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# A look at the Current Situation of Iranian Molecular Diagnostic Methods and the Implementation of Required Future Policy: A Review Article

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**ABSTRACT**

Today, molecular diagnostic methods have an unignorably position in diagnostic laboratories. It is estimated that 60-70% of all decisions depend on molecular detection methods. However, many Iranian physicians still do not fully trust the newly developed protocols in particular. If necessary, they request some confirmatory tests available to ensure a final decision.

The purpose of this short study is to investigate the causes of uncertainty in these tests and current challenges in Iranian clinical centers. Therefore, all the effective cases from receiving the samples to publishing the patient reports are looked up.

Significant parameters including pre-analytical, analytical and post-analytical parameters are studied in this study. The reason for some of the current limitations is discussed based on released documents and reported periodic inspections according to published standard criteria. Based on the results, the need for fundamental revisions in some parts of the relevant bodies is clearly identified.

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## Introduction

It is assumed that the results of diagnostic tests should be reliable and consistently interpretation in the same parts of a sample by different laboratories (1,4).

The importance of standardizing laboratory SOPs and minimizing uncertainties should be considered from the pre-analytical stage to the preparation of the final results (5,7).

Obviously, the quality of these results must be constantly increased. Diagnostic errors have been reported in all countries, causing permanent injury or even death to patients (18,13).

Patients and physicians are deeply concerned about these errors in their health care system. Therefore, physicians request that, at least in some important cases, simultaneous testing be performed in two laboratories to make the correct interpretation and final decision.

At present, Iranian physicians often complain of uncertainty about the results (14,15).

These uncertainties, which are mostly related to molecular methods, may be due to several problems. Some of these problems may be due to government policies. In this study, we try to explain some of the limitations and other chal nges of clinical laboratories.

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## literature review

### *Laboratory materials and equipment*

In order to perform the correct tests to achieve its laboratory mission, each laboratory must ensure its own equipment and verify its performance. In addition to the role of materials and equipment, the accuracy of the results depends on several other parameters from the receipt of specimens to the report of patients' results.

Some studies report a range of 10-15% for diagnostic errors, while no research has been conducted on clinical diagnostic laboratories in Iran or documents have been published (16,17).

The National Medical Devices Directorate (NMDD) is a government office that approves required laboratory materials and devices (18,21).

Unfortunately, accrediting equipment, according to the complainant, takes a long time in the NMDD. Verification of unauthorized equipment has been reported in some cases.

Thus, this situation has caused medical centers to use invalid devices when needed. On the other hand, the lack of active supervision has also encouraged some laboratories to buy unqualified and cheap equipment and materials.

### *Definitions and Reference intervals*

Each laboratory supplies the approved equipment according to the criteria and calculation methods of its country. Unfortunately, we have to procure many materials and kits from other countries. These resources are sourced in their own way from East Asia to the United States. Therefore, each laboratory may have its own definition based on the materials used and diagnostic kits with their own interpretations such as International Unite, dynamic range, quantitative calculation methods.

Reference intervals in the clinical laboratory are another widely used decision tool. This plays an important role in interpreting laboratory results. Several studies have revealed that reference intervals vary greatly, even when laboratories use the same method. Most reference intervals used are based on short laboratory studies, while they should be the result of valid clinical trial studies in Iran (22,23).

Obviously, this will lead to different clinical interpretations. Therefore, it increases the risk for patients and may cause unnecessary testing to be repeated. According to the Australian approach, the selecting of reference intervals requires evidence that needs to be evaluated by a checklist for different criteria.

There are currently no published documents or articles on this topic. Periodic inspections have shown that most General Directorate of Laboratory Affairs (GDLA)
do not have a clear view of checklists.

The Australians items are as follows

1-Definition of analyte.
2. Define assays used, accuracy and specificity of analyte.
3. Checking the interference the differences of pre-analytical procedures.
4. Define RI and its principle (e.g. central 95%).
5. Describe evidence for selection of common RIs data sources .
6. Consider partitioning based on age, sex, etc
7. Define degree of rounding.
8. Assess clinical considerations of the RI and use of common RI.
9. Document and implement.

### *Harmonization of analytical issues*

Coordination of procedures in laboratory medicine is recognized as a need to improve the quality of diagnostic tests. Mismatch of analytical issues is one of the most influential parameters that is often ignored and can often lead to other problems (24,27).

Clinical and Laboratory Standards Institute (CLSI) and Joint Committee for Traceability in Laboratory Medicine (JCTLM) are two organizations that provide guidance on this issue. In addition, several other organizations have a key role to play in improving standardization and coordination of measurements (24,27).

CLSI and JCTLM are the two organization for providing guidelines at this issue. Besides, several other organizations have also original role on improvement of standardization and harmonization of assays such as:

-The International Federation of Clinical Chemistry (IFCC),
-The European Federation of Clinical Chemistry and Laboratory Medicine (EFLM),
- The American Association for Clinical Chemistry (AACC),
- The World Health Organization,
- International Consortium for Harmonization of Clinical Laboratory Results (ICHCLR)

The responsibility for issuing a formal SOP is with the Health Reference Laboratory (RHL). There are several things that need to be coordinated (e.g. sample type, different test accuracy for each sample,etc.), but only a few documents have been publishedIt seems necessary to invite academic members or specialists to form various scientific committees. The task of these committees is to provide specific answers to laboratory questions or to provide specific recommendations and SOPs in each issue (28,29).

### *EQAS program and Auditing*

The Iranian HRL also monitors the quality of diagnostic tests in all clinical diagnostic centers that work with GDLA. They check laboratory conformity using standard guidelines for all clinical laboratories.

They have enough power to point out any problems or introduce them as a well-functioning laboratory. At present, no independent studies are available on the success and weakness of the current quality assurance program in Iranian laboratories, although much effort has been made to implement quality assurance throughout the country (30).

These programs should indeed identify systematic errors in diagnostic procedures that may not be revealed by internal QA processes. In addition, the audit program is another key strategy for controlling weakness and improving laboratory results, and is part of a quality assessment that may in some cases provide better results (e.g. diagnosis of tuberculosis).

The Office of Laboratory Affairs (OLA) of each university has authority in this matter. This office is located in the Vice Chancellor for Treatment of each university and involves in surveillance on clinical laboratories.

The main task of this office is to arrange regular audits, which are currently not done properly. Despite of activity of these authorized bodies with last decade, rout of unreliability and uncertainty of those unique tests has not been reduced. (31).

Undoubtedly, there should be some potential barriers to the effectiveness of our EQAS implementation, such as availability of proficiency testing and the proper conduct of audits in laboratories.

However, it is reported that the regular performance of internal audits is often overlooked. Despite the potential and critical role of auditing in improving the quality of clinical care, the audit evaluation has not been scientifically evaluated or adequately reported.

### *Technical officer*

Some of these uncertainties are obviously related to the laboratory performance. Periodical inspections have revealed some other errors in the routine work of clinical laboratories, even in reputable labs. In fact, the accuracy of all laboratory processes should be supervised by technical authorities. Unfortunately, several reports confirm significant number of technical authorities are unaware on the quality of diagnostic procedures. Laboratories that want to be accredited must participate in training programs or workshops to meet the following standard criteria; trained staff, use of quality control for inspect equipment, availability of approved workspace, valid diagnostic protocols.

In addition, the technical supervisors of each laboratory must have sufficient pathophysiological knowledge about each test to perform or modify diagnosis procedures. These technical assistants are qualified for the best guarantee of using internal and external quality assessment and having successful laboratory quality assurance program (24,31).

## Conclusion

The study of the efficient parameters investigated on the performance of laboratory tests shows that various factors play a role in the uncertainty of the answers. Lack of proper supervision law, incompetence of auditors, laboratory costs, staff skills are some of the things that have led to testing in non-standard conditions. Determining the quality of special tests and allocating the appropriate cost to it can be the most useful measures.

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