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Title: A Review on Prospect of Creatinine Meter as a Point-of-Care Device for Instant Renal Function Check

Authors: Sneha Maiti,
Department of Electronics and Communication Engineering,
Haldia Institute of Technology, ICARE, Haldia, India

Smarajit Maiti
Department of Medical Laboratory Technology,
Haldia Institute of Health Sciences, ICARE, Haldia, India.

Correspondence: Sneha Maiti.

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Abstract:
Renal failure remains a global health concern, with high rates of morbidity and mortality. This necessitates early and accurate detection of kidney dysfunction. Creatinine, a by-product of muscle metabolism, serves as a key biomarker for assessing renal health. We reviewed here existing strategies of creatinine analysis. While conventional detection techniques, such as the Jaffe reaction, are widely used, they suffer from low specificity, interference by non-creatinine substances, and the use of hazardous reagents like picric acid. These limitations hinder timely and accurate diagnosis, especially in point-of-care (POC) and home settings. In recent years, innovative sensing strategies including electrochemical, spectroscopic, and molecularly imprinted polymer (MIP)-based systems have emerged, offering enhanced sensitivity, selectivity, and miniaturization capabilities for portable applications.
This review paper explores the development of a robust, accurate, and user-friendly POC creatinine meter by integrating advanced enzymatic sensing with optimized signal transduction technologies. The device aims to overcome current limitations by enabling real-time creatinine monitoring in both clinical and non-clinical environments. Emphasis is placed on improving precision at low creatinine concentrations, minimizing cross-reactivity, and ensuring cost-effective fabrication. A comparative analysis of existing techniques—such as the Jaffe method, enzymatic assays, ion-selective electrodes, and turbidimetric and photometric approaches—is presented. Furthermore, the paper proposes a prospective design strategy for a next-generation creatinine POC meter capable of capillary blood analysis. This article might focus on the prospective development of scalable, field-deployable creatinine meters that can transform early-stage kidney health management.

***Keywords*: Kidney function test, Jaffe reaction, creatinine meter, POC device, sensor based signaling.**

INTRODUCTION:

Renal failure is a very prevalent condition that has a high rate of morbidity and death (1-3). Controlling the course of the disease and enhancing patient outcomes depend heavily on early identification. Serum creatinine, which is commonly determined via the Jaffe reaction, is a crucial biomarker for evaluating kidney function. Blood creatinine levels typically range from 0.84 to 1.21 mg/dL. Nevertheless, the Jaffe method has a number of

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drawbacks, such as poor sensitivity, low precision, and interference by nonspecific substances such ammonium ions (4). Furthermore, the technique uses picric acid, which is hazardous and flammable, raising questions about safety in lab and medical settings. More accurate and dependable creatinine detection methods have been developed as a result of these limitations (4).

Researchers have investigated a range of different detection techniques, such as spectroscopic, electrochemical, and chromatography-based technologies, in order to overcome these difficulties. To improve specificity and sensitivity, sensor technologies that include enzymes, molecularly imprinted polymers (MIPs), and nanoparticles have also been created. Theoretically, these developments aim to enhance creatinine detection selectivity, signal amplification, and molecular recognition. Practically speaking, the goal is to create sensors that are small, easy to use, and extremely sensitive and accurate so that patients can perform point-of-care testing (POCT) for self-monitoring (4-7).

Molecularly imprinted electro- chemiluminescence-based sensors have proven to be the most accurate of the many detection techniques. These sensors have an incredibly low detection limit of 0.5 nM and function within a linear concentration range of 5–1 mM (8). They also offer a resolution of 2 million measurable points, guaranteeing extremely precise and thorough results. This strategy's theoretical foundation is utilizing electro-chemiluminescence to maximize signal creation while reducing background interference from other biomolecules (8). In real-world applications, the reduction in size of these sensors could transform clinical diagnostics by increasing the accessibility of high-precision creatinine monitoring. Before they can be widely used for routine medical use, more research is necessary to confirm their long-term reliability, cost-effectiveness, and ease of use.

One tool for determining the amount of creatinine in blood or urine is a creatinine meter. The amount of creatinine, a waste product produced by muscle metabolism, can reveal kidney health. Normal creatinine levels indicate good kidney function, however high levels may indicate renal disease. Creatinine meters come in two primary varieties:

Creatinine meters for blood: These instruments determine the amount of creatinine present in a little blood sample, usually obtained by venipuncture or fingerstick (9). They are portable and can be used for routine kidney health monitoring at clinics, hospitals, or even homes.

Significance and emergence of kidney function evaluation

Evaluation of kidney function is important because it aids in determining the general health of the kidneys, identifies early disease indicators, and tracks how well therapies for diseases like chronic kidney disease (CKD) are working. The procedure has been simplified by the introduction of more accurate and practical techniques, such as estimated glomerular filtration rate (eGFR), which makes integration into standard clinical practice simpler. Even smallest deterioration of kidney function has massive devastating effects on overall health status. This leads to quick accumulation of toxic substances in the body that affects heart and brain very fast. Moreover, kidney damage becomes irreversible frequently resulting permanently damage to the body. Unlike glucose or other biochemical parameters smallest increase of blood creatinine level signifies initiation of major kidney damage. Additionally, this ailment has few symptoms; therefore it goes undiagnosed in the early stages. As a result, patients are typically timed out when the screening results are positive. Some other confounding factors like diabetes, chronic liver disease and cardiac anomalies significantly increase the chance of kidney failure. So, instant screening and early detection of kidney function may save hundreds of lives.

Kidney function marker creatinine and its instant screening

A vital tool for people with chronic renal disease or at risk for kidney dysfunction, several portable home monitoring devices enable patients to follow their kidney health and check their creatinine levels on a regular basis.

In healthcare settings, using a creatinine meter for point-of-care (POC) testing has various benefits, especially when it comes to speed, convenience, and quick decision-making. Below is a summary of its main applications:

Instant Diagnosis of Kidney function:

Healthcare professionals may evaluate kidney function without waiting for lab results thanks to creatinine meters, which often deliver readings in a matter of minutes. This is particularly helpful in acute care or emergency situations where prompt diagnosis and treatment are essential. Acute Kidney Injury (AKI) Detection: POC creatinine testing can assist in the prompt detection of acute kidney injury (AKI) in intensive care units (ICUs) or emergency rooms. Prompt identification of AKI can result in more successful treatments and stop additional kidney damage (10).

Simplified Clinical Workflow:
POC creatinine meters allow for on-the-spot testing at the patient's bedside, cutting down on delays and doing away with the need to send blood samples to a lab. When working with severely ill patients or in hectic hospital settings, this can be especially helpful.

Better Patient Management: Without waiting for lab-based results, medical professionals may promptly evaluate kidney function and modify treatment strategies accordingly, improving patient care and cutting down on wait periods for essential treatments.

Point-of-Care Examinations in Remote Locations Accessibility: In rural or isolated locations where laboratory testing facilities might not be easily accessible, creatinine meters might be utilized. Without having to transfer patients or samples to far-off hospitals, this can assist medical professionals in these locations in performing critical kidney function testing.

Convenient and Portable: A lot of POC creatinine meters are small, lightweight, and easy to use, which makes them perfect for use in places with inadequate medical facilities.

Routine checking of kidney function Following Surgery and Treatment Immediate Post-Operative Monitoring: To monitor kidney function and make sure there are no kidney-related issues following surgery, particularly one involving the kidneys, creatinine levels can be measured right away. POC meters speed up and simplify this evaluation. Medication and Dialysis Adjustments: Patients receiving dialysis or taking specific drugs frequently have their creatinine levels checked. POC testing enables medical professionals to make real-time adjustments to medications or dialysis treatments, guaranteeing that the patient is getting the right kind of care.

Rapid Response to Critical Situations:
The POC creatinine meter enables medical professionals to promptly ascertain whether kidney failure or other complications are present in urgent care or critical care settings where patients may exhibit signs of kidney dysfunction or other conditions that impact kidney health. Observation While Receiving Fluid Therapy: When treating patients undergoing intense fluid therapy, creatinine levels are crucial. POC creatinine testing can assist medical professionals in real-time renal function monitoring and treatment plan modification to prevent consequences like kidney failure or fluid overload.

Monitoring of Chronic Kidney Disease (CKD):
Frequent Monitoring: It's critical to regularly check creatinine levels in patients with chronic renal disease. During clinic appointments, a POC creatinine meter can be used to monitor the course of the disease and assist in making prompt decisions about therapy or care plan modifications. Prevention of consequences: POC testing can help prevent future consequences, such as renal failure or the need for dialysis, in patients with CKD by detecting large changes in creatinine levels early.

Different procedures of kidney function testing

1. Jaffe Reaction (Colorimetric Method):

One of the most popular techniques for determining creatinine is the Jaffe reaction. It involves the formation of a colored complex by the interaction of creatinine with alkaline picrate (picric acid), which is subsequently quantified using spectrophotometry.
The brief mechanism is sample's creatinine combines with alkaline picrate to produce an orange-red hue. The amount of creatinine in the sample directly correlates with the color's intensity. And that is compared with a standard calibration curve observed at510 nm of wavelength. It is an easy and cheap method but limitations include; influence of interfering chemicals in the sample i.e. proteins or ketones, not suitable for POC testing because time consuming for large number of sample (11).

2. The Enzymatic Approach

Compared to the Jaffe reaction, the enzymatic method is more precise and specific. The conversion of creatinine to other compounds, which can subsequently be quantified, is specially catalyzed by enzymes. Creatinine is catalyzed into creatine and water by the enzyme creatininase. A further enzymatic process is required to make color-change reactions which are measured spectrophotometrically. It has less interference problem of other

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chemicals but this process is more complicated than the Jaffe approach and necessitates the use of more reagents and chemicals (12).

3. Ion-Selective Electrodes (ISE):
Ion-selective electrode technology can be used to measure creatinine levels by detecting the concentration of creatinine ions in a sample. A creatinine-selective electrode is used to measure the potential difference between the electrode and the sample. The electrode responds to the specific ions of creatinine in the sample, producing a signal that correlates with creatinine concentration. This method provides a direct and precise measurement of creatinine without the need for complex chemical reactions. Requires calibration with known standards, and may still be influenced by the presence of other ions or substances (13).

4. Spectrophotometric or Photometric Approach
This technique measures the amount of light absorbed by a colorful compound that is produced when creatinine combines with a particular reagent. After series of reaction steps the colorful product absorbs light of a particular wavelength is measured by a photometric sensor. The absorbance which is directly proportional to creatinine concentration is measured by the *creatinine meters* and is more users friendly. This approach is susceptible to influence from other compounds in the sample (14).

5. Capillary Electrophoresis (CE):
CE is an analytical method that uses an electric field to separate ions according to their size and charge. In CE, an electric field is used to separate the creatinine from other substances according to its mobility after a sample is placed into a capillary tube. By measuring the strength of the signal produced when creatinine flows through a detector typically a UV detector the creatinine concentration is ascertained. Benefits: Very exact findings can be obtained by accurately separating creatinine from interfering compounds. This technique requires specialist equipment, making it more complicated than other approaches and possibly impractical for point-of-care testing (15).

6. Turbidimetric Approach
When creatinine in the sample combines with a certain reagent, a precipitate or turbidity is formed. The reagent and creatinine combine to produce an insoluble combination, which makes the sample murky. A light scattering detector is used to determine the degree of turbidity and the amount of scattering is correlated with the concentration of creatinine. This method is easily implemented and applicable to point-of-care testing. Other materials or particles in the sample that produce turbidity may have an impact. Each method has its advantages in terms of specificity, complexity, and ease of use.
The Jaffe reaction and enzymatic methods are most commonly used in creatinine meters for point-of-care testing, with the choice of method depending on the application, available technology, and need for accuracy (16).

CURRENT SCENARIO OF GLOBAL USAGE OF CREATININE METER

Nowadays, a range of POC devices can be used to test creatinine in a number of clinical settings, including community-based screening at health camps, clinical emergencies, and risk assessments prior to the administration of contrast material, such as in MRIs. Worldwide, POC creatinine analyzers are based on both blood gas and non-blood gas sources. These are produced and sold by several businesses under various brand names, such as Stat Sensor and Dri-Chem 4000 for non-blood gas kinds or i-STAT and IRMA TRUpoint for blood gas types. (17).
Although the majority of non-analytical creatinine meter devices rely on enzymatic techniques, there are differences in the final point color/signal generation and calculations. These mostly include enzymatic with indicator absorbance, enzymatic with dye absorbance, enzymatic with dye reflectance, and enzymatic with amp biosensor. The majority of methods employ a full blood sample together with consumables like dry slides, cartridges, or sensor cassettes (18).
POC is now used by 10–15 devices worldwide to measure whole blood or serum/plasma creatinine. Positive bias still affects POC creatinine gadget manufacturers to varying degrees. Most devices have poor precision when blood creatinine levels are low (19). As the prevalence of CKD increases worldwide, there is an increasing need for efficient screening methods to assess CKD risk. A POC device needs to have fast turnaround times and robust analytical performance specifications in addition to capillary sample in order to correctly categorize CKD risk (19). No device currently meets these requirements. More research is required in this situation in order to create new approaches for the development of more reliable POC devices.

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OUTLINED A PROSPECTIVE STRATEGY TO DEVELOP A DEPENDABLE CREATININE METER POC DEVICE

1. Sample exposure to strip sensor (fig 1)
A small volume (typically a drop) of blood or serum is applied onto the enzyme-immobilized region of the sensor surface. Creatininase and Creatine Oxidase, the key enzymes are immobilized here on a biocompatible matrix (e.g., chitosan or Nafion) on the surface of the working electrode (Table 1).

2. Enzymatic Conversion of Creatinine

Step 1: Creatininase (creatinine amidohydrolase) catalyzes the hydrolysis of creatinine to creatine.

Step 2: Creatine oxidase then oxidizes creatine to sarcosine, simultaneously generating hydrogen peroxide (H_2O_2) as a byproduct at pH ~7.4, 25–37°C.

Stoichiometric production of H_2O_2 is proportionate to the creatinine concentration present in the sample.

3. Electrochemical Oxidation of H_2O_2

The H_2O_2 diffuses to the working electrode (WE) surface, where it undergoes electrochemical oxidation according to the following reaction: $H_2O_2 \rightarrow O_2 + 2H^+ + 2e^-$

This oxidation reaction generates a measurable faradaic current, directly proportional to the local H_2O_2 concentration—and hence, to the initial creatinine level. The sensor comprises a conventional three-electrode system:

Working Electrode (WE): Carbon or platinum-based, where oxidation occurs.
Reference Electrode (RE): Ag/AgCl, providing a stable reference potential (~+0.6 V vs. RE).
Counter Electrode (CE): Completes the circuit and allows current flow.

Table 1. Tabulated data show the requirements of different components in Biochemical layer. and Electronics layer. Possible best combination of device components are, Microcontroller: ESP32 (for better performance and wireless support), ADC: Built-in 12-bit ADC of ESP32, LCD: I2C 16x2 LCD display, Sensor output: From transimpedance amplifier (op-amp) to analog input, Additional features: Optional serial data output

BIOCHEMICAL LAYER	
Component	**Details**
Enzymes	Creatininase + Creatine Oxidase (co-immobilized)
Substrate	Glass, gold, or screen-printed carbon electrode (SPCE)
Working Electrode	Carbon/Platinum (H_2O_2 sensitive)
Reference Electrode	Ag/AgCl
Counter Electrode	Carbon/Platinum
ELECTRONICS LAYER	
Component	**Function**
Transimpedance Amplifier (TIA)	Converts tiny electrode current into voltage
Op-Amp (e.g., TLV2372, LMP91000)	Used in TIA and buffering
Analog-to-Digital Converter (ADC)	Reads voltage output
Microcontroller (e.g., Arduino Nano, ESP32)	Converts ADC to digital value and displays it
Display (OLED/16x2 LCD)	Displays creatinine in mg/dL
Power Source	Battery or USB

4. Signal Amplification via Transimpedance Amplifier

Due to the low magnitude of the oxidation current (nanoampere to microampere range), direct measurement is impractical. To address this, the current signal is amplified using a transimpedance amplifier (TIA) that is a low-noise operational amplifier (e.g., TLV2372), it converts the current to a corresponding voltage signal using a high-value feedback resistor (typically 10 MΩ): $V_{out} = -I_{(we)} \times R_{(f)}$. This voltage signal now represents the electrochemical activity corresponding to the creatinine concentration (Table 1).

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5. Signal Acquisition and Processing
The output voltage is interfaced with an analog-to-digital converter (ADC) integrated within a microcontroller unit (e.g., Arduino Nano or ESP32). The ADC digitizes the voltage for computational processing. Using a creatinine standards calibration curve, the microcontroller translates the digitized signal into a concentration value (typically reported in mg/dL or µmol/L). The physiological relevant value is 0.5–5.0 mg/dL).

6. Data Display and Output
The final creatinine concentration is displayed on a compact OLED or LCD module interfaced with the microcontroller. The system provides a rapid, user-readable output, enabling near real-time point-of-care diagnostics.

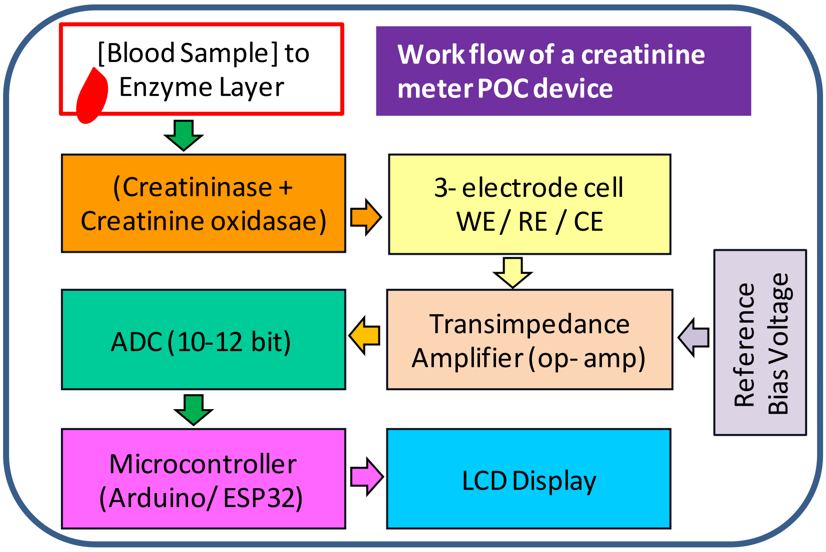

Figure 1. Outlined diagram and work flow of a prospective creatinine meter

Prospective key features of this flow:

Specificity: The enzymatic method focuses directly on creatinine, avoiding interference from other substances commonly found in blood or urine.

Rapid Results: The process is designed to provide results quickly, making it ideal for point-of-care testing.

Accuracy: Since the enzymatic reaction specifically targets creatinine, it leads to highly accurate and reliable measurements of creatinine levels.

This flow diagram outlines the process of a creatinine meter that uses the enzymatic method, which is regarded as the most reliable and accurate approach for measuring creatinine concentration.

POSSIBLE TECHNICAL CHALLENGES

Enzyme Stability and Shelf-life: Enzyme immobilization on chitosan/Nafion matrices may degrade over time under variable humidity or temperature—impacting sensor reliability.2. Sample Matrix Complexity: Blood contains interferents (ascorbic acid, uric acid, glucose, etc.) that can undergo side reactions or oxidize —leading to false positives.

Signal Drift and Noise: Despite TIA use, baseline drift, capacitive charging, and electrode fouling can impact long-term measurements. Routine baseline correction or built-in diagnostic checks would be helpful. ESP32/Arduino are good for prototyping but may not be optimized for battery life, form factor, or regulatory approval in final products.

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AREAS MAY BE DEVELOPED:

Interference Management may include permselective membranes (e.g., Nafion or polyphenol coatings) or a dual-electrode system for background subtraction. Enzyme stability can be maintained by freeze-dried enzyme films or encapsulation methods. Calibration might include on-strip reference standards or allow user calibration for improved accuracy. User friendly handling may be achieved by developing a mobile app interface or Bluetooth data output for improved usability and remote health monitoring. Manufacturability transition can be done from Arduino/ESP32 to a custom ASIC or low-power MCU for commercialization.

CONCLUSION

In summary, the creatinine meter for point-of-care testing is a powerful tool that offers rapid, convenient, and reliable assessment of kidney function. It enhances clinical decision-making, supports early intervention, and improves patient outcomes, particularly in settings like emergency care, intensive care units, and chronic disease management. Its use in both hospital and home settings provides flexibility, especially for patients who need continuous monitoring of kidney health.

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