Metabolic Nephrology

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Abstract

Nephrology faces a paradox. The prevalence of kidney disease is rising, in spite of advances in diagnostic, preventive and therapeutic strategies. This has kindled interest in the discipline. Once considered a subspecialty of general medicine, nephrology has evolved into a broad discipline. This encompasses diverse fields like transplant medicine, dialysis medicine, onconephrology, interventional nephrology, and immunonephrology. Notably, most causes, clinical manifestations, complications, comorbidities, and therapeutic targets in kidney disease are metabolic in nature. This underscores the need to recognize Metabolic Nephrology as a distinct and emerging subspecialty. This allows holistic addressal of the metabolic origins and consequences of kidney disease. It will also foster the development of preventive, pharmacologic, etiology-specific and replacement therapies.

DOI: https://doi.org/10.47391/JPMA.25-72

Introduction

Nephrology is a vast field, which studies the health and disease of kidney and associated structures. It uses the knowledge of anatomy, physiology, and biochemistry, along with advances in diagnostic sciences, to craft optimized regimens for prevention and management of kidney disease. This allows protection and promotion of kidney health, as well as overall well-being.

Changing Challenges

Over the past decades, the morbidity and mortality associated with kidney disease has changed dramatically. Chronic kidney disease (CKD) has emerged as a major pandemic, threatening the survival of nearly 11% of all adults.[1] The aetiology of CKD has changed as well- while previously uncontrolled hypertension was the major cause of CKD, diabetes is now the main contributor to CKD burden.[2] As per an estimate, CKD is projected to be the 5th

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Table-1: Scope and Spectrum of Metabolic Nephrology.

- Renal physiology
  - o Deep understanding of electrolyte, acid-base, and fluid balance
  - o Tubular handling of solutes, minerals, and metabolites
  - o Hormonal regulation (RAAS, vasopressin, PTH, FGF23, others)
- Etiology of kidney disease
  - o Diabetes, obesity, hypertension, dyslipidaemia
  - o Exposure to metabolic toxins (e.g., heavy metals, oxalate, uric acid)
  - o Genetic/metabolic disorders (e.g., primary hyperoxaluria, cystinosis, Fabry disease)
  - o CKD in preterms- foetal origins of CKD (low nephron endowment)
  - o Hyperfiltration injury in kidney donors
  - o Gut microbiome and kidney health
- Pathogenesis of kidney disease
  - o Metabolic and haemodynamic injury pathways
  - o Glomerular hyperfiltration, mitochondrial dysfunction, crystal deposition
  - o Oxidative stress, inflammation, endothelial dysfunction
  - o Interplay of genetics, epigenetics, and metabolomics
- Clinical features of kidney diseases
  - o Acute kidney injury (including toxic/metabolic causes)
  - o Chronic kidney disease (including metabolic progression factors)
  - o Nephrolithiasis and crystallopathies
  - o Metabolic glomerulopathies (e.g., lipoprotein glomerulopathy, gouty nephropathy)
  - o Tubulopathies and inherited transporter/channelopathies (e.g., Gitelman, Bartter, RTA)
- Screening, diagnostic risk stratification and monitoring tests
  - o Albuminuria, eGFR, NT-proBNP, urinary electrolytes and oxalate
  - o Metabolic profiling (e.g., lipid, uric acid, amino acid, and glycaemic panels)
  - o Genomic, proteomic and metabolomic tools for precision nephrology
  - o Advanced imaging for nephrolithiasis and bone disease
- Complications of kidney disease
  - o Acute: hyperkalaemia, acidosis, tumour lysis syndrome, volume overload
  - o Chronic: renal osteodystrophy, anaemia, dyslipidaemia, sarcopenia
  - o Cardiometabolic complications: atherosclerosis, heart failure with preserved ejection fraction (HFpEF)
- Comorbid diseases
  - o Endocrinopathies: diabetes mellitus, thyroid disorders, adrenal disease
  - o Metabolic syndrome, PCOS, obesity-related glomerulopathy
  - o Disorders of bone and mineral metabolism, hypogonadism, and mitochondrial diseases
- Curative interventions
  - o RAAS blockers, MRAs (e.g., finerenone), GLP-1 receptor agonists, SGLT2 inhibitors
  - o Uric acid-lowering therapies, oxalate-lowering agents, citrate therapy

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highest cause of years of life lost globally by 2040.[3] However,there is a silver lining to this. Recent developments in diagnostics, drugs and devices have allowed early treatment. Whereas more effective screening leads to prompt diagnosis and management of CKD along with identifying its risk factors, and complications.[4]

Expanding Horizons

This seemingly quixotic situation- an increase in prevalence, and improvement in preventive as well as prescriptive measures, has spurred interest in nephrology. The subject, hither to considered as a subspecialty of medicine, has become a broad discipline in its own right. It includes branches as varied as transplant medicine, dialysis medicine, onconephrology, interventional nephrology, and immunonephrology.[5-7] The vast majority of causes, clinical features, complications, comorbid conditions, and consequence of kidney disease, as well as its investigation and interventions, however, are metabolic in nature.[8,9] This suggests that metabolic nephrology should be identified and developed as a distinct specialty.

Neoteric Nomenclature

Metabolic nephrology may be defined as the science which studies the metabolic aspects of kidney health and disease, including diagnosis, prevention, and management. This is limited not only to clinical, but also public health aspects of nephrology. Table 1 describes the various domains of metabolic nephrology. Metabolic nephrology is a multidisciplinary science, led by a nephrologist, with the active participation of other team members. These should include experts from diagnostic sciences such as biochemistry, clinical disciplines including endocrinology, and allied professions such as dialysis technology, nephrology nursing, and dietetics. Table 2 lists some interventions that form the science of metabolic nephropathy.

Table-1: *Continued from previous page.*

- Gene therapy and enzyme replacement for rare metabolic nephropathies
- Dietary and lifestyle modifications tailored to metabolic profiles
- Integrated therapy

- Preventive aspects
  - Early screening in high-risk populations (obese, diabetic, stone formers)
  - Nutritional interventions and metabolic counselling
  - Public health strategies for early intervention in metabolic disorders
  - Lifelong monitoring of inherited metabolic kidney diseases
- Collaborative interfaces
  - Endocrinology (metabolic control), Urology (stone disease), Rheumatology (crystal disorders), Genetics, and Nutrition
  - Establishment of multidisciplinary Metabolic Stone Clinics and Inherited Renal Disease Clinics.

Table-2: Therapeutic interventions in metabolic nephropathy.

- Lifestyle interventions
  - Kidney-friendly diet and Personalized nutrition
  - Personalized exercise programmes
  - Behavioural modifications- tobacco and alcohol cessation
- Prevention and promotive pharmacotherapy
  - RAAS blockers
  - Mineralocorticoid receptor antagonists
  - SGLT2 inhibitors
  - GLP1 receptor agonists
- Etiology-specific therapy
  - Glucose lowering drugs
  - Blood pressure lowering drugs
  - Urate/Oxalate lowering therapy
  - Cystine binding thiol drugs
  - Enzyme replacement therapy e.g., agalsidase
  - Biological therapy
- Supportive therapy
  - pH maintenance
  - Electrolyte balance
  - Mineral and bone health
  - Vitamin and micronutrient optimization
- Kidney replacement therapy
  - Individualized dialysate composition
  - Pre-transplant preparation (donor and recipient)
  - Peri-transplant stewardship
  - Post-transplant care (donor and recipient)

Health for All

Metabolic nephrology will be able to harness the advances of modern medicine, and translate them into achieving better kidney health. This will also help in accomplishing overall health. The benefit of such an approach will accrue not only to the nephrology fraternity, or persons living with metabolic kidney disease, but also to other health care professionals, and society at large. A lead may be taken by starting focussed chapters or interest groups within existing professional organizations, such as the International Society of Nephrology[10] and the Transplantation Society.[11] Colleagues from the sister disciplines mentioned above should be invited to share their expertise and contribute to cross pollination of ideas. This is an important step, if we wish to stem the growing pandemic of chronic kidney disease.

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