapsibility of the IVC are used as a surrogate for right atrial pressure (RAP)/central venous pressure. An IVC diameter ≤ 2.1 cm and collapsibility >50% indicates normal RAP of 3 mm Hg (0-5 mm Hg); while IVC > 2.1 cm with < 50% inspiratory collapse indicates high RAP of 15 mm Hg (10-20 mm Hg). IVC needs to be differentiated from aorta. IVC passes through the liver, while aorta is separated from it and passes in front of the vertebral column (spine shadows are frequently seen posterior to aorta). IVC enters the right atrium just above the diaphragm whereas origin of the aorta is not seen at this level. Furthermore, aorta has anterior branches (celiac and superior mesenteric artery are seen in this clip) whereas IVC does not have major anterior tributaries outside the liver.

4. **Increased cortical echogenicity, which could be acute kidney injury or chronic kidney disease.**

There is increased brightness of the cortex bilaterally (compare with that of liver on the right). Normal renal cortex is usually hypoechoic (less bright) or sometimes isoechoic (similar brightness) to that of liver or spleen. Increased cortical echogenicity is seen in chronic kidney disease (correlates with interstitial fibrosis, tubular atrophy, and glomerulosclerosis in histologic studies) and acute kidney injury where inflammatory infiltrates and proteinaceous casts reflect sound waves. CKD is typically associated with decreased kidney length and cortical thickness, which is not seen here.

5. **Foley catheter is misplaced.**

Note the balloon in the prostate, which means it was prematurely inflated in the prostatic urethra. Moreover, the Foley balloon hasn’t passed prostatic urethra in this case. Urinary bladder is filled with urine indicating that the Foley is ineffective in draining it. Foley’s catheters can get obstructed due to debris or bladder clots but if that is the case, the balloon would be within the bladder surrounded by urine.
POCUS in practice: The Premise

Nephrology practice often involves complex decision making. Traditionally, this has been guided by clinical examination (Inspection, palpation, percussion & auscultation) and judgement. **Point of care ultrasound (POCUS) in Nephrology** (NEPH-POCUS) adds an important and more objective, fifth dimension (Insonation) to this assessment and can aid at key moments in decision making.

NEPH-POCUS as envisaged goes beyond just scanning the kidney. It offers a wide gamut of other studies that can inform on the volume status of the patient, haemodialysis adequacy, vascular access, and cardiovascular health. (Table).

It consists of quick, limited bedside ultrasonographic assessment that seeks to answer simple yes or no questions. Is the patient truly volume overloaded? Have I dialysed him sufficiently? Does the patient have a kidney that can be biopsied? Are there suitable veins for AVF creation? It is not a replacement of a more comprehensive radiological assessment by a field expert (radiologist, cardiologist). Potentially integrating all these assessments by a single provider (the Nephrologist), leads to less fragmentation of decision making and more efficient, quicker problem resolution.

The Problem (The Hocus in POCUS):

NEPH-POCUS provides complementary information to the discerning nephrologist, that is often more accurate than clinical examination. However, there appears to be a lack of formal and dedicated training in POCUS in most nephrology training centres in India. We did a quick online survey of DM/DrNB trainees and young nephrologists across top institutes in India and the data emerging was stark. 64% of the respondents trained in reputed public health hospitals and the rest in DrNB centres of excellence. Though 96% of the respondents felt that POCUS was an essential tool in their daily nephrology practice, only 23.8% could attest to the fact that they had formal, targeted POCUS training during their 3 years of otherwise rigorous nephrology tutelage (Figure1). 48% of registrars were only exposed to an 'observe and do' approach, often from seniors/teachers, who were themselves not formally trained in POCUS. 26% of trainees were self-taught POCUS practitioners, often through online modules and you-tube videos.

<table>
<thead>
<tr>
<th>Domain</th>
<th>List of NEPH-POCUS skills to be learned</th>
<th>Pivotal areas where it enables clinical decision making</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VOLUME STATUS ASSESSMENT</strong></td>
<td>IVC Diameter and Collapsibleness</td>
<td>Aids dry weight assessment</td>
</tr>
<tr>
<td></td>
<td>Lung B lines or comet tails detection</td>
<td>Decisions on diuretics versus fluid</td>
</tr>
<tr>
<td></td>
<td>Pleural effusion assessment</td>
<td>Decisions in hyponatremia management!</td>
</tr>
<tr>
<td><strong>FOCUSED CARDIAC ASSESSMENT</strong></td>
<td>Qualitative assessment of LV</td>
<td>HD prescription</td>
</tr>
<tr>
<td>(FoCUS)</td>
<td>Presence of RA/RV dilatation</td>
<td>Judging tolerability of the patient to HD.</td>
</tr>
<tr>
<td></td>
<td>Presence of pericardial effusion</td>
<td></td>
</tr>
<tr>
<td><strong>KUB SCREENING</strong></td>
<td>To assess location of kidneys and size</td>
<td>Decide on biopsy</td>
</tr>
<tr>
<td></td>
<td>To rule out obstruction</td>
<td>Urgency of care (?) RPGN.</td>
</tr>
<tr>
<td></td>
<td>Renal biopsy</td>
<td>Triaging patient in a busy OPD</td>
</tr>
<tr>
<td></td>
<td>To screen for post biopsy hematomas</td>
<td>Reversible AKI (Obstruction)</td>
</tr>
<tr>
<td></td>
<td>To assess bladder status and residual urine</td>
<td></td>
</tr>
<tr>
<td><strong>KIDNEY GRAFT SCREENING</strong></td>
<td>To assess for renal allograft doppler flow, obstruction, collection.</td>
<td>Immediate post Tx period decision making</td>
</tr>
<tr>
<td><strong>VASCULAR ACCESS</strong></td>
<td>HD catheter insertion</td>
<td>No controversies here! Invaluable!</td>
</tr>
</tbody>
</table>
Pedagogy towards POCUS, as a part of the curriculum was considered limited and only a minority (9%) of the respondents could conclude that adequate focus and time was given to this specific skill (Figure 2). This, sadly, is not unique to India. A recent paper from the United States assessed nephrology program directors, fellows and graduates from top nephrology training institutes and found that no group felt adequately trained in POCUS. Reasons identified were lack of trained teachers, not enough, focused POCUS training and high equipment expense. Truly, there seems to be some hocus in this POCUS!

The solution: A Proposal

POCUS is an important core competency in Nephrology. We pride ourselves as being a speciality that integrates holistic care of patients. NEPH-POCUS cements that ability. Learning POCUS is like starting a new language. It needs to be an immersive, intensive, hands-on experience that is taught and practiced through the three years of training. For new learners (both young and old), gaining the psycho-motor-visual coordination skills required for POCUS needs time, repetition and patience. Busy programs tend to find it easier to write a referral out to Radiology for doing the same assessment. Therefore, the institution of NEPH-POCUS has to be systematic and intentional. And most importantly, it needs to be taught by trained experts. To begin with, we must teach the teachers! As a bridge until more competency is gained, we could seek the help of our radiology colleagues to partake in teaching nephrology trainees, the art of POCUS. The CJASN editorial on this topic in 2022 recommends ten scans per POCUS application directly supervised by a POCUS trained faculty member. Would nephrology programs be able to find time, intention and resources to implement this?

Online Resources:

Till training takes on a more structured approach to NEPH-POCUS skill acquisition in India, we would like to share some links to exciting online resources for POCUS.

https://nephropocus.com/about/
https://www.renalfellow.org/pocus-gallery/
https://www.theisn.org/blog/2021/02/15/follow-the-pocus-curriculum-on-the-isn-academy/

Dr Harshavardhan TS
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Critical Kidney Conundrums

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

Across
2. Triangle used as landmark for a central percutaneous approach to the Internal jugular vein
3. Tissue extracts from rabbit kidneys that helped prove that kidneys contribute to hypertension
4. In mechanically ventilated patients with PEEP ≥ 10cm H2O, the PEEP-test study evaluated the increase in this index with reduction of PEEP (to 5 cm H2O) to detect fluid responsiveness
9. Name given to normal appearance of right ventricular outflow tract, aorta and left atrium in parasternal long axis view of cardiac POCUS (based on a famous novel by Alexandre Dumas)
11. The 'Trident' sign is a classical MRI brain finding associated with dyselectrolytemia causing this disease
12. This maneuver is done to prevent a venous air embolism from lodging in the lungs
13. Minimum pressure in mm Hg for qualifying as abdominal compartment syndrome, an important cause of AKI

Down
1. Recent European trial comparing outcomes of hemodiafiltration with high flux hemodialysis
4. This electrolyte present in intravenous fluids is notorious to increase the risk of delayed graft function in patients undergoing kidney transplantation
5. This solution was a serendipitous discovery when distilled water was accidentally substituted by tap water in experiments on frog hearts
6. This ECG wave, although classically associated with hypothermia, may also be seen in severe hypercalcemia
7. Clinically meaningful renal composite outcome used as the primary and secondary outcome respectively in SMART and SALT-ED trials
8. This trial showed that, in adults with septic shock, the number of kidney failure-free days was not improved with early vasopressin vs norepinephrine
9. Following World War II, Frank, Seligman and Fine undertook experiments and performed PD in AKI using a modified _______ solution
10. The anti-angiogenic protein produced from placenta, which is responsible for manifestations of pre-eclampsia

Answers to the Crossword are available on page 23
Residents’ Corner

Mastering the Mock Exam:
A chance to unlock one’s potential

I was lucky to get an opportunity to attend the mock nephrology exam conducted at Madras Medical Mission Hospital, Chennai under the aegis of Mumbai Kidney Foundation and endorsed by the Indian Society of Nephrology. The humidity in Chennai was no respite from the heat wave back home in Delhi, but the food was definitely comforting. We were given the choice between long cases, short cases, histopathology discussions, and viva discussions prior to the examination itself. We reached the prestigious Madras Medical Mission hospital at 9 am sharp and got to know that I would be an observer for day 1 as I had been allotted ward rounds for day 2 of the examination. On day 1, I got to attend the best of the students who were presenting their respective allotted cases to behemoths of nephrology. It was an awe inspiring experience. The auditorium was packed with students who had come from all over the country to get a taste of the exam and to refine their knowledge of the field. The examiners were kind and considerate and made sure everyone was at ease. The cases in the two auditoriums were evenly distributed and we were free to attend either one. The best characteristic of the mock examination was the lucidity with which the examiners cleared our doubts and that we were allowed to ask questions about the subject as well. Discussions with the examiners allowed us to gain insights into our performance and areas of improvement. Day one concluded with spotters in the main auditorium and we were clearly explained everything and the manner of answering was also elucidated. The interaction we had with our colleagues was refreshing and I did meet a few friends from the other side of the country.

Day 2 started early in the smaller auditorium and I went ahead with my allotted ward rounds. The case scenarios were presented on the screen and the interaction with the examiners was genuine and comforting. We were treated as colleagues by the examiners and that gave us hope, a hope that someday we would be standing on the other side of the table. The thought that we would some day help new nephrologists and guide them, make their exam process easier, was a warm feeling that will stay with me till the day I actually execute it. I reached home with a sense of clarity and new found confidence and maybe even as a better nephrologist, with the knowledge gained from behemoths of the field in my mind.

Mock exams may be embraced as a catalyst for growth and improvement. I hope ISN continues to conduct such events in future so as to help students recognize their strengths, confront their weaknesses and refine their study techniques.

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Chronic active antibody-mediated rejection (ABMR) is a common complication in kidney transplant recipients and a leading cause of graft loss. Standard-of-care (SOC) therapy includes plasmapheresis and intravenous immunoglobulins (IVIG). However, non-responsive patients require additional and alternative treatments, as recommended by the 2019 Expert Consensus from the Transplantation Society Working Group. Tocilizumab, an IL-6 receptor antagonist, has been investigated as a potential therapy for chronic active ABMR with donor-specific antibodies (DSAs) and transplant glomerulopathy that does not respond to conventional treatments. Studies suggest that Tocilizumab may stabilize graft function and prevent histological lesion progression. In this report, we present the case of a young living related renal allograft recipient with chronic active ABMR who received experimental therapy with Tocilizumab.

This is a case of a 30-year-old man with chronic kidney disease (CKD) and hypertension. He underwent a renal transplant in February 2019. Initially, his creatinine levels were stable, but in May 2019, they started to rise and methylprednisolone was given. In January 2020, his creatinine increased further, and a graft biopsy revealed active ABMR and acute TCMR. Treatment with plasmapheresis and IVIG was administered, resulting in a decline in creatinine. However, by October 2020, his creatinine rose again, and a second graft biopsy showed chronic active ABMR and borderline active TCMR. He had fungal pneumonia and was treated with voriconazole, as well as antivirals for hepatitis C. Despite modifications in immunosuppression, his creatinine continued to increase, and subsequent biopsies confirmed ongoing rejection. In June 2022, another biopsy revealed mixed chronic active ABMR and chronic TCMR. Tocilizumab therapy was initiated in September 2022, and the patient experienced pancytopenia but eventually recovered. In March 2023, his creatinine remained elevated with significant proteinuria, and he received the fourth dose of Tocilizumab. Currently, his graft function is stable with a serum creatinine of 4 to 4.3 mg/dl. (Details in Figure)

Currently, there is an unmet need for managing chronic active ABMR, as no approved therapy exists. Conventional treatments include plasmapheresis, IVIG, and steroids, with additional options such as rituximab and bortezomib. Notably, a study by Choi et al reported graft survival and patient survival rates of 80% and 91% at 6 years, respectively, in Tocilizumab-treated ABMR patients. Another study by Lavacca et al. used Tocilizumab as a first-line therapy in fifteen chronic ABMR patients and observed improvements in graft function and proteinuria, along with a reduction in donor-specific antibodies.
Our case report demonstrates a patient with chronic active ABMR who experienced a sustained rise in serum creatinine despite receiving various standard-of-care therapies. However, after receiving four doses of Tocilizumab, and with cautious modulation of net immunosuppression, infection, and metabolic control, our patient exhibited a stable serum creatinine level of around 4.0-4.3 mg/dl during the past 7 months. This indicates a likely role of Tocilizumab in retarding the progression of chronic ABMR to end-stage kidney disease (ESKD) and providing a longer dialysis-free interval for our patient.

Given the evidence from previous studies and our own case, Tocilizumab should be considered as a rescue therapy in patients with chronic ABMR. Further evaluation of graft survival and overall patient survival is needed to fully assess the benefits of Tocilizumab in chronic ABMR.

To conclude, Tocilizumab can be sought as an alternative therapy to standard-of-care therapy in patients with chronic active ABMR. Results have been promising with this therapy as various case reports suggest. Our case report also suggests the possibility that Tocilizumab can retard the progression of chronic ABMR and, thereby, provide a prolonged dialysis-free life to these patients. Tocilizumab is, therefore, a promising avenue in the field of renal transplant.

KEYWORDS
Chronic active antibody mediated rejection, Tocilizumab, plasmapheresis, IVIG

"The utility of Tocilizumab in chronic antibody mediated rejection is yet to be established due to paucity of published literature. Future well planned prospective and randomized trials would enlighten us on its utility and limitations."

- Dr. Shyam Bihari Bansal

The views and opinions expressed in the cartoon (Stay Tooned) are that of the cartoonist and not that of his/her employer.
A 41-year-old lady presented with pyrexia of unknown origin for two months, proteinuria (uPCR 7.8) and serum creatinine of 0.8mg/dl. Renal biopsy showed large lymphoid cells with increased nuclear-to-cytoplasmic ratio, prominent nucleoli with brisk mitotic activity within the glomerular capillaries and peritubular capillaries. These cells were positive for CD20 and BCL2, and negative for CD3. Immunofluorescence study for immunoglobulins, complements and light chains was negative. The diagnosis of renal intravascular large B-cell lymphoma (IVLBCL) was made.

IVLBCL is a rare, highly aggressive type of extranodal non-Hodgkin lymphoma in which the neoplastic lymphoid cells selectively proliferate within the lumina of blood vessels, particularly capillaries, with no obvious extracellular tumour masses. The preferential growth within blood vessel lumina is because the tumour cells lack cell surface proteins CD29 (β1 integrin) and CD54 (ICAM-1) which is required for transmigration across the endothelium, thereby confining the cells within vascular spaces.

IVLBCL usually occurs in the 6th and 7th decades, with no gender predilection. Clinically, two patterns have been recognized depending on the geographical origin of the patients; classical (western variant) and haemophagocytic syndrome-associated (Asian variant). Most common organs involved in the ‘western variant’ are brain and skin. The ‘Asian variant’ is characterized by hemophagocytic syndrome, fever, multiorgan failure, hepatosplenomegaly and bone marrow involvement.

Renal IVLBCL is extremely rare, presenting with fever, anaemia, acute kidney injury (AKI) and proteinuria. The obliteration of the glomerular and peritubular capillaries by tumour cells causes podocyte and tubular epithelial injury, resulting in proteinuria and AKI.

The differential diagnoses include other B-cell and T-cell lymphomas. The characteristic proliferation of the neoplastic cells exclusively within the vessels along with immunohistochemistry establishes the diagnosis.

Images: Please take a look at the Cover Images

Anila Abraham Kurien, MD, Jayasenthilnathan S, MD, Abhinesh Vijayakumar, DM

ISN CROSSWORD ANSWERS

ACROSS
2. SEDILLOT -The essential surface anatomy of the Sedillot triangle consists of the borders formed by the sternal head of the sternocleidomastoid muscle medially, the clavicular head of the sternocleidomastoid laterally, and the superior border of the medial third of the clavicle inferiorly. The internal jugular vein lies immediately posterior to the apex of Sedillot’s triangle with a frequency of 97% on the right and 79% on the left, and is thus relatively superficial in location at a needle depth of 1.0–1.5 cm

3. RENIN By the end of the nineteenth century, Tigerstedt, a Finnish professor of physiology working at the Karolinska Institute, and his assistant Bergman analyzed the effect of renal extracts on arterial pressure. They discovered the presence of a pressor compound in the renal tissue of the rabbit, and based on its origin, they named it Remin

4. CARDIAC In the PEEP-test study, an increase in cardiac index of >8.6% on reducing PEEP to 5 cmH2O was found to be a predictor of volume responsiveness in mechanically ventilated patients with a PEEP ≥10 cm H2O.

9. THREEMUSKATEERS In the parasternal long axis (PLAX) view, right ventricular outflow tract (RVOT), aorta (Ao) and left atrium (LA) roughly occupy one-third of the image and hence are nicknamed, "three musketeers. When one of these structures enlarges, we can get a sense of severity by observing their relative proportions.

11. ODS A symmetrical trident-shaped area in the central pons is a characteristic finding on T2-weighted and FLAIR MR images in Osmotic demyelination syndrome. The ventrolateral pons and the pontine portion of the corticospinal tracts typically are spared. Decreased signal intensity throughout affected areas, with no mass effect, is a classic finding on T1-weighted images.

12. DURANT Durant et al. demonstrated that dogs that were subjected in experiments to air emboli were more tolerant of air infusion, while lying on their left sides. This position placed the right ventricular outflow tract in a position inferior to the right ventricular cavity, allowing the air bolus to migrate superiorly, removing the obstruction to blood flow. Trendelenburg position also prevents embolism from occluding the outflow tract by
placing the right ventricular cavity in a more superior position

13. TWENTY Intra-abdominal hypertension is defined as a sustained intra-abdominal pressure (IAP) ≥12 mm Hg & abdominal compartment syndrome as IAP ≥ 20 mm Hg associated with new organ dysfunction or failure. IAP is measured through a bladder transducer.

DOWN

1. CONVINCE: This multicentric randomised controlled trial compared HDF (convection volume ≥23 litres) with HD in patients requiring kidney-replacement therapy. Despite not being able to recruit the planned number of patients, it found that the use of high-dose hemodiafiltration resulted in a lower risk of death from any cause than conventional high-flux hemodialysis.

4. CHLORIDE High chloride is implicated in increasing the risk of delayed graft function (DGF) by afferent arteriolar vasoconstriction via the tubuloglomerular feedback. BEST-Fluids was a randomised controlled trial comparing normal saline with low chloride balanced crystalloid solution amongst patients receiving a deceased donor kidney transplant. Intravenous fluid therapy with balanced crystalloid solution reduced the incidence of DGF compared with saline.

5. RINGERLACTATE RL was developed due to the observations of Sydney Ringer when he noted the effect of inorganic salts on heart muscle when distilled water was accidentally replaced by tap water.

6. OSBORN The main ECG abnormality seen with hypercalcaemia is shortening of the QT interval. In severe hypercalcaemia, there may be Osborn waves, seen as a positive deflection at the J point in precordial and true limb leads.

7. MAKE30 The NIDDK in a 2010 workshop put forth that a composite of death, dialysis and sustained loss of kidney function would be an appropriate end-point for phase 3 studies of AKI. Hence, the term MAKE (major adverse kidney events), analogous to MACE was introduced. MAKE within 30 days (MAKE30) was used as the primary and secondary outcome respectively in the SMART and SALT-ED studies.

8. VANISH The trial was a 2x2 factorial, double-blinded RCT in adult patients who had septic shock requiring vasopressors despite fluid resuscitation within a maximum of 6 hours after the onset of shock. There was no significant difference in the number of kidney failure free days in the vasopressin vs norepinephrine groups.

9. TYRODE Renal failure cases seen in world war II may have accelerated the development of renal replacement therapy. Tyrode’s solution was used initially by Frank, Seligman and Fine for PD. Read more about the history of PD in the words of Twardowski here.

10. sFLT1 In 2003, the Karumanchi group reported that the placentas of women with preeclampsia strikingly over-express a soluble receptor for the angiogenic factors, vascular endothelial growth factor (VEGF) and placental growth factor. Soluble fms-like tyrosine kinase-1 (sFLT-1) acts as an antagonist of VEGF and placental growth factor by binding and sequestering these growth factors from interaction with their receptors.
The 53rd Annual National Conference of Indian Society of Nephrology

14th - 17th December, 2023
ITC Royal Bengal, Kolkata

Registration is open at
www.isncon2023.com

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Scientific Luminary Spotlight

**Dr George Bakris**
Member of the National Kidney Foundation’s Board of Directors; Professor of Medicine and Director of the American Society of Hypertension’s Comprehensive Hypertension Center at the University of Chicago Medicine

**Dr Sandip Mitra**
Consultant Nephrologist at Manchester Royal Infirmary; Expert Advisor for Dialysis at the National Horizons Scanning centre, Dept. Of Public Health & Epidemiology, University of Birmingham

**Dr Amit Garg**
Associate Dean, Clinical Research, Schulich School of Medicine & Dentistry, Site Director, Institute for Clinical Evaluative Sciences (ICES) Western Facility

**Dr Dorry Segev**
Professor, Department of Surgery at NYU Grossman School of Medicine, Director, Center for Surgical and Transplant Applied Research (C-STAR)

**Dr Camille Kotton**
Clinical Director of Transplant and Immunocompromised Host Infectious Diseases in the Infectious Diseases Division at the Massachusetts General Hospital

**Dr Masaomi Nangaku**
Professor and Head, Department of Nephrology, University of Tokyo Graduate School of Medicine
The 53rd Annual National Conference of Indian Society of Nephrology
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LINA-DKD
Linagliptin 5 mg Tablets

SAFETY WITH NO ADJUSTMENT