Research in Molecular Medicine

Risk Factors, Etiology, Pathology, and Diagnostic Methods for Acute Kidney Injury: A Review Study

Tamer A Addissouky[1, 2, 3*], Majeed MA Ali[1], Ibrahim El Tantawy El Sayed[2], Yuliang Wang[4], Ayman El Baz[5, 6], Naglaa Elarabany[7, 8], Ahmed A Khalil[9]

1. Department of Medical Laboratories, Al-Hadi University College, Baghdad, Iraq.
2. Department of Biochemistry, Faculty of Science, Menoufia University, Menoufia, Egypt.
3. MLS Ministry of Health, Alexandria, Egypt.
4. School of Agriculture and Biology, Shanghai Jiao Tong University, Shanghai, China.
5. Department of Basic Medical Sciences, Faculty of Medicine, Ibn Sina University for Medical Sciences, Amman, Jordan.
6. Department of Medical Biochemistry and Molecular Biology, Faculty of Medicine, Mansoura University, Mansoura, Egypt.
7. Department of Biology, Sajir College of Arts and Science, Shaqra University, Shaqra, Saudi Arabia.
8. Department of Zoology, Faculty of Science, Damietta University, Damietta, Egypt.
9. Department of Pathology, Baystate Medical Center, Springfield, United States.

Use your device to scan and read the article online

Citation Addissouky AA, Ali MMA, El Tantawy El Sayed I, Wang Y, El Baz A, Elarabany N, et al. A Review of Advancing Toward Early Prediction and Personalized Precision Medicine for Acute Kidney Injury. Research in Molecular Medicine. 2022; 10(4):193-204. https://doi.org/10.32598/rmm.10.4.1265.1

https://doi.org/10.32598/rmm.10.4.1265.1

Article Type:
Review Paper

Article info:
Received: 20 Aug 2022
Revised: 15 Sep 2022
Accepted: 10 Oct 2022

Keywords:
Acute kidney injury, Imaging modalities, Biomarker panels, Nanotechnology, Traditional medicines, Artificial intelligence

ABSTRACT

Background: Acute kidney injury (AKI) is characterized by a rapid decline in kidney function, resulting in significant morbidity and mortality. This review summarizes our knowledge of AKI risk factors, pathogenesis, prediction, diagnosis, and emerging management approaches.

Materials and Methods: A comprehensive literature search was conducted to summarize current knowledge on AKI. Five electronic databases were searched using various combinations of search terms related to AKI's risk factors, pathogenesis, prediction, diagnosis, and management approaches. The databases included PubMed, Embase, Web of Science, CINAHL, and Cochrane Central Register of Controlled Trials. Relevant publications were limited to those written in English from 2016 to 2024, but some prior studies were included if highly seminal. Reference lists were also reviewed to find other sources. The full texts of all possibly relevant articles were assessed for inclusion. Data were extracted on study details and findings concerning AKI causes, biomarkers, prediction strategies, diagnostic techniques, treatments, and perspectives to enhance prevention and outcomes. Quality was considered during data extraction, prioritizing well-performed randomized controlled trials, systematic reviews, and large epidemiological studies. Case reports and select editorials were included to summarize specific topics. Extracted data were narratively synthesized to provide an overview of current AKI knowledge and highlight opportunities for mitigating its impact. Through searching multiple databases using applicable index terms, hand searching reference lists, screening and extracting pertinent published literature, this review aims to understand AKI complications and advance solutions from the existing evidence base.

Results: This review summarizes current knowledge on AKI risk mechanisms, diagnostic approaches, emerging therapies and implications of personalized medicine leveraging multi-omics for optimizing prediction and precision treatment.

Conclusion: Despite progress, AKI has remained challenging. However, integrative approaches leveraging new technologies offer hope for improving AKI prevention and management.

*** Corresponding Author:**
Tamer A Addissouky, PhD.
Address: *Department of Medical Laboratories, Al-Hadi University College, Baghdad, Iraq.*
E-mail: *tedesoky@gmail.com, tedesoky@science.menofia.edu.eg*

Introduction

Acute kidney injury (AKI), previously termed acute renal failure, is characterized by a rapid decline in kidney function occurring over hours to weeks [1]. It is a common and highly consequential clinical condition, affecting over 13 million people worldwide each year [2]. AKI is associated with significant morbidity and mortality, especially when severe or sustained. Even small changes in serum creatinine, indicative of minor AKI, are linked to a higher risk of chronic kidney disease (CKD), end-stage renal disease, and death [3]. So far, the KDIGO (Kidney Disease: Improving Global Outcomes) group has provided the most widely used definition of AKI. Their criteria include an increase in serum creatinine by ≥0.3 mg/dL within 48 hours or a 1.5-fold rise over baseline within 7 days [4]. Additional criteria incorporate urine output, with oliguria defined as <0.5 mL/kg/h for 6 hours. AKI frequently manifests without classic oliguria, emphasizing the importance of creatinine monitoring.

Etiologies of AKI include prerenal causes such as volume depletion, intrinsic kidney injury from ischemia or nephrotoxins, and postrenal obstruction of urine flow. Risk factors include patient demographics, comorbidities, medications, and clinical settings [5]. The pathophysiology of AKI is complex and not well understood. However, some common pathways have been elucidated. Ischemia or toxic agents incite tubular epithelial and vascular endothelial cell damage, prompting inflammatory, oxidative stress, and apoptotic responses [6]. These conditions reduce glomerular filtration, intraparenchymal congestion, and impaired tubular reabsorption and secretion. Maladaptive repair can promote interstitial fibrosis. The clinical picture represents the downstream effects of kidney microcirculation and cellular dysfunction [7].

Detection and severity categorization of AKI rely on clinical indicators like urine output and serum creatinine. However, creatinine is an imperfect marker with delayed increase after injury due to its kinetics and variable production. This issue has spurred substantial research into novel biomarkers representing distinct pathophysiologic pathways [8]. Examples include neutrophil gelatinase-associated lipocalin (NGAL) for tubular damage, kidney injury molecule-1 (KIM-1) for cellular regeneration, and liver fatty acid binding protein (L-FABP) for hypoxia. Multiplex biomarker panels are also emerging to improve diagnostic and prognostic accuracy [9].

AKI management is predominantly supportive, removing nephrotoxic agents and restoring volume and electrolyte homeostasis. No effective pharmacotherapies exist to directly treat established AKI or interrupt progressive injury [10]. Renal replacement therapy by intermittent hemodialysis or continuous venovenous hemofiltration may be used in severe AKI or certain clinical situations like tumor lysis or hyperkalemia. Overall care focuses on mitigating complications like volume overload and metabolic derangements. Following an AKI episode, monitoring for CKD development is essential [11].

This review comprehensively presents the current state of knowledge on AKI prediction, diagnosis, pathogenesis, and emerging therapies. It provides a wide-ranging overview of promising technologies like biomarkers, artificial intelligence, nanomedicine, and multi-omics that can potentially transform AKI prevention and care. Identifying critical innovations across the translational spectrum will inform future directions.

Pathogenesis and etiology of AKI

The pathogenesis of AKI is complex and multifactorial, involving hemodynamic, inflammatory, and cytotoxic mechanisms that manifest in kidney dysfunction. Understanding these pathways is key for developing targeted therapies [12]. Prerenal azotemia from reduced renal perfusion is a common cause. Volume depletion, congestive heart failure, or impaired blood flow autoregulation can diminish perfusion pressure. This condition leads to preferential shunting to vital glomeruli and ischemic tubular injury. Restoring perfusion often rapidly reverses mild AKI, underscoring the importance of hemodynamic factors [13].

Ischemic AKI arises when impairment of blood flow explicitly involves the kidneys. Causes include renal artery disease, thromboembolism, shock, and major surgery. Ischemia triggers endothelial dysfunction, release of cytokines, complement activation, and leukocyte accumulation [14]. Reperfusion elicits oxidative stress and mitochondrial damage. Prolonged severe ischemia causes necrosis of tubules and vascular endothelium. Apoptosis and autophagy may also contribute to problems [15].

Nephrotoxic AKI follows exposure to exogenous toxins or metabolites. Medications are a common cause, particularly aminoglycosides, amphotericin, and cisplatin. Contrast agents, myoglobin in rhabdomyolysis, and hemoglobin in hemolysis can also incite toxicity. Most nephrotoxins generate reactive oxygen species, causing

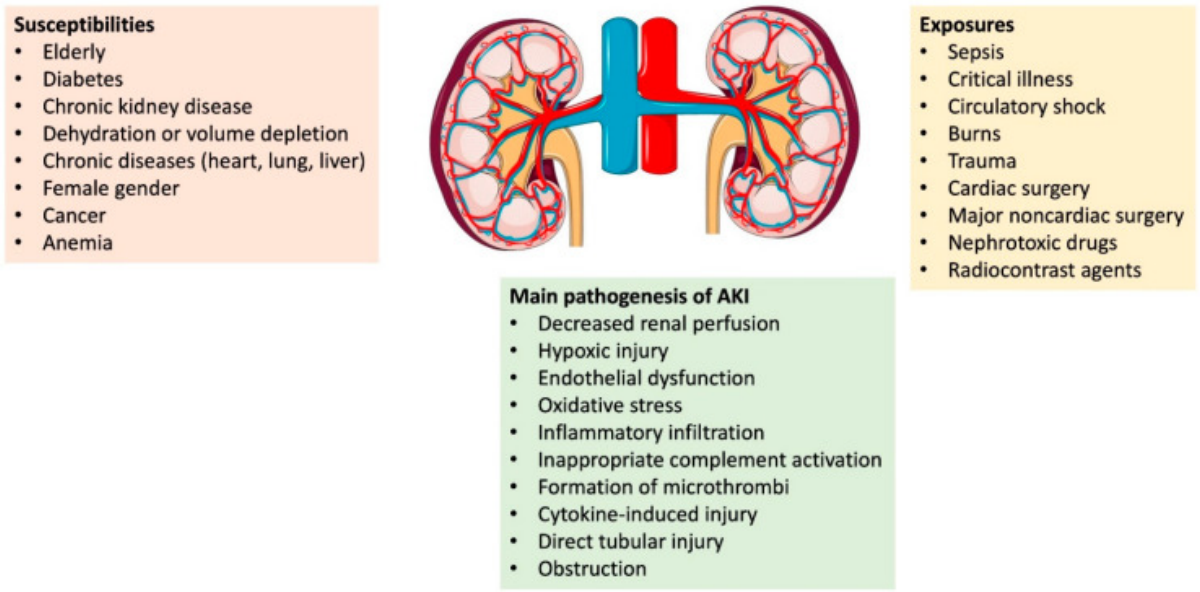

Figure 1. Risks and pathogenesis of AKI

tubular apoptosis and sloughing. Others directly damage membranes or clog tubules. Risk factors like volume depletion or CKD augment susceptibility [16].

Sepsis accounts for approximately 50% of AKI in critically ill patients. Sepsis provokes intrarenal hemodynamic changes, direct cellular injury, and dysregulated immunity. Endothelial dysfunction and impaired autoregulation reduce glomerular filtration. Proinflammatory cytokines, oxidative stress, apoptosis, and microvascular thrombosis all contribute. The resultant septic AKI often manifests without classic hypoperfusion, oliguria, or rhabdomyolysis [17]. Prerenal azotemia manifests primarily in hemodynamic changes. Ischemic insults cause more proximal tubular damage. Nephrotoxins often affect distal tubules and collecting ducts. The glomerular filtration rate universally declines, but proteinuria and hematuria signify glomerular involvement.

Histology can localize lesions but is rarely obtained. After the initial insult, maladaptive repair processes can worsen the injury. Persistent inflammation, hypoxia, and cellular senescence promote fibrosis. This condition leads to chronic tubulointerstitial scarring and impaired kidney function. AKI survivors have an elevated risk of eventually developing CKD [18]. The pathogenesis involves complex vascular, tubular, and inflammatory changes leading to reduced glomerular filtration and impaired tubular function. AKI can occur more frequently following specific triggers or in vulnerable populations due to several shared disease mechanisms, as depicted in Figure 1 [19].

Several factors modify the risk and severity of AKI through unclear mechanisms. Advanced age, male gender, black race, and low income are demographic factors. CKD is a major risk factor, lowering the threshold for AKI. Diabetes mellitus, heart failure, liver disease [20, 21], and immunocompromised states also are risk factors. Obesity, hypertension, smoking, alcoholism, and acidic urine confer smaller risks. Genetic factors may contribute but require further study [22]. Table 1 summarizes major categories of injury mechanisms that can lead to AKI, including key mediators within each category and some of the main molecular pathways elicited downstream. Grouping by broad mechanism category and listing specific triggers and cellular/molecular sequelae helps provide readers with a quick yet comprehensive overview of the interrelated pathways that converge to cause AKI.

Advances in early AKI prediction

The late and unreliable nature of serum creatinine has spurred extensive research into early biomarkers and predictive models for AKI. These innovations aim to enable earlier intervention and improve outcomes. Novel damage markers detectable before creatinine rise have shown promise for early AKI diagnosis. NGAL is among the most studied [23]. This 25-kDa protein is expressed in low levels systemically but upregulated and excreted by the kidney after ischemic or nephrotoxic AKI. Both urine and plasma NGAL levels correlate with the severity and timing of AKI in diverse clinical settings. However, systemic confounders like CKD and

Table 1. Pathogenesis and pathophysiology pathways leading to acute kidney injury

Category	Mediators	Molecular Mechanisms
Hemodynamic	Renal hypoperfusion-ischemia/reperfusion injury	ATP depletion, hypoxia-inducible factor activation, endothelial dysfunction
Inflammatory	Sepsis, immune response	Cytokine and chemokine release, complement system activation, leukocyte infiltration
Cytotoxic	Nephrotoxins, free radicals	Apoptosis/necrosis pathways, mitochondrial damage, oxidative stress

systemic inflammation may reduce its specificity [24]. KIM-1 is a transmembrane glycoprotein undetected in normal kidneys but upregulated >100-fold after proximal tubule injury. Urinary KIM-1 rises 12-24 hours after cardiac surgery or contrast exposure before detectable creatinine elevation [25]. It also correlates with AKI severity and duration. Limitations include persistence after injury and nonspecific elevation in CKD [26]. Other urinary biomarkers like interleukin-18 (IL-18), L-FABP, and cystatin C demonstrate similar early rise after varied AKI etiologies [27]. No single marker provides perfect discrimination, prompting interest in biomarker panels. A 7-marker panel including KIM-1, NGAL, L-FABP, and IL-18 demonstrated improved early diagnostic performance for cardiorenal syndrome compared to individual markers. Customizable panel design and machine learning integration may further optimize predictive capacity as research continues [28].

Electronic health record (EHR) data offer an opportunity for real-time AKI prediction. Automated tracking of creatinine, urine output, and clinical parameters enables risk algorithms to identify patients on a concerning trajectory before meeting AKI criteria. For example, a score integrating vital signs, medications, and prior lab trends predicted stage 2-3 AKI 24 hours before creatinine-based diagnosis. Machine learning increases predictive ability when applied to longitudinal EHR data [29]. Clinical risk scores can also be combined with novel biomarkers. A decision tree model incorporating the Toxic renal injury biomarkers and ethnicity-AKI score (which considers demographics, diagnoses, and vitals) with a urine biomarker panel improved the prediction of severe AKI compared to either alone. This issue demonstrates the predictive synergy of multimodal data. Integrating risk factors, biomarkers, and EHR trends into predictive analytics and alert systems provides the greatest potential to maximize lead time for AKI intervention [30]. Table 2 outlines some key emerging AKI biomarkers categorized by type and relevant attributes like biomarker source, time of elevation after AKI onset, performance characteristics, and biological significance. Grouping biomarkers into logical categories and listing key features in a concise table enables readers to easily compare and contrast the various novel options to improve early AKI detection and management compared to traditional markers like serum creatinine.

Molecular biology and pathology

AKI arises from diverse cellular and molecular derangements that converge to impair kidney function. Elucidating these pathways is key to developing targeted therapies. Several putative pathological mechanisms may promote the development of acute kidney disease (AKD) following AKI [31]. These mechanisms include

Table 2. AKI biomarkers

Category	Biomarker	Source	Time of Elevation	Performance	Sig.
Damage	NGAL	Urine, blood	<24 hours	Sensitive, early marker	Tubular injury
	KIM-1	Urine	12-24 hours	Specific for AKI	Proximal tubule regeneration
	L-FABP	Urine	<12 hours	Early indicator	Renal tubule hypoxia
Functional	Cystatin C	Blood	<24 hours	GFR marker	Detects renal dysfunction earlier than Cr
Regenerative	YKL-40	Urine	48-72 hours	Indicates recovery	Tubular epithelial repair

Abbreviations: NGAL: Neutrophil gelatinase-associated lipocalin; KIM-1: Kidney injury molecule-1; L-FABP: Liver fatty acid binding protein; YKL-40: Chitinase-3-like protein 1.

renal tubular epithelial cell cycle arrest, epigenetic alterations, chronic inflammation mediated by cytokines like interleukin and tumor necrosis factor-alpha, mitochondrial dysfunction, excessive reactive oxygen species production, failed regeneration of proximal tubule cells, endothelial dysfunction, metabolic changes like altered fatty acid oxidation, and over activation of the renin-angiotensin system signaling cascade via angiotensinogen conversion to angiotensin I and subsequently angiotensin II binding to angiotensin type-1 receptors. Elucidating the contributions of each pathway to maladaptive repair after AKI may reveal therapeutic targets for preventing progression to AKD [31]. Ischemic AKI triggers complex changes in gene transcription and expression. Hypoxia inhibits mitochondrial oxidative phosphorylation, depleting ATP and disrupting cellular processes. Hypoxia-inducible factors (HIFs) are upregulated, along with glucose transporters, to augment anaerobic glycolysis. However, excessive HIF activation also increases inflammation and apoptosis. Other ischemia-responsive genes like p53, heat shock proteins, and nitric oxide synthases demonstrate similar dichotomous effects [32]. Reperfusion elicits further damage through oxidative stress. Reactive oxygen species injure cell membranes, proteins, and DNA while activating proinflammatory and pro-apoptotic signaling cascades. The complement system is activated by ischemic tissue, exacerbating inflammation upon restoration of blood flow. Mitochondrial permeability transition pore formation is another key mediator of reperfusion injury [33]. Sepsis-induced AKI also demonstrates intricate molecular changes [34]. Bacterial components like lipopolysaccharides bind toll-like receptors, triggering cytokine and chemokine release [35]. Tumor necrosis factor-α, interleukin-1β, interferon-γ, and other proinflammatory mediators create a cytokine storm [36]. They also recruit and activate neutrophils and macrophages [37]. Counterregulatory anti-inflammatory cytokines like IL-10 temporarily restrain excessive inflammation. If the proinflammatory response prevails, microvascular dysfunction, bioenergetic failure, and apoptosis result. Nephrotoxins prompt cell-specific molecular alterations that impair function. Aminoglycosides and cisplatin accumulate in proximal tubule cells, activating pathways causing apoptosis and necrosis. Rhabdomyolysis incites inflammation, vasoconstriction, and tubular obstruction by myoglobin, hampering function. Contrast agents directly damage tubule cell membranes and mitochondrial function. Molecular mechanisms mediate nephrotoxin entry, accumulation, and downstream dysfunction [38]. Histologic examination demonstrates AKI's effects across kidney structures. Light microscopy reveals diffuse tubular dilatation and flattening in early AKI. Brush border loss signifies proximal tubule injury. Necrotic debris and cast formation obstruct flow. Proliferative cells replace epithelium starting days after AKI onset. Interstitial inflammation and microvascular congestion develop. With prolonged or severe AKI, patchy tubular loss leaves denuded basement membranes. Glomerular changes like dilation and endothelial injury occur later. Chronic lesions include tubular atrophy and interstitial fibrosis [39].

Diagnostic imaging

Diagnostic imaging is not routinely required to diagnose AKI, which relies on clinical data like serum creatinine. However, specific modalities can provide valuable anatomic and functional information to evaluate AKI etiology and severity. Renal ultrasound helps assess structural changes and obstruction. Hydronephrosis visible on ultrasound implicates postrenal etiologies. Intrarenal dilation signifies intrinsic renal dysfunction. Subtle increases in kidney size and echogenicity occur early in AKI. Doppler ultrasound can detect diminished renal artery flow from prerenal causes or renal artery stenosis. Ultrasound is non-invasive and avoids contrast or radiation, making it well-suited for AKI evaluation [40]. Computed tomography (CT) offers more detailed structural delineation. Contrast-enhanced CT can identify renal artery occlusion, infarction, or cortical necrosis that may underlie AKI. Obstructive nephrolithiasis, retroperitoneal fibrosis, and other urologic abnormalities are visible. However, contrast agents pose a risk of worsening AKI. Newer dual-energy CT protocols maximize parenchymal enhancement while minimizing contrast dose [41]. Functional magnetic resonance imaging (MRI) techniques are also being studied. Blood oxygen level-dependent (BOLD) MRI exploits the oxygenation-dependence of hemoglobin's magnetic properties to assess tissue oxygenation [42]. Renal BOLD-MRI demonstrates reduced medullary oxygenation in experimental AKI models and some human studies. Arterial spin labeling MRI quantifies renal perfusion using magnetically labeled inflowing blood protons. This tool reveals declined cortical perfusion in septic AKI patients. Such functional MRI approaches are still being translated to clinical AKI and require standardized methodology [43]. Nuclear medicine studies offer additional functional details but involve ionizing radiation [44]. Tc-99m DTPA scintigraphy uses glomerular filtration of radiolabelled DTPA (diethylenetriaminepentaacetic acid) to measure single-kidney glomerular filtration rate (GFR) [45]. Split renal function and obstruction can be assessed. 123I-iothalamate or Tc99m MAG3 allows concurrent imaging and GFR quantification. PET (positron emission tomog-

raphy) tracers like 18F-FDG are also studied to characterize AKI metabolic patterns and inflammation [46].

Nanomedicine and multi-omics

Nanotechnology and omics fields expand our understanding of AKI pathogenesis and enable novel diagnostics and treatments. Integrating these new approaches with traditional methods will be key to tackling AKI [47]. Nanomaterials possess customized structural, functional, electrical, and optical properties. Their minute size facilitates interactions with biomolecules and access to injured tissue. In AKI, nanotechnology aims to enable early diagnosis, interrupt pathogenic pathways, and promote recovery [48]. Several nanomaterial-based sensors hold promises for early AKI detection. Quantum dots and gold nanoparticles conjugate with antibodies or aptamers to detect urine biomarkers like KIM-1 with high sensitivity and stability. Graphene and carbon nanotube platforms also allow multiplex biomarker measurement. Chip-based nanosensors also utilize biomarker affinity to improve AKI prediction [49]. Nanoparticle therapeutic delivery is another active area. Liposomes, dendrimers, carbon nanotubes, and polymeric nanoparticles efficiently encapsulate drugs and genes, protecting cargo from degradation and facilitating controlled release [50]. These particles enhance the delivery of anti-inflammatory, antioxidant, and regeneration-promoting agents to injured kidney sites. Limiting off-target effects improves safety [51].

Multi-omics fields are also elucidating AKI biology. Genomics analyzes genetic variability affecting AKI risk and outcomes. Several inflammatory, oxidant stress and cell cycling gene susceptibility variants have been identified [52]. Pharmacogenomics examines genetic determinants of drug response, like nephrotoxicity. Transcriptomics defines genomic expression changes in AKI using microarrays and RNA sequencing [53]. Affected regulatory and functional pathways are revealed across AKI models [54]. Proteomics quantifies proteins and peptides via mass spectrometry to profile AKI-induced changes. Urine proteomics demonstrates changes in tubule injury, inflammation, and repair markers within hours of cardiac surgery [55]. Comparing proteomic signatures to conventional biomarkers provides mechanistic insights. Metabolomics similarly catalogs metabolic fingerprints of AKI using techniques like gas chromatography-mass spectrometry. Mapping deranged metabolic pathways helps localize dysfunction [56].

Integrating multi-omics data with physiologic monitoring and imaging provides a comprehensive systems biology perspective on AKI. Machine learning applied to these multidimensional datasets may improve diagnosis, risk stratification, and treatment selection accuracy. However, overcoming technical challenges in data integration and interpretation remains a barrier.

Emerging therapeutics and traditional medicine

Currently, no effective targeted treatment exists for AKI. Supportive care has remained the standard treatment. However, various emerging pharmacotherapies and traditional medicines are under investigation to interrupt AKI pathogenesis and promote repair. Several novel drug classes target impaired perfusion and oxygen delivery in AKI. In animal models, vasodilators like fenoldopam, atrial natriuretic peptide, and anti-thrombotic agents like thromboxane inhibitors improve renal blood flow. However, human trials show limited benefit for clinically established AKI [57]. Anti-inflammatory agents like curcumin and stem cell therapies may mitigate deleterious injury cascades. Curcumin demonstrates antioxidative and anti-inflammatory properties in AKI models by modulating NF-kB, COX-2, and other pathways [58]. Mesenchymal stem cells promote beneficial immunomodulation, angiogenesis, and cell regeneration when administered early after AKI. Results from ongoing clinical trials are eagerly anticipated [59]. Promoting tubular repair and regeneration is another strategy [60]. Several growth factors, like Insulin-like growth factor 1, hepatocyte growth factor, and epidermal growth factor, restored functional and structural integrity in experimental AKI by activating cell proliferation, migration, and survival programs [61]. However, concerns exist regarding unintentional angiogenesis or fibrosis. Small clinical trials show promise but require replication [62]. Novel biomarkers like KIM-1 and NGAL also have therapeutic potential. Besides diagnostics, these endogenous proteins may participate in protective pathways that could be pharmacologically augmented to ameliorate AKI. Clinical translation is still preliminary but represents an intriguing prospect [63]. Certain traditional medicine therapies show promise for integrating into AKI management [64]. The polysaccharide astragalus membranaceus has antioxidant, anti-inflammatory, and immune-boosting properties with low toxicity [65]. Acupuncture and herbal blends from systems like Ayurveda and Traditional Chinese Medicine remain largely unstudied for AKI [66, 67]. However, their ability to address interconnected physiological systems may confer benefits. Herbs like ginger, ginseng, and hawthorn may mitigate oxidative stress and inflammation while improving renal perfusion. Acupuncture could similarly rectify imbalanced

homeostasis to hasten recovery. Appropriate clinical trials are needed.

Emerging role of artificial intelligence and machine learning in AKI management

The advent of massive data and advanced analytics is transforming medicine, including the detection, diagnosis, and management of AKI. Artificial intelligence (AI) and machine learning offer enormous potential to improve predictive capabilities and support clinical decision-making for AKI patients [68]. Machine learning applied to EHR enables automated early warning systems for AKI risk. Algorithms can continuously analyze data trends in creatinine, vital signs, fluid balance, medications, and past medical history to identify patients progressing toward AKI. Alerts notify clinicians to intervene before substantial kidney damage accrues. Deep learning enhances predictive capabilities by integrating longitudinal data and complex interactions [69].

AI can also help AKI diagnosis by detecting patterns invisible to humans across multimodal data sources. A convolutional neural network analyzing time-series serum creatinine, urine output, and clinical variables identified AKI episodes on par with nephrologist review. Adding real-time biomarker data may further enhance diagnostic accuracy. Natural language processing of clinical notes provides additional clinical context [70]. Besides diagnosis, AI algorithms can support various aspects of AKI management as follows.

- Predicting AKI recovery, dialysis needs, or other outcomes based on temporal lab patterns and trends. This measure facilitates prognostication and care planning.

- Recommending medications and dosing by identifying risk factors for nephrotoxicity and contraindications. This proposal prevents iatrogenic harm.

- Determining optimal fluid management by continuously analyzing intake/output data and volume status indicators. This act promotes hemodynamic stability [71].

- Triaging patients for specialist referral or ICU transfer based on risk stratification. This measure allocates resources to the highest needs [72].

- Suggesting personalized nutritional interventions based on labs, medication, fluid status, and physiologic data. This measure prevents electrolyte derangements and protein-energy wasting.

The possibilities are limitless, but extensive validation is required to ensure the safety and efficacy of these measures. Human-AI collaboration, with the algorithm providing insights for physician evaluation, maybe the ideal model for enhancing AKI care.

Challenges accompanying AI integration include data biases, generalizability across institutions, and acceptance by clinicians. To realize the potential of AI in AKI, solutions must be thoughtfully designed and rigorously tested, with patient benefit as the major goal. However, machine learning promises to revolutionize AKI prediction, diagnosis, and evidence-based management in the coming years [73-76].

Personalized medicine and lifestyle approaches for AKI management

Unique patient factors underlie AKI risks, manifestations, and outcomes. Personalized medicine leveraging genetics, biomarkers, and lifestyle data aims to deliver tailored prevention and management to improve outcomes [77]. Pharmacogenomics examines genetic variants affecting drug metabolism and response. Coding polymorphisms in hepatic enzymes like CYP3A5 alter the metabolization of immunosuppressants and influence toxicity. Identifying high-risk genotypes allows personalized dosing to minimize adverse events. Variants in drug transporters within kidney tubules also modify elimination and nephrotoxicity [78]. Preventive pharmacotherapy like renin-angiotensin-aldosterone system inhibition in high-risk groups requires balancing benefits against side effects for the individual. Avoiding iatrogenic insults such as radiocontrast procedures or certain medications in susceptible patients remains paramount. Within intensive care, daily medication review, judicious volume management, and vigilance for new onset risk factors can prevent AKI in at-risk individuals [79]. Genetic susceptibility to sepsis and septic AKI is an active area of study. Candidates include genes regulating inflammation (TNF, IL-6), endothelial function (eNOS), and coagulation (PAI-1) [80]. Genotyping may eventually guide AKI prevention or early intervention in infection-prone individuals. Other polymorphisms linked to oxidative stress, apoptosis, and healing pathways likely influence AKI recovery and sequelae [81].

Biomarkers provide complementary precision data by tracking real-time kidney damage [82]. A urinary biomarker panel demonstrated improved prediction of AKI recovery versus clinical models alone [83]. Incorporating novel biomarkers with genetics and clinical features could optimize highly personalized prognosis. Selected

markers may also predict response to therapies targeting particular pathophysiologic pathways [84].

Lifestyle modification represents another facet of individualized AKI prevention and management. Patients with chronic conditions like hypertension, diabetes, and CKD require counseling on diet, physical activity, weight control, and avoidance of nephrotoxic substances to reduce AKI risk. These same principles aid rehabilitation after AKI. Nutrition assessment and protein intake optimization are critical. Stress management and mental health support address psychosocial aspects influencing outcomes [85].

The future outlook for eradicating and managing AKI

Despite extensive research, AKI has remained a common and challenging syndrome. However, progress in elucidating mechanisms, predicting onset, and mitigating sequelae provides hope for improving future prevention and management. Systems approach leveraging massive data, and AI may transform prediction. Integrating novel biomarkers, genetic risks, and EHR trends into machine-learning models will enable earlier risk identification in varied settings. Wearables monitoring individual physiology may also contribute real-time data. With sufficient lead time, targeted prevention in susceptible people could significantly reduce AKI incidence [86]. A better understanding of AKI subtypes will open doors for tailored therapy. The division into flow-dependent hemodynamic, septic, nephrotoxic, and obstructive AKI is likely too simplistic. Molecular phenotyping, bioinformatics, and AI-based pattern recognition applied to multi-omics data may reveal distinct endotypes with optimal treatment responses. Matching specific interventions like vasodilators, anti-cytokines, or stem cells to AKI endotypes could dramatically improve outcomes [87]. Innovations in modulating the immune response hold promise [88]. Regulatory T cells help contain inflammation and promote tissue recovery [89]. Therapies promoting Treg mobilization are being explored [90]. Tolerogenic dendritic cells and mesenchymal stem cells may similarly mitigate immunopathology and enhance repair [91]. Optimizing the balance between pro- and anti-inflammatory forces is critical. Biomaterials and cell therapies help reconstitute kidney structure and function by replacing damaged and apoptotic cells [92]. Scaffolds seeded with progenitor cells facilitate endogenous regeneration [93]. Renal organoids generated from patient-derived induced pluripotent stem cells recapitulate kidney cell diversity, enabling disease modeling and drug screening [94].

Despite these advances, prevention will remain imperative. Population health initiatives promoting awareness of AKI risk factors and prevention in at-risk groups can help drive change. Policy and institutional changes will also effectively minimize nephrotoxin exposure, ensure prompt recognition, and provide appropriate follow-up for AKI patients. Ultimately, eradicating AKI will require integrative approaches across the translational spectrum, from public health to personalized nanomedicine.

Conclusion

Diverse mechanisms such as hemodynamic, inflammatory, and cytotoxic derangements are involved in causing functional impairment. Despite clinical risk factors and fundamental scientific advances, prediction and diagnosis have remained challenging. While serum creatinine is widely used, its delayed rise prompts the development of novel biomarkers and algorithms to enable earlier detection. Supportive care predominates, given the lack of targeted therapies. However, innovative options, including stem cells, growth factors, and traditional medicines, show promise in experimental models. Integrating multi-omics data and artificial intelligence constitutes the future of personalized prediction and management. However, prevention through risk factor modification and nephrotoxin avoidance remains paramount. Continued research across the translational spectrum is imperative to unravel the intricacies of AKI and translate discoveries into tangible patient benefits.

Recommendations

Moving forward, a systems biology approach leveraging multi-omics data integration with physiological monitoring and imaging will likely provide the most comprehensive perspective on AKI subtypes and enable precision management. Machine learning methodologies should be applied to these expansive datasets to reveal predictive patterns and therapeutic targets. Development and validation of AKI biomarker panels with greater sensitivity and biological specificity than creatinine should continue. Novel drugs and traditional medicines warrant testing in robust randomized controlled trials using standardized endpoints. Personalized medicine integrating pharmacogenomics, novel biomarkers, and lifestyle modification should be employed to optimize prevention and rehabilitation. Public health initiatives promoting awareness and avoidance of nephrotoxins require expansion. Ultimately, conquering AKI will necessitate integrative efforts across the biomedical research spectrum.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors contribution's

Study design, data collection, writing and final approval: All authors; Ensuring the accuracy: Tamer A Addissouky.

Conflict of interest

The authors declared no conflict of interest.

Acknowledgements

The authors thank all the researchers and the supported universities that have made great efforts in their studies.

References

[1] Joannidis M, Meersch-Dini M, Forni LG. Acute kidney injury. Intensive Care Med. 2023; 49(6):665-8. [DOI:10.1007/s00134-023-07061-4] [PMID]

[2] Bikbov B, Fortino I, Leoni O, Nobili A, Tettamanti M. Burden of acute kidney injury among adult hospital patients in the Italian Lombardy Region: A 20-Year Real-World Data Analysis. Nephron. 2023; 147(10):599-607. [PMID]

[3] Bani Hani A, Abu Abeeleh M, Al-Najjar S, Alzibdeh A, Mansour S, Bsisu I, et al. Incidence, risk factors and outcomes of acute kidney injury in surgical intensive care unit octogenarians at the Jordan University Hospital. BMC Geriatr. 2023; 23(1):266. [DOI:10.1186/s12877-023-03975-2] [PMID]

[4] Massoth C, Küllmar M, Pajares Moncho A, Susana GS, Grigoryev E, Ivkin A, et al. Implementation of the Kidney Disease Improving Global Outcomes guidelines for the prevention of acute kidney injury after cardiac surgery: An international cohort survey. Eur J Anaesthesiol. 2023; 40(6):418-24. [DOI:10.1097/EJA.0000000000001837] [PMID]

[5] Almazmomi MA, Esmat A, Naeem A. Acute kidney injury: Definition, management, and promising therapeutic target. Cureus. 2023; 15(12):e51228. [DOI:10.7759/cureus.51228] [PMID]

[6] Yu Y, Li C, Zhu S, Jin L, Hu Y, Ling X, et al. Diagnosis, pathophysiology and preventive strategies for cardiac surgery-associated acute kidney injury: A narrative review. Eur J Med Res. 2023; 28(1):45. [DOI:10.1186/s40001-023-00990-2] [PMID]

[7] Addissouky TA, Khalil AA, El Agroudy AE. Assessment of potential biomarkers for early detection and management of Glomerulonephritis patients with diabetic diseases. Am J Clin Pathol. 2023; 160(Supplement_1):S18–9. [DOI:10.1093/ajcp/aqad150.040]

[8] Højagergaard MA, Beske RP, Hassager C, Holmvang L, Jensen LO, Shacham Y, et al. Neutrophil Gelatinase-Associated Lipocalin (NGAL) in Patients with ST-Elevation Myocardial Infarction and Its Association with Acute Kidney Injury and Mortality. J Clin Med. 2023; 12(11):3681. [DOI:10.3390/jcm12113681] [PMID]

[9] Albert A, Radtke S, Blume L, Bellomo R, Haase M, Stieger P, et al. Neutrophil gelatinase-associated lipocalin cutoff value selection and acute kidney injury classification system determine phenotype allocation and associated outcomes. Ann Lab Med. 2023; 43(6):539-53. [DOI:10.3343/alm.2023.43.6.539] [PMID]

[10] Khandelwal A, Satariano M, Doshi K, Aggarwal P, Avasarala V, Sood A, et al. Management and outcomes of acute kidney injury due to burns: A literature review. J Burn Care Res. 2024; 45(2):323-37. [DOI:10.1093/jbcr/irad121] [PMID]

[11] Krishnasamy S, Sinha A, Bagga A. Management of acute kidney injury in critically Ill children. Indian J Pediatr. 2023; 90(5):481-91. [DOI:10.1007/s12098-023-04483-2] [PMID]

[12] Bordoni L, Kristensen AM, Sardella D, Kidmose H, Pohl L, Krag SRP, et al. Longitudinal tracking of acute kidney injury reveals injury propagation along the nephron. Nat Commun. 2023; 14(1):4407. [DOI:10.1038/s41467-023-40037-y] [PMID]

[13] Shan D, Wang YY, Chang Y, Cui H, Tao M, Sheng Y, et al. "Dynamic Cellular changes in acute kidney injury caused by different ischemia time. IScience. 2023; 26(5):106646.[PMID]

[14] Liu Y, Deng S, Song Z, Zhang Q, Guo Y, Yu Y, et al. MLIF modulates microglia polarization in ischemic stroke by Targeting EEF1A1. Front Pharmacol. 2021; 12:725268. [PMID]

[15] Kwiatkowska E, Kwiatkowski S, Dziedziejko V, Tomasiewicz I, Domański L. Renal microcirculation injury as the main cause of ischemic acute kidney injury development. Biology (Basel). 2023; 12(2):327. [DOI:10.3390/biology12020327] [PMID]

[16] Yasrebi-de Kom IAR, Dongelmans DA, Abu-Hanna A, Schut MC, de Lange DW, van Roon EN, et al. Acute kidney injury associated with nephrotoxic drugs in critically ill patients: A multicenter cohort study using electronic health record data. Clin Kidney J. 2023; 16(12):2549-58.[DOI:10.1093/ckj/sfad160] [PMID]

[17] Zarbock A, Nadim MK, Pickkers P, Gomez H, Bell S, Joannidis M, et al. Sepsis-associated acute kidney injury: Consensus report of the 28th Acute Disease Quality Initiative workgroup. Nat Rev Nephrol. 2023; 19(6):401-17. [DOI:10.1038/s41581-023-00683-3] [PMID]

[18] Niculae A, Gherghina ME, Peride I, Tiglis M, Nechita AM, Checherita IA. Pathway from acute kidney injury to chronic

kidney disease: Molecules involved in renal fibrosis. Int J Mol Sci. 2023; 24(18):14019. [DOI:10.3390/ijms241814019] [PMID]

[19] Turgut F, Awad AS, Abdel-Rahman EM. Acute kidney injury: Medical causes and pathogenesis. J Clin Med. 2023; 12(1):375. [DOI:10.3390/jcm12010375] [PMID]

[20] Addissouky TA. Detecting liver fibrosis by recent reliable biomarkers in viral hepatitis patients. Am J Clin Pathol. 2019; 152(Supplement_1):S85.[Doi:10.1093/ajcp/aqz117.000]

[21] Addissouky TA, El Agroudy AE, El-Torgoman AM, El Sayed IE, Ibrahim EM. Efficiency of alternative markers to assess liver fibrosis levels in viral hepatitis B patients. Biomed Res. 2019; 30(2):1-6. [Link]

[22] Addissouky TA, Ali M, El Tantawy El Sayed I, Wang Y. Revolutionary innovations in diabetes research: From biomarkers to genomic medicine. Iran J Diabetes Obes. 2023; 15(4):228-42. [DOI:10.18502/ijdo.v15i4.14556]

[23] Swolinsky JS, Hinz RM, Markus CE, Singer E, Bachmann F, Halleck F, et al. Plasma NGAL levels in stable kidney transplant recipients and the risk of allograft loss. Nephrol Dial Transplant. 2024; 39(3):483-95. [DOI:10.1093/ndt/gfad226] [PMID]

[24] Komaru Y, Oguchi M, Sadahiro T, Nakada TA, Hattori N, Moriguchi T, et al. Urinary neutrophil gelatinase-associated lipocalin and plasma IL-6 in discontinuation of continuous venovenous hemodiafiltration for severe acute kidney injury: A multicenter prospective observational study. Ann Intensive Care. 2023 ;13(1):42. [DOI:10.1186/s13613-023-01137-6] [PMID]

[25] Brilland B, Boud'hors C, Wacrenier S, Blanchard S, Cayon J, Blanchet O, et al. Kidney injury molecule 1 (KIM-1): A potential biomarker of acute kidney injury and tubulointerstitial injury in patients with ANCA-glomerulonephritis.Clin Kidney J. 2023; 16(9):1521-33. [DOI:10.1093/ckj/sfad071] [PMID]

[26] George M, Pillai K, Suseela KV. Kidney injury molecule-1 as a urinary biomarker for aminoglycoside induced acute kidney injury, among non-critically Ill children. Indian J Pediatr. 2023. [DOI:10.1007/s12098-023-04987-x]

[27] Addissouky TA, Wang Y, Megahed FAK, El Agroudy AE, Tantawy El Sayed IE, El-Torgoman AM. Novel biomarkers assist in detection of liver fibrosis in HCV patients. Egypt Liver J. 2021; 11(86):1-5. [DOI:10.1186/s43066-021-00156-x]

[28] Rajendran S, Xu Z, Pan W, Ghosh A, Wang F. Data heterogeneity in federated learning with Electronic Health Records: Case studies of risk prediction for acute kidney injury and sepsis diseases in critical care. PLOS Digit Health. 2023; 2(3):e0000117. [DOI:10.1371/journal.pdig.0000117] [PMID]

[29] Atia J, Evison F, Gallier S, Hewins P, Ball S, Gavin J, et al. Does acute kidney injury alerting improve patient outcomes? BMC Nephrol. 2023; 24(1):14. [DOI:10.1186/s12882-022-03031-y] [PMID]

[30] Fuhrman DY, Stanski NL, Krawczeski CD, Greenberg JH, Arikan AAA, Basu RK, et al. A proposed framework for advancing acute kidney injury risk stratification and diagnosis in children: A report from the 26th Acute Disease Quality Initiative (ADQI) conference. Pediatr Nephrol. 2024; 39(3):929-39. [DOI:10.1007/s00467-023-06133-3] [PMID]

[31] Kung CW, Chou YH. Acute kidney disease: An overview of the epidemiology, pathophysiology, and management. Kidney Res Clin Pract. 2023; 42(6):686-99. [PMID]

[32] Nørgård MØ, Svenningsen P. Acute Kidney Injury by Ischemia/Reperfusion and Extracellular Vesicles. Int J Mol Sci. 2023; 24(20):15312. [DOI:10.3390/ijms242015312] [PMID]

[33] Wang Y, Jiang H, Zhang L, Yao P, Wang S, Yang Q. Nanosystems for oxidative stress regulation in the anti-inflammatory therapy of acute kidney injury. Front Bioeng Biotechnol. 2023; 11:1120148. [DOI:10.3389/fbioe.2023.1120148] [PMID]

[34] Addissouky TA, Khalil AA. Detecting lung cancer stages earlier by appropriate markers rather than biopsy and other techniques. Am J Clin Pathol. 2020; 145(Supplement_1):S146–7. [DOI:10.1093/ajcp/aqaa161.320]

[35] Nakazawa D, Takeda Y, Kanda M, Tomaru U, Ogawa H, Kudo T, et al. Inhibition of Toll-like receptor 4 and Interleukin-1 receptor prevent SARS-CoV-2 mediated kidney injury. Cell Death Discov. 2023; 9(1):293. [DOI:10.1038/s41420-023-01584-x] [PMID]

[36] Addissouky TA, El Agroudy AE, Khalil AA. Developing a novel non-invasive serum-based diagnostic test for early detection of colorectal cancer. Am J Clin Pathol. 2023; 160(1):S17. [DOI:10.1093/ajcp/aqad150.037]

[37] Vallés PG, Gil Lorenzo AF, Garcia RD, Cacciamani V, Benardon ME, Costantino VV. Toll-like receptor 4 in acute kidney injury. Int J Mol Sci. 2023; 24(2):1415. [DOI:10.3390/ijms24021415] [PMID]

[38] Mok V, Nixon J, Hu J, Ma D. The impact of perioperative acute kidney injury/failure on short and long surgical outcomes. Anesthesiol Perioper Sci. 2023; 1(9).[DOI:10.1007/s44254-022-00001-3]

[39] Gleeson PJ, Crippa IA, Sannier A, Koopmansch C, Bienfait L, Allard J, et al. Critically ill patients with acute kidney injury: Clinical determinants and post-mortem histology.Clin Kidney J. 2023; 16(10):1664-73. [DOI:10.1093/ckj/sfad113] [PMID]

[40] Fujii K, Nakayama I, Izawa J, Iida N, Seo Y, Yamamoto M, et al. Association between intrarenal venous flow from Doppler ultrasonography and acute kidney injury in patients with sepsis in critical care: A prospective, exploratory observational study. Crit Care. 2023; 27(1):278. [DOI:10.1186/s13054-023-04557-9] [PMID]

[41] Berglund F, Eilertz E, Nimmersjö F, Wolf A, Nordlander C, Palm F, et al. Acute and long-term renal effects after iodine contrast media-enhanced computerised tomography in the critically ill-a retrospective bi-centre cohort study. Eur Radiol. 2024; 34(3):1736-45. [DOI:10.1007/s00330-023-10059-7] [PMID]

[42] Francis ST, Selby NM, Taal MW. Magnetic resonance imaging to evaluate kidney structure, function, and pathology: Moving toward clinical application. Am J Kidney Dis. 2023; 82(4):491-504. [PMID]

[43] Zhang Z, Chen Y, Zhou X, Liu S, Yu J. The value of functional magnetic resonance imaging in the evaluation of diabetic kidney disease: A systematic review and meta-analysis. Front Endocrinol (Lausanne). 2023; 14:1226830. [PMID]

[44] Altarelli M, Jreige M, Prior JO, Nicod Lalonde M, Schneider AG. Renal scintigraphy to predict persistent renal failure

after acute kidney injury: An observational study. J Nephrol. 2023; 36(4):1047-58. [DOI:10.1007/s40620-023-01569-0] [PMID]

[45] Patschan D, Patschan S, Matyukhin I, Hoffmeister M, Lauxmann M, Ritter O, et al. Metabolomics in acute kidney injury: The experimental perspective. J Clin Med Res. 2023; 15(6):283-91. [DOI:10.14740/jocmr4913] [PMID]

[46] Anand Kumar R, Maran T, Davidson J, Hassan I. Nuclear medicine imaging findings in end-stage renal disease and renal transplant complications. Clin Radiol. 2023; 78(5):333-9. [PMID]

[47] Hu J, Li Y, Zhang X, Wang Y, Zhang J, Yan J, et al. "Ultrasensitive Silicon Nanowire Biosensor with Modulated Threshold Voltages and Ultra-Small Diameter for Early Kidney Failure Biomarker Cystatin C. Biosensors. 2023; 13(6):645. [DOI:10.3390/bios13060645] [PMID]

[48] Yang K, Shang Y, Yang N, Pan S, Jin J, He Q. Application of Nanoparticles in the diagnosis and treatment of chronic kidney disease. Front Med (Lausanne). 2023; 10:1132355. [PMID]

[49] Chen Q, Wang X, Yuan C, Nan Y, Huang Q, Ai K. 2D-nanomaterials for AKI treatment. Front Bioeng Biotechnol. 2023; 11:1159989. [DOI:10.3389/fbioe.2023.1159989] [PMID]

[50] Addissouky TA, El Tantawy El Sayed I, Ali MMA, Wang Y, El Baz A, Elarabany N, et al. Shaping the future of cardiac wellness: Exploring revolutionary approaches in disease management and prevention. J Clin Cardiol. 2024; 5(1):6-29. [DOI:10.33696/cardiology.5.048]

[51] Huang Z, Chun C, Li X. Kidney targeting peptide-modified biomimetic nanoplatforms for treatment of acute kidney injury. J Control Release. 2023; 358:368-81. [PMID]

[52] Patschan D, Patschan S, Matyukhin I, Ritter O, Dammermann W. Metabolomics in acute kidney injury: The clinical perspective. J Clin Med. 2023; 12(12):4083. [DOI:10.3390/jcm12124083] [PMID]

[53] Li Z, Lu Y, Yang L."Imaging and spatial omics of kidney injury: Significance, challenges, advances and perspectives. Med Rev (2021). 2024; 3(6):514-520. [DOI:10.1515/mr-2023-0046] [PMID]

[54] Pejchinovski I, Turkkan S, Pejchinovski M. Recent advances of proteomics in management of acute kidney injury. Diagnostics (Basel). 2023; 13(16):2648. [DOI:10.3390/diagnostics13162648] [PMID]

[55] Paranjpe I, Jayaraman P, Su CY, Zhou S, Chen S, Thompson R, et al. Proteomic characterization of acute kidney injury in patients hospitalized with SARS-CoV2 infection. Commun Med.2023; 3(1):81. [DOI:10.1038/s43856-023-00307-8] [PMID]

[56] Chen J, Zheng QY, Wang LM, Luo J, Chen KH, He YN. Proteomics reveals defective peroxisomal fatty acid oxidation during the progression of acute kidney injury and repair. Heliyon. 2023; 9(7):e18134. [PMID]

[57] Karimzadeh I, Barreto EF, Kellum JA, Awdishu L, Murray PT, Ostermann M, et al. Moving toward a contemporary classification of drug-induced kidney disease. Crit Care. 2023; 27(1):435. [DOI:10.1186/s13054-023-04720-2] [PMID]

[58] Chen Q, Nan Y, Yang Y, Xiao Z, Liu M, Huang J, et al. Nanodrugs alleviate acute kidney injury: Manipulate RONS at kidney. Bioact Mater. 2022; 22:141-67. [DOI:10.1016/j.bioactmat.2022.09.021] [PMID]

[59] Wang Y, Jiang H, Zhang L, Yao P, Wang S, Yang Q. Nanosystems for oxidative stress regulation in the anti-inflammatory therapy of acute kidney injury. Front Bioeng Biotechnol. 2023; 11:1120148. [PMID]

[60] Oo AP, Riaduzzaman MN, Alsaman MI, Rubel AR, Pisharam J, Khalil MAM, et al. Factors predictive of development of acute kidney injury in patients with covid-19 in Brunei Darussalam. Cureus. 2023; 15(4):e37230. [DOI:10.7759/cureus.37230] [PMID]

[61] Addissouky TA, Ali MMA, El Tantawy El Sayed I, Wang Y. Recent advances in diagnosing and treating helicobacter pylori through botanical extracts and advanced technologies. Arch Pharmacol Ther. 2023; 5(1):53-66. [DOI:10.33696/Pharmacol.4.045]

[62] Mattinzoli D, Molinari P, Romero-González G, Bover J, Cicero E, Pesce F, et al. Is there a role in acute kidney injury for FGF23 and Klotho? Clin Kidney J. 2023; 16(10):1555-62. [DOI:10.1093/ckj/sfad093] [PMID]

[63] Edelstein CL. Biomarkers in acute kidney injury." biomarkers of kidney disease. 2016; 241-315. [DOI: 10.1016/B978-0-12-803014-1.00006-6]

[64] Addissouky TA, Khalil AA, El Agroudy AE. Assessing the efficacy of a modified triple drug regimen supplemented with mastic gum in the eradication of helicobacter pylori infection. Am J Clin Pathol. 2023; 160, I(Supplement_1):S19. [DOI:10.1093/ajcp/aqad150.041]

[65] Kalariya Y, Kumar A, Ullah A, Umair A, Neha F, Madhurita F, et al. Integrative medicine approaches: Bridging the gap between conventional and renal complementary therapies. Cureus. 2023; 15(9):e46033. [DOI:10.7759/cureus.46033] [PMID]

[66] Addissouky TA, Megahed F, Elbaz A, El Sayed I. Efficiency of mixture of olive oil and figs as an antiviral agents: A review and perspective. Int J Med Sci Health Res. 2020; 4(4):107-11. [Link]

[67] Jin Q, Liu T, Ma F, Yang L, Mao H, Wang Y, et al. Therapeutic application of traditional chinese medicine in kidney disease: Sirtuins as potential targets. Biomed Pharmacother. 2023; 167:115499. [PMID]

[68] Addissouky TA, El Tantawy El Sayed I, Ali MMA, Wang Y, El Baz A, Khalil AA, et al. Latest advances in hepatocellular carcinoma management and prevention through advanced technologies. Egypt Liver J. 2024; 14(2). [DOI:10.1186/s43066-023-00306-3]

[69] Bajaj T, Koyner JL. Artificial intelligence in acute kidney injury prediction. Adv Chronic Kidney Dis. 2022; 29(5):450-60. [DOI:10.1053/j.ackd.2022.07.009] [PMID]

[70] Yu X, Ji Y, Huang M, Feng Z. Machine learning for acute kidney injury: Changing the traditional disease prediction mode. Front Med (Lausanne). 2023; 10:1050255. [PMID]

[71] Kashani KB, Awdishu L, Bagshaw SM, Barreto EF, Claure-Del Granado R, et al. Digital health and acute kidney injury: Consensus report of the 27th Acute Disease Quality

Initiative workgroup. Nat Rev Nephrol. 2023; 19(12):807-18. [DOI:10.1038/s41581-023-00744-7] [PMID]

[72] Addissouky TA, Wang Y, El Sayed IE, Baz AE, Ali MM, Khalil AA. Recent trends in Helicobacter pylori management: harnessing the power of AI and other advanced approaches. Beni-Suef Univ J Basic Appl Sci. 2023; 12(1):80. [Link]

[73] Wu C, Zhang Y, Nie S, Hong D, Zhu J, Chen Z, et al. Predicting in-hospital outcomes of patients with acute kidney injury. Nat Commun. 2023; 14(1):3739. [DOI:10.1038/s41467-023-39474-6] [PMID]

[74] Addissouky TA, El Sayed IET, Ali MMA, Wang Y, El Baz A, Elarabany N, et al. Oxidative stress and inflammation: Elucidating mechanisms of smoking-attributable pathology for therapeutic targeting. Bull Natl Res Cent. 2024; 48(16). [DOI:10.1186/s42269-024-01174-6]

[75] Addissouky TA, El Sayed IE, Ali MM, Wang Y, El Baz A, Khalil AA, Elarabany N. Molecular pathways in sepsis pathogenesis: Recent advances and therapeutic avenues. J Cell Immun. 2024; 5(6):174-83. [DOI: 10.33696/immunology.5.183]

[76] Addissouky TA, Ali MMA, Sayed IETE, Wang Y. Emerging advanced approaches for diagnosis and inhibition of liver fibrogenesis. Egypt J Intern Med. 2024; 36(19). [DOI:10.1186/s43162-024-00283-y]

[77] Reizine NM, O'Donnell PH. Modern developments in germline pharmacogenomics for oncology prescribing. CA Cancer J Clin. 2022; 72(4):315-32. [DOI:10.3322/caac.21722] [PMID]

[78] Schlosser P, Scherer N, Grundner-Culemann F, Monteiro-Martins S, Haug S, Steinbrenner I, et al. Genetic studies of paired metabolomes reveal enzymatic and transport processes at the interface of plasma and urine. Nat Genet. 2023; 55(6):995-1008. [DOI:10.1038/s41588-023-01409-8] [PMID]

[79] Alshahrani S. Renin-angiotensin-aldosterone pathway modulators in chronic kidney disease: A comparative review. Front Pharmacol. 2023; 14:1101068. [DOI:10.3389/fphar.2023.1101068] [PMID]

[80] Addissouky TA, El Sayed IE, Ali MM, Alubiady MH. Optical insights into fibrotic livers: Applications of near-infrared spectroscopy and machine learning. Arch Gastroenterol Res. 2024; 5(1):1-10. [DOI: 10.33696/Gastroenterology.5.048]

[81] Stasi A, Franzin R, Caggiano G, Losapio R, Fiorentino M, Alfieri C, et al. New frontiers in sepsis-induced acute kidney injury and blood purification therapies: The role of polymethylmethacrylate membrane hemofilter. Blood Purif. 2023; 52(Suppl 1):1-14. [PMID]

[82] Addissouky TA, El Tantawy El Sayed I, Ali MMA, Wang Y, El Baz A, Khalil AA, et al. Can vaccines stop cancer before it starts? Assessing the promise of prophylactic immunization against high-risk preneoplastic lesions. J Cell Immunol. 2023; 5(4):127-40. [DOI:10.33696/immunology.5.178]

[83] Al-Husinat L, Alsabbah A, Hmaid AA, Athamneh R, Adwan M, Hourani MN, et al. Norepinephrine may exacerbate septic acute kidney injury: A narrative review. J Clin Med. 2023; 12(4):1373. [DOI:10.3390/jcm12041373] [PMID]

[84] Conticini E, Naveen R, Sen P, Singh M, Rathore U, Anuja AK, et al. Renal injury, biomarkers, and myositis, an understudied aspect of disease: Prospective study in the myocite cohort. Front Med (Lausanne). 2023; 10:1127657. [PMID]

[85] Alkhatib L, Velez Diaz LA, Varma S, Chowdhary A, Bapat P, Pan H, et al.Lifestyle modifications and nutritional and therapeutic interventions in delaying the progression of chronic kidney disease: A review. Cureus. 2023; 15(2):e34572. [DOI:10.7759/cureus.34572] [PMID]

[86] Tang Z, Cui T, Liu H, Jian J, Li D, Yang Y, Ren T. Wearable chemosensors in physiological monitoring. Chemosensors. 2023; 11(8):459. [DOI:10.3390/chemosensors11080459]

[87] Li DD, Li N, Cai C, Wei CM, Liu GH, Wang TH, et al. A molecular network-based pharmacological study on the protective effect of Panax notoginseng rhizomes against renal ischemia-reperfusion injury. Front Pharmacol. 2023; 14:1134408. [DOI:10.3389/fphar.2023.1134408] [PMID]

[88] Addissouky TA, Ali MMA, El Tantawy El Sayed I, Wang Y, El Baz A, Elarabany N, et al. Preclinical promise and clinical challenges for innovative therapies targeting liver fibrogenesis. Arch Gastroenterol Res. 2023; 4(1):14-23. [DOI: 10.33696/Gastroenterology.4.044]

[89] Lee K, Thompson EA, Gharaie S, Patel CH, Kurzhagen JT, Pierorazio PM, et al. T cell metabolic reprogramming in acute kidney injury and protection by glutamine blockade. JCI Insight. 2023; 8(12):e160345. [PMID]

[90] Goto H, Kinoshita M, Oshima N. Heatstroke-induced acute kidney injury and the innate immune system. Front Med (Lausanne). 2023; 10:1250457. [DOI:10.3389/fmed.2023.1250457] [PMID]

[91] Guerrero-Mauvecin J, Villar-Gómez N, Rayego-Mateos S, Ramos AM, Ruiz-Ortega M, Ortiz A, et al. Regulated necrosis role in inflammation and repair in acute kidney injury. Front Immunol. 2023; 14:1324996. [DOI:10.3389/fimmu.2023.1324996] [PMID]

[92] Fu Z, Zhang Y, Geng X, Chi K, Liu C, Song C, et al. Optimization strategies of mesenchymal stem cell-based therapy for acute kidney injury. Stem Cell Res Ther. 2023; 14(1):116. [DOI:10.1186/s13287-023-03351-2] [PMID]

[93] Wang W, Zhang M, Ren X, Song Y, Xu Y, Zhuang K, et al. Single-cell dissection of cellular and molecular features underlying mesenchymal stem cell therapy in ischemic acute kidney injury. Mol Ther. 2023; 31(10):3067-83. [PMID]

[94] Soranno DE, Rodell CB. Novel therapeutics: Can hydrogels work to treat kidney disease? Nephron. 2023; 147(12):769-73. [PMID]