



REVIEW ARTICLE

Point-of-Care Testing for Autoimmune Rheumatic Diseases: Benefits and Barriers

Yashwant Kumar^{1*}, Alka Bhatia²

¹Department of Immunopathology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

²Experimental Medicine and Biotechnology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

*Correspondence Author: Yashwant Kumar, *Email:* dryashwant@gmail.com.

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Abstract: Point-of-care testing (POCT) is a near-patient detection technique that could provide results within minutes. Compared to conventional laboratory testing, POCT is more beneficial particularly in emergency and urgent care settings. Detection of antinuclear antibodies and autoantibodies against extractable nuclear antigens are critical for the diagnosis and management of autoimmune rheumatic diseases (AIRD). At present, these autoantibodies are detected using conventional methods that take hours or days in centralized laboratories. POCT for AIRD is hardly practiced as they are chronic illnesses which are seen as clinical emergencies occasionally. Since POCT provides instant results, it may be life-saving in critically ill and confusing cases, particularly those admitted to intensive care units with multisystem organ failure. POCT is also very useful in rural and remote health-care centers, addressing the needs of emergent disease detection. This review aims to provide an overview of the potential use of POCT in AIRD as well as discuss the types, benefits, and shortcomings of POCT devices, and the hurdles that prevent their widespread clinical use.

Keywords: Point-of-care testing, Autoimmune rheumatic disorders, Antinuclear antibodies, Autoantibodies

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1 Introduction

Autoimmune rheumatic diseases (AIRD) represent one of the most common chronic disorders of connective tissue and musculoskeletal system. These disorders are believed to affect 3 – 5% of the world's population with a prevalence rate ranging from 2 to 10/1000 population. In recent years, an increase in the cases of these disorders has been noted [1-3]. AIRD are characterized as heterogeneous disorders that affect the joints, muscles, and multiple organs and cause significant morbidity and mortality in patients from different age groups. AIRD include but are not limited to rheumatoid arthritis (RA), systemic

lupus erythematosus (SLE), primary Sjögren's syndrome, systemic sclerosis (scleroderma), idiopathic inflammatory myositis, and the systemic vasculitis [4].

The various forms of AIRD share the common features such as constitutional symptoms, sicca symptoms, arthralgia, arthritis, hematological, renal, pulmonary, and neurological involvement. Thus, a diagnosis that can accurately identify the correct disease type of AIRD may be difficult, and a thorough examination and detailed laboratory investigations are required for making a correct diagnosis. Of note, almost 50% of patients with apparent AIRD remain undiagnosed for several months even after a regular follow-up. In the next

few years following the initial medical consultation, they develop AIRD with persistent and well-defined symptoms [5,6]. Rapid onset disease could happen to some of these patients who need to seek medical attention in the emergency department. Immediate diagnosis of such cases is always challenging as many of the clinical features resemble a wide range of ailments, for example, infections, malignancies, allergic, and other immunological disorders. Under emergencies, patients could be nearing the point of organ failure and even death. In this setting, an easy-to-use and efficient laboratory device such as point-of-care testing (POCT) that is available at the bedside is of immense value [7].

Many AIRD are associated with a different set of autoantibodies that not only help in diagnosis but are also highly useful for disease categorization, prediction of flares, and in monitoring the efficacy of therapy. The current practice is to detect these autoantibodies in blood samples in a centralized laboratory where testing is performed on conventional laboratory equipment by the trained technical staff. Such type of analysis is labor-intensive, expensive, and time-consuming as it takes several hours or days before the results are available. On the other hand, POCT is simpler and can be done in the absence of a proper laboratory setup [8]. Because of several advantages and with the increasing availability of this innovative and affordable technology, POCT is gaining popularity among the clinicians. Current knowledge regarding utility, pros, and cons of POCT in AIRD may help in improving the already available tests and developing new ones to facilitate its widespread use in clinical setting. This review, therefore, aims to critically dissect various aspects of POCT in the context of AIRD. Some of the potential assays, types of devices, advantages, and limitations are discussed.

2 The current scenario of laboratory diagnosis of AIRD

Diagnosing AIRD is a challenging task as it depends upon the clinical stage of the disease. Although the classification criteria for different rheumatic diseases are available, the diagnostic criteria for some of these disorders are not well defined [9]. The most important element for the diagnosis of AIRD is the medical history of patients. Physical and

imaging examinations are coupled with serological marker-based tests for making a diagnosis.

Often, serum autoantibodies are the only objective serological markers that can pinpoint the specific AIRD. A list of different autoantibodies commonly used for AIRD in emergency settings is available elsewhere [10]. Although together they are called antinuclear antibodies (ANA), their targets can also be found in the cytoplasm outside the nuclear compartment (e.g., Ribo-P protein, and Jo-1). Each of these antibodies is associated with a specific type of AIRD. Some of these autoantibodies (i.e., dsDNA, histones, CENP, and Scl-70) are highly specific for a disease while others (e.g., RNP and lamins) may be found in more than one disease or sometimes two or more autoantibodies may be present in a particular AIRD [11,12]. As far as their role in pathogenesis is concerned, few of the autoantibodies are involved in the tissue damage while others have diagnostic importance only or act as markers of disease development [13]. The presence of these autoantibodies in sera of a patient helps the clinician not only in confirming an autoimmune disorder but also to confine it into the best fitting category of AIRD [14].

Indirect immunofluorescence ANA test (IF-ANA) is the first and foremost test performed in a suspected case to detect multiple autoantibodies. The selection of specific markers or autoantibodies, and their interpretation is done based on the clinical observations and results of IF-ANA [9]. For example, in a hypothetical case, a clinician examining a female patient visiting an emergency unit with shortness of breath, cough, and chest pain finds it difficult to come to a diagnosis. In such a scenario, the clinician will order a range of clinical, radiological, and laboratory investigations, such as ECG, chest X-ray, complete blood counts, routine biochemistry test, and immunoassays such as IF-ANA. A positive IF-ANA test indicates an underlying AIRD such as systemic sclerosis that may be confirmed by subsequent specific ANA testing. IF-ANA is performed in a centralized laboratory; the results are available after hours or a few days, depending on the type of laboratory facility. Thus, the availability of a POCT device for the detection of ANA could be life-saving.

Similarly, other serological immunoassays such as antineutrophil cytoplasmic antibody (ANCA)

testing are equally important for detecting acute-onset autoimmune vascular diseases, for example, granulomatosis with polyangiitis or renal pulmonary syndrome, where availability of a POCT would help the clinician in making an immediate diagnosis and implementing the appropriate therapy. There are other scenarios as well where patients were initially presented to dermatology, neurology, nephrology, pulmonary medicine, oncology, or any other departments, but later on were diagnosed to have an autoimmune disorder such as SLE, neuromyelitis optica, vasculitis, and RA. Therefore, the specific serological tests to detect autoantibodies associated with these disorders not only facilitates the correct diagnosis but also help to predict disease severity, impending disease or relapse, the extent of organ involvement, and disease progression (Table 1) [15-17].

3 POCT devices

POCT has the potential to change the current practice in providing medical care to patients with AIRD in tertiary care, primary health centers, or remote medical facility, especially in the case where access to laboratory testing is restricted or delayed. The testing in a centralized lab is time-consuming as it is done in multiple steps

divided into pre-analytic (withdrawal of blood, its transport, and processing), analytic (analysis and result interpretation), and post-analytic (report preparation, and delivery to treating unit) phases (Figure 1). As a result, the chance of drop out will increase if the patient is required to make multiple visits to the hospital. POCT that could provide immediate results may help the clinician to diagnose the disease and decide the treatment during the same visit, indirectly reducing the time of patient hospitalization [18]. With such an advantage, new, simple, and cost-effective POCT techniques capable of delivering rapid, qualitative as well as quantitative information are gaining popularity in various medical specialties.

3.1 Mechanisms and technologies

In the context of AIRD, all the assays detecting one or the other autoantigens are based on the principle of immune complex or autoantigen-antibody complex formation [19]. This immunological reaction may allow both qualitative assessment of an analyte or, more importantly a quantitative measurement of its concentration. Recent advances in the field of immunosensor technologies have provided few assays with a high degree of accuracy in quantitation

Table 1. Complications of AIRD presenting as clinical emergencies

| Disease | Acute/emergency symptoms | Autoantibody |
|--|--|---|
| Systemic lupus erythematosus (SLE) | Neuropsychiatric SLE (encephalitis, stroke, seizures, and psychosis), alveolar hemorrhage, pneumonia, renal failure, transverse myelitis, catastrophic antiphospholipid syndrome, cytopenias, myocardial infarction, pericardial tamponade, mesenteric vasculitis, pancreatitis, fetal heart block | Anti-dsDNA/sm/ nucleosome/histone and other autoantibodies |
| Systemic sclerosis, Sjogren's syndrome and mixed connective tissue disorders | Pulmonary arterial hypertension, alveolar, hemorrhage, renal crisis, esophageal dysmotility, digital ischemia, right-sided heart failure, hypokalemic paralysis | Anti-RNP/CENP/RNA polymerase I, Anti-SSA/SSB/ topoisomerase I |
| Rheumatoid arthritis | Alveolar hemorrhage, atlanto-axial subluxation, cricoarytenoid arthritis, cytopenias, myocardial infarction, dysrhythmias, gastrointestinal hemorrhage catastrophic antiphospholipid syndrome | Anti-CCP |
| Granulomatosis with polyangiitis/ microscopic polyangiitis/ Goodpasture's syndrome | Subglottic stenosis, hypopharyngeal ulcers, pulmonary hemorrhage, acute renal failure | Anti-PR3/MPO/GBM |
| Antiphospholipid syndrome | Deep vein thrombosis, pulmonary thromboembolism retinal artery occlusion, fetal loss | APLA, β 2GPI |
| Dermatomyositis/polymyositis | Muscle weakness, dystonia, acute lung injury, respiratory failure, dysphagia, bowel perforation | Anti-Jo-1 |
| Parainfectious manifestations | Reactive arthritis, septic arthritis, pyogenic myositis | - |

AIRD: Autoimmune rheumatic diseases

and low detection limit. They are based on diverse mechanisms (i.e., lateral flow; electrochemical, optical, and microgravimetric sensor) and are available in different configurations [17,20-31]. Of these, surface plasmon resonance (SPR) sensor-based technique is the most rapid but requires high cost for miniaturization; hence, this technique is not suitable to be used as POCT [32]. Lateral flow-based methods are commonly used but have their shortcomings in the delivery of qualitative results, and those requiring antigen tags are of limited practical value [33]. Assays based on

electrochemical amplification using autoantigens are promising due to the low cost involved in their development as miniaturized, disposable sensor chips.

3.2 Types of POCT devices

In recent years, several platforms or POCT devices that are based on one or other methods mentioned above have been designed. They are classified based on their key elements: type of sensor used, basic principle, complexity, mode of measurement, as well as nature of use, etc. (Table 2) [34,35].

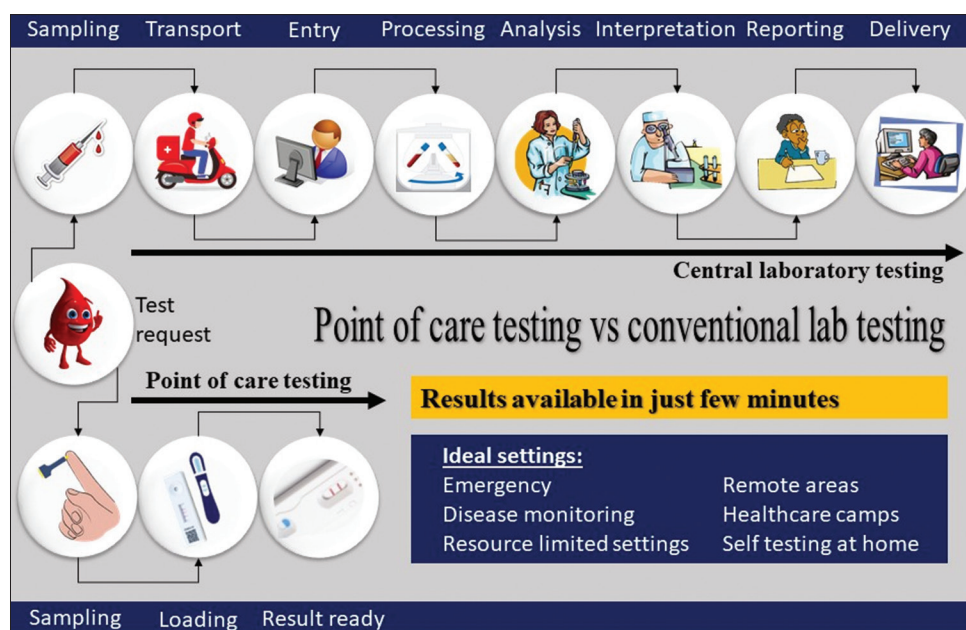


Figure 1. A comparison of patient sample testing by the conventional laboratory and by a point-of-care device. In case of conventional or centralized laboratory testing, the sample has to pass through multiple steps divided into pre-analytic (i.e., sample withdrawal and labeling, transportation to the laboratory, entry of sample details into the laboratory information system, and processing of the sample); analytic (i.e., sample analysis and result interpretation); and post-analytic phases (i.e., report preparation, and delivery). Hence, the conventional testing system is very laborious. On the other hand, point-of-care testing requires only a few steps, i.e., sample collection, testing/loading, and result analysis; final results are usually ready within few minutes.

Table 2. Types of POCT devices

| POCT device class | Examples |
|---|---|
| Type 1a: Qualitative POCT methods | Lateral flow assay (LFA)-based test strips or read-out devices |
| Type 1b: Unit-use POCT systems | Electrochemical or thin film sensor based hand held devices |
| Type 2: Benchtop POCT instruments | Test strips, cartridge, multichannel devices |
| Type 3: Viscoelastic coagulation analyzers | Coagulation analysis system based on optical aggregometry, thromboelastometry |
| Type 4: Continuous POCT measurement methods | Invasive/non-invasive continuous metabolic parameters monitoring devices |
| Type 5: Molecular biological POCT analyzers | PCR based analytical systems |
| Type 6: Direct-to-consumer testing (DCT) | Rapid test for pregnancy |

POCT: Point of care testing

3.2.1 Type I devices

Type Ia devices primarily represent a qualitative strip-based method that produces results as either positive or negative. The strips are made of a porous matrix containing dried reagents; a color change of the reagents is suggestive of the results. On the other hand, type Ib devices are the simplest form of POCT that is able to produce quantitative results. They are single-use strips that require a reader device, for example, a glucometer [36].

3.2.2 Type II devices

These POCT devices are complex and use different principles. Some examples of this type of device include spectrophotometry-based clinical chemistry analyzers, simple hematology analyzers, immunoassay, and blood gas analyzers [37].

3.2.3 Type III devices

These include complex instruments that are compatible with POCT. Thus, the operation requires qualified and trained personnel. One example of type III device is a coagulation analyzer [34].

3.2.4 Type IV devices

These devices are useful in continuous monitoring of a parameter, for example, continuous glucose monitoring. They have the potential to replace invasive devices, and they can be embedded in the subcutaneous tissue [38].

3.2.5 Type V devices

These are molecular biology-based devices that are particularly promising for the detection of infections. An important example is the real-time polymerase chain reaction-based Xpert system that uses a set of microfluidic cartridges and is able to yield raw data within an hour. The instrument has been used for the detection of various types of bacterial and viral infections. Recently, this instrument has been further proven by the rapid detection of the severe acute respiratory syndrome-Coronavirus-2 responsible for the COVID-19 pandemic [39,40].

3.2.6 Type VI or direct-to-consumer test

It is a recently introduced category where patients can choose a POCT for the measurement of a particular biochemical parameter. A common

example of this device is glucometer that can be used by patients to measure blood glucose level at home [34,41].

3.2.7 Miscellaneous devices

Devices based on other technologies such as lab-on-a-chip devices are a suitable tool for rapid testing at low-resource settings. However, the test involving this device requires a chip reader. The researchers, therefore, are working toward miniaturization of the chip reader and its integration into the chip itself. Paper-based microfluidic (PBMF) diagnostics is another low-cost option for POCT. It is similar to lateral flow immunoassay, utilizing porous cellulose-based material as a solid phase and a patterned, three-dimensional microfluidic paper for transfer of fluids. PBMF, however, is cheaper as well as user friendly [10,42]. Recently, microfluidic paper-based analytical device that relies on bioluminescence resonance energy transfer (BRET) switches for analyte recognition and colorimetric signal generation has also been added to the list of POCT device. The device uses BRET-based antibody sensing proteins that are integrated into vertically assembled multiple layers of paper [43].

3.3 Emerging POCT devices for AIRD

Application of POCT technology to the field of rheumatology is truly a work in progress. Some of the POCT devices with sensitivity and specificity comparable to the gold standard IF-ANA are in the final testing phase (**Table 3**). One such device based on lateral flow has the advantage of detecting individual antibodies, for example, dsDNA or multiple autoantibodies such as anti-Sm or anti-phospholipid antibodies, on the same strip [44]. Another reliable and user-friendly rapid test that involves the use of an anti-cyclic citrullinated peptide (CCP) for detecting RA has sensitivity and specificity comparable to ELISA [20]. Anti-CCP is an autoantibody that targets a circular peptide containing an unusual amino acid called citrulline and can be detected in blood in the very early stage of RA. It is considered a better diagnostic marker of RA than rheumatoid factor (RF) due to its higher sensitivity and specificity [45,46]. Anti-CCP POCT has recently been commercialized but its widespread availability and general acceptability in rheumatology are yet to be realized [29].

Table 3. Recently proposed POCT for AIRD

| Analyte/auto-antibody | Associated AIRD | Detection method/platform | Clinical sample | Assay time | Ref |
|-----------------------|-----------------|--|-----------------|------------|------|
| ANA | AIRD | PRI | Whole blood | 15 min | [9] |
| Anti-dsDNA | SLE | Electrochemical containing E-DNA like sensor | Serum | ~3 min | [10] |
| | | Electrochemical immunoassay | | ~30 min | [11] |
| | | Quartz crystal microbalance immunosensor | | ~60 min | [12] |
| | | SPR biosensor chip | | ~5 min | [13] |
| Anti-chromatin | SLE | Electrochemical flow- through immunosensor | Serum | 20 min | [14] |
| Anti-SSA | SjS | LIPSTICKS | Serum, saliva | ~15 min | [15] |
| Anti-La/Ro60/Ro52 | SjS | QLIPS | Serum | 25 min | [16] |
| Anti-MCV/RF | RA | LFIA | Whole blood | 15 min | [17] |
| Anti-CCP | RA | Gold based lateral flow | Serum | ~10 min | [18] |
| Anti- β 2GPI | APLA syndrome | SPR biosensor chip | Serum | ~5 min | [19] |
| Anti-MPO/PR3 | Vasculitis | Rapid lateral flow | Serum | 20 min | [20] |

AIRD: Autoimmune rheumatic diseases; POCT: Point-of-care testing; SLE: Systemic lupus erythematosus; SjS: Sjogren's syndrome; RA: Rheumatoid arthritis; APLA: Antiphospholipid; PRI: Photonic ring immunoassay; SPR: Surface plasmon resonance; LIPSTICK: Luciferase immunoprecipitation sticks; QLIPS: Quick version of luciferase immunoprecipitation systems; LFIA: Lateral flow immunochromatographic assay; SPR: Surface plasmon resonance

4 Benefits of POCT

An ideal POCT should fulfill the World Health Organization's ASSURED criteria of the following characteristics: *Affordable*, *Sensitive*, *Specific*, *User-friendly*, *Rapid*, *Equipment-free*, and *Delivered* to needy [47,48]. Any test fulfilling these criteria can increase work efficiency in situations where an immediate diagnosis is an utmost goal. Inefficiency can be very frustrating for healthcare workers because it costs money, wastes time, and compromises quality. Overcrowding in the emergency department seriously hampering clinician's work efficiency is a widely acknowledged problem and that is a place where one cannot afford to compromise with competence as it may have an adverse impact on disease outcome. POCT in all such settings may enable decisions to be made more quickly in patients who visit an emergency unit due to one or other complications of AIRD [49-51].

The POCT, as an alternative, offers several advantages. Most important among all is their rapid turnaround time. Besides, it can be performed at the bedside. Hence, a POCT saves time taken during pre- and post-analytic phases that involve the use of conventional laboratory

testing. It bypasses several steps, for example, sample transport, data entry, sample processing, and result validation. The ease of performing POCT is therefore attractive especially for the management of critically ill patients [52]. It also eliminates the chances of several errors that may take place in conventional laboratory testing, for example, the chances of non-receiving of results due to misplaced samples during transit, wrong labeling, or samples sent in wrong containers. POCT minimizes pre-analytical errors such as inappropriate or inadequate sampling, improper packaging of samples, and misidentification of patients. Issues of post-analytical errors caused by the incorrect transmission of results are also resolved. Even if a test is negative, the result is equally important as it may eliminate the requirement of expansive autoantibody profile testing or may also avoid an appointment/opinion from an autoimmunity specialist.

Further charm of POCT includes its minimal invasiveness relative to conventional laboratory testing since blood testing using POCT is possible with just a drop of blood obtained by finger prick. This may be extremely useful in neonates or infants, where sampling may be an issue. There is no need for any high-end equipment that, in addition to its running and maintenance cost, frequently takes

significant warm-up time before it is ready for analysis. POCT devices are mostly maintenance-free or come in the form of a single-use disposable strip, card, or cassette containing all the reagents required for the chemical reaction [53]. Most patients of AIRD require frequent monitoring of their clinical condition and autoantibody levels, for which they need to visit frequently to a nearby private laboratory or the hospital. POCT can assist the patient in self-assessment of the disease; therefore, it is convenient and can reassure the patient of his disease status without a visit to the clinician (**Table 4**). With further advances in technology and their mass production, routine use of POCT in AIRD is likely in the coming years [9].

5 Barriers to POCT

POCT has immense potential in bedside diagnosis of AIRD and the planning of early treatment. However, its availability and large-scale use may take considerable time as this will require additional support in the form of infrastructure, dedicated funds, and active participation by the institute, public and private sectors [54]. Furthermore, the bulk production of POCT kits or reagents is not easy as most of the serological screening or diagnostic assays for AIRD are antibody-based. These disease-specific antibodies comprise only a tiny fraction of

total serum immunoglobulin. Non-specific binding of immunoglobulin is another hurdle towards the development of a reliable antibody sensor. Several other barriers also impede their use in routine diagnostic practice (**Table 4**). These may be economic (e.g., high costs and financial issues), regulatory (e.g., poor-quality products), policy-related (e.g., lack of proper guidelines for the use of POC tests), user/provider perceptions and social or cultural barriers. Besides, several other factors, such as dedicated workforce, reagents, and supplies, test platform, screening/confirmatory value, and sensitivity/specificity, also play an important role in successful implementation of POC testing [55].

5.1 Economic barriers

Studies indicate that POCT is more expensive when compared to laboratory testing [56]. The majority of these studies have been carried out in primary care settings, and only a few have incorporated a proper economic evaluation [57-60]. So far, these studies demonstrate a very confusing picture of their diagnostic value and economic aspects because the analysis of the cost-effectiveness of a POCT system is difficult, and cost comparison studies against traditional central laboratory testing methods are complex. Despite significant cost-effectiveness in terms of little infrastructure cost involved and rapid

Table 4. Benefits and barriers for POCT in AIRD

| Benefits | Barriers |
|---|---|
| Fast turnaround time (TAT) | Cost may be higher |
| Easy to perform | Limited sensitivity and specificity |
| Can be done at bedside | Limited information |
| Minimal or non-invasive | Limited acceptability |
| Less sample quantity needed | Need of trained manpower |
| No need of sample transportation | Need of quality control |
| Minimum or no sample processing | Additional burden on clinical staff |
| Minimum or no need of instrumentation | Needs monitoring of storage and expiry |
| Disposable or minimum maintenance | Risk of interference |
| Avoids maintenance of large inventory | Pre-analytical errors |
| Can meet growing demand | Analytical bias |
| Can improve clinical outcome and facilitate early discharge | Difficulty in connecting with electronic medical record |
| Useful in emergency setting | Limited availability and manufacture |
| Utility in remote or resource limited settings | Competition with centralized labs |
| Reduces number of visits | |
| Can be performed at home (self-testing) | |

AIRD: Autoimmune rheumatic diseases, POCT: Point-of-care testing

delivery of results, the higher cost-per-test of POCT as compared to automated testing in a centralized laboratory may be a setback. Since POCT devices or kits are manufactured as single-use tests rather than bulk reagents, such formats raise the cost of testing compared to reagents used in high-volume central laboratories. The challenges to reducing the cost are manifold, for example, lack of proper investment, stunted sale, geographical restrictions, and lack of broad acceptance. In addition, the tests may not be accepted by laboratories having budget-related issues. Furthermore, despite its convenience, POCT does require a significant amount of support from the laboratory to keep the quality of testing in check. Above all, the regulatory control requirements of POCT products and their use depend on the area where they are marketed, and the guidelines in that area may vary for different products [61,62]. Despite these odds, the POCT use for AIRD has the potential to radically change the process of care, and minimize the utilization of resources by, for example, reducing emergency admissions, reducing hospitalizations, reducing the length of stay, as well as enabling care to be delivered closer to home [56].

5.2 Quality assurance and regulatory barriers

Rapid delivery of test results by POCT helps the clinician in enhancing the quality of patient care. As per Clinical Laboratory Improvement Amendments guidelines, all laboratories performing patient testing, including POCT, should adhere to good laboratory practice to assure the accuracy of test results. However, quality assurance is a major challenge associated with POCT. In general, a POCT is performed by clinical staff on duty, whose primary responsibility is to manage patients. They are not as qualified as a trained laboratory person and have inadequate knowledge of quality control (QC) and quality assurance practices. This sometimes may result in errors [63]. In a centralized laboratory, the technical staff is entirely dedicated to specimen, collection, analysis, QC, and instrument maintenance. While in the patient care unit, the clinical staff is devoted to patient care with less emphasis on POCT and related tasks such as QC and documentation [64]. Moreover, the clinical staff also has limited laboratory training and experience to perform POCT. As a result,

the pre-analytical, analytical, and post-analytical variables in a POCT may be compromised. Appropriate tests and QC documentation may be challenging for the clinical staff that mandates them to be familiar with the specific requirements of their accreditation body since documentation, records, and data logs are essential for regulatory compliance and accreditation [55].

Another issue is that the majority of POCT devices require visual interpretation of tests and the staff. Furthermore, the POCT results need to be manually entered into a patient's file or electronic health record. Some POCT devices produce digital results that need to be scanned or entered manually into a patient's record. Fortunately, some of the newer POCT devices can directly transfer the results into electronic records, thereby relieving the staff with the extra burden. This, however, increases the cost as well as requires assistance from information technology professionals [65].

Unless properly received, recorded, and maintained, the POCT devices can compromise patient results and in turn, may affect the course of treatment for patient care. Hence, the nurses and other clinical staff handling the POCT device or reagents must be familiar with the proper use and storage of POCT reagents [66]. They need to maintain a record for the ordering, receipt of shipments, storage, expiration dates, distribution of reagents, and storage conditions. After opening these reagents or device, they must update the new expiration date [67]. There are also QC issues associated with POCT [68]. The person performing the test is inherently responsible for the success or failure of these devices. Some POCT may require daily QC check and thus, the staff on duty is supposed not only to document but also to identify the logs. Another issue is routine maintenance and regular care of the devices used for POCT and the appropriate use of their refrigerated controls. They should always be taken out of the refrigerator about 15 – 30 min before performing a test and must be re-refrigerated after use. Clear guidelines related to the storage of reagents and controls need to be incorporated into the standard operating procedure (SOP) for POCT. All this can be achieved by their proper training before testing and documenting their competency at regular intervals. There may be a POCT management team to coordinate and arrange

all such training programs and the documentation process [69].

Similar to devices and equipment in a centralized laboratory, the POCT devices need routine maintenance. Since certain types of cleaning substances may damage POCT devices, their cleaning and disinfection must be performed as per manufacturer's instructions. Poor sanitation of these devices may invite nosocomial and antibiotic-resistant organisms and can lead to the transmission of infectious diseases [70]. It is also necessary to explicitly mention the cleaning and disinfection procedures of these devices in the SOP because these portable and handheld devices are used on many patients in the hospital [71].

It is important to understand that POCT is generally performed on whole blood rather than processed samples, and stable reference materials are currently unavailable for calibration purposes. A mutually acceptable reference material, therefore, is required to avoid technical differences when comparing the performance between POCT and centralized laboratory [72]. Furthermore, different models of POCT devices may give nonmatching results that are also different from those derived from centralized laboratory instruments [73]. An alternative solution to these problems is to set up a satellite laboratory where trained laboratory staff performs POCT by complying with the accreditation standards related to quality assurance, but doing so would come with an added cost that may be inhibitory for small hospitals or clinics with low budgets. In other words, it is important to apply the concepts of conventional laboratory testing in POCT, mimicking the process from pre-analytical to post-analytical phase to reduce the rate of errors [50].

5.3 Policy-related barriers

The adoption of a POCT in a community or clinical setting depends on the nature of the healthcare system in the region [55]. Due to the lack of regulatory policies for POCT diagnostics in many countries, the risk of widespread use of sub-standard POCT kits or devices is inevitable. Hence, national policies regarding evaluation, certification, funding, training, and research of POC diagnostics should be devised to guide the widescale implementation of POCT [74,75].

Current guidelines and policy documents do not provide clear recommendations on how to include POCT in diagnostic algorithms for AIRD. The guidelines also lack in terms of crucial components such as training, quality assurance, maintenance, and overall management of a decentralized POCT program at the level of communities and health-care centers [76]. There is a need to address all these regulatory challenges to avoid delayed approval of POCT and increase its accessibility in an effort to improve clinical outcomes of AIRD. Furthermore, the formulation of national policy guidelines/regulations on supply chain management of POCT diagnostics will ensure consistency of supply, appropriate use, and quality testing [74,77,78]. Since POCT reagents are manufactured only in selected countries, their shipping to another country may be delayed due to cross-border regulations. The customs may hold up the delivery of laboratory supplies, thereby shortening the shelf life of the reagents. Furthermore, delays in customs clearance may expose reagents to adverse storage conditions. This aspect also deserves our attention, and a change in policy is required to promote and encourage the use of POCT [79].

6 Conclusion

The centralized laboratory and POCT share a common goal of providing quality laboratory test results. In the present scenario, there is a need to reduce unnecessary testing and duration of stay of patients in the hospital. With the availability of POCT, it will be possible to make an early decision about disease management by bringing clinical laboratory testing closer to the patients. This will save time, reduce the unnecessary expenses for hospital care as well as increase the operational efficiency of the health-care institution. With an increase in POCT menu, reliability, and availability in the coming years, the use of POCT for the diagnosis of AIRD is likely to increase. The POCT devices are expected to require lesser human handling and become more digitalized and electronic. This gradual transformation will help minimize bias and errors. In the foreseeable future, POCT devices hold promise for an upgrade in their test sensitivity and specificity, and the stability and shelf life of the reagents will also improve. Therefore, POCT has tremendous potential to revolutionize current diagnostic practices in AIRD.

Conflicts of interest

None to declare

Author contributions

Y.K. conceived, designed, and wrote the manuscript. A.B.H. reviewed drafts of the paper and gave valuable inputs. Both the authors read and approved the final manuscript.

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