ORIGINAL RESEARCH ARTICLE

Clinical Chemistry and Autoverification: A Path Less Traversed

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Received on: 28 March 2024; *Accepted on:* 27 April 2024; *Published on:* 18 May 2024

Abstract

Aims and background: Autoverification (AV) is an application of artificial intelligence that uses computer-based algorithmically established rules for release of patient reports. This allows effective time management, prevents probable laboratory errors, and ensures consistent results. However, not many labs have adopted AV into practice due to hesitations concerning cost-effectiveness, lack of robust software and informatics support along with dearth of knowledge for its implementation. Additionally, there is scant published literature on AV implementation.

This study has been conducted as an attempt to outline benefits of AV and address the existing gaps.

Methods: The study was conducted in the Department of Clinical Chemistry of a standalone lab. Autoverification implementation was done in stepwise manner. (i) Test selection and developing algorithms, (ii) Setting-up rules in middleware to prevent release of erroneous results, (iii) User acceptance testing (UAT), (iv) Going-live.

Results: Efficacy of AV system was gauged based on following factors. (i) AV passing rate—initial 53.7–85.4% later was achieved with inclusion of more parameters and extension of tolerance limit, (ii) Significant improvement was observed in TAT for both immunoassay (from 88.28 to 97.32%) and routine chemistry (from 82.7 to 95.68%), (iii) decreased error rates as evidenced by reduced number of amended reports, (iv) reduction in staff required for manual verification allowing their utilization for other departmental activities.

Conclusion: Implementation of AV by laboratories provides efficient and cost-effective work opportunities with scope for continuous growth. However, it doesn't preclude the need for careful quality control.

Keywords: Algorithms, Automation, Autoverification**,** Clinical chemistry, Laboratory information systems, Turn-around-time.

Indian Journal of Medical Biochemistry (2024): 10.5005/jp-journals-10054-0233

Aims and Background

Clinical diagnostic laboratories are faced with continuous challenges to deal with the increased workload and concurrently deliver consistent and reliable reports. Accomplishing the above encompasses optimization of workflow processes, provision of better services through new initiatives while preserving cost control and reducing the error rates of the total testing process. The estimated error rate in the total testing procedure is 30–75% for preanalytical, 4–30% for analytical, and 9–55% for postanalytical phase. [1]

Technological advances in laboratory automation has significantly reduced errors occurring at the analytical phase. Likewise, introduction and adoption of modern information technologies alike Laboratory Information Systems (LIS) and/or middleware has secured the flow of data minimizing transcription errors.

Introduction of a tool to validate test results without manual intervention, using predetermined rules and can minimize the possibility of error additionally in the post analytical phase.[2,3]

The process of manual test verification poses several challenges. Additionally, the evaluation process is subjective and not standardized and varies from person to person depending on their training level, experience, or "professional judgement".[4] Hence, the total effectiveness of manual verification in clinical laboratories is variable, unknown and susceptible to errors.

Autoverification (AV) is an application of artificial intelligence for diagnostic laboratories that uses set of rules algorithmically established either in the middleware or LIS for release of patient reports. It selectively verifies test results that meets the criteria while holding back the unacceptable and potentially erroneous results for manual verification and other corrective action. This allows effective time management, prevents probable laboratory errors, and provides more consistent test results. Selection of autovalidation rules and the criteria that are to be implemented are specific for each laboratory setting.

In order to improve the operational efficiency, the study laboratory designed and implemented the AV system profiled in this report as a measure to improve turnaround time (TAT), consistency of result verification, and to reduce the workload of staff for optimum utilization in other areas.

Due to the limited number of literature available on the topic, this study aims to contribute to the understanding of the AV process by providing a detailed description of the setting up of the entire AV process, and an evaluation of the benefits brought by its implementation to the laboratory.

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How to cite this article: Datta RR, Bansal A. Clinical Chemistry and Autoverification:A Path Less Traversed. Indian J Med Biochem 2024;28(2):36–40.

Source of support: Nil

Conflict of interest: None

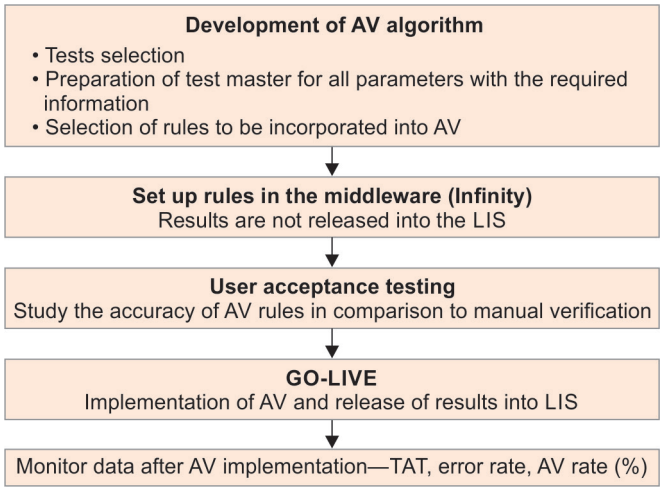

Fig. 1: Figure showing stepwise execution of AV implementation

Methods

Settings

This study was conducted in the Department of Clinical Chemistry of a national reference lab of a diagnostic chain that caters to around 4,000 samples received per day from most parts of the country.

The clinical chemistry and immunoassay parameters are being routinely performed on Cobas-Pro (Roche Diagnostics, Mannheim, Germany). The information technology tool used for AV implementation was the middle ware (Infinity) provided by Roche Diagnostics. The core laboratory has a supervisor and three clinical laboratory technologists that were tasked with validation and maintenance of AV rules along with manual review of AV held reports. There is also a full-time medical technologist engaged for quality control and improvement.

The concerned laboratory has a practice of processing patient samples only after quality control levels are found to be within acceptable limits. In the presence of an outlier, necessary corrective actions are taken subsequent to which patient samples are processed. Thus, control failure was not included in the algorithm for establishing AV.

Execution of AV implementation was done in a step-wise manner as depicted in Figure 1.

1. Development of an Algorithm for Setting up Auto-verification

Appropriate designing of the autovalidation algorithm along with clear and unambiguous definition of AV rules are prerequisites for AV implementation.[2,3,5–7] The algorithm for the clinical chemistry was developed according to the CLSI AUTO10—A guideline.[2] The following steps were executed:

1.1 Selection of the candidate tests which included 113 commonly assayed biochemical and immunoassay parameters.

1.2 Preparation of a test master spreadsheet having complete information for each candidate parameter.

The test master should be inclusive of the following details:

i. Test name
ii. Reference range – which should be gender and age specific. The lower limit and the upper limit of the reference range for the parameter should be clearly defined.
iii. Units of reporting.
iv. Recommended dilution by the manufacturer for each included parameter.
v. Limit checks/tolerance limit—Limit checks were developed using different methods for different parameters like reference range, critical values and analytical measurement range (AMR) for the analyte as defined by the manufacturer.

The AV process was initiated by incorporating reference ranges as tolerance limits for the selected parameters. With continued user acceptance testing (UAT), the tolerance limit was increased up to the AMR for the parameters that frequently encountered higher values. Critical values were set as the tolerance limit for the following parameters: Albumin, bilirubin, chloride, creatinine, glucose, lipase, magnesium, phosphorus, potassium, sodium, urea and uric acid. User acceptance testing was considered acceptable when results released were within the defined tolerance limits.

2. Setting up Rules in the Middleware (Infinity)

2.1 The following rules were selected for incorporation into the middleware (infinity) to prevent the release of erroneous results.

i. Instrument alarms analytical flags from the analyzer were considered as AV stopping criteria.
ii. Analytes without reference ranges.
iii. Results having alphanumeric characters are withheld during AV.
iv. Results with values beyond the defined tolerance limit.
v. Results with panic (critical) values. Results with panic values not autoverified. These are then immediately notified and documented manually.
vi. Delta check: Delta check was incorporated to detect significant deviations in the results of the critical parameters which may arise due to intra-individual variations or as a result of sample integrity issues or analytical disparities. Incorporating delta check for the potentially life-threatening laboratory results ensured immediate medical attention. Results were checked retrospectively to detect discrepancies and errors. In the absence of any errors, the results were manually verified and notified to the clinician concerned. The duration of delta check was 7 days. AV was halted if a variation of 10% was observed in the results of these critical parameters in the past seven days.
vii. Consistency checks involving different analytes were incorporated into the AV system. Consistency rule checks are cross-checks that allow correct release of results of two or more different correlated tests. The consistency checks applied by the lab during AV implementation are as follows:
   – Insulin postprandial values is less than insulin fasting - AV stops.
   – Glucose post-prandial values is less than glucose fasting – AV stops.
   – Direct bilirubin value is more than total bilirubin – AV stops.
   – VLDL and LDL calculation stops when triglyceride levels are >400 mg/dL – AV stops.

Autoverification is halted under these conditions. The results are then manually reviewed after checking for the reason of discrepancy and after correlating with the clinical history of the patient.

2.2 Formula for calculated parameters like percentage saturation, albumin/globulin ratio, BUN/creatinine ratio, cholesterol/HDL ratio, LDL cholesterol calculation, Non-HDL cholesterol calculation, LH/FSH ratio, Free PSA/PSA ratio were included for auto calculation and AV.

These algorithms and rules were incorporated into the middleware leveraged for AV.

3. Verification of Auto Validation Algorithm/User Acceptance Testing (UAT)

Before introduction of auto validation in routine practice, extensive UAT was done as per CLSI guidelines to ensure sustainable functioning of the defined rules and algorithms in the middleware and thus prevent the release of erroneous results. The limit checks, delta checks, and consistency checks were applied to the candidate tests to assess errors in AV settings. The tests results had to pass through a middle window in the LIS where it was manually checked for errors without releasing the results to the physicians. Accurate transfer of results from the instrument to the middle window was verified. Results that passed all AV rules would be categorized as auto-released. Any pitfalls observed during the process were amended and then subjected to manual verification (MV) before delivery to the clinicians. A technical staff was daily rostered for manual review of reports that were held back on AV to avoid delay in release of results. The entire process was accomplished in a phase-wise manner with gradual inclusion of the parameters, extension of tolerance limits and step wise inclusion of limit check with extensive UAT done at each step. Autoverification at each step was closely monitored.

4. The Process of UAT

Persisted for a year before the lab went live with av under constant monitoring for the error rate, autoverification percentage and turn-around time (TAT).

5. Facility for Rapid Termination of AV

In case of any untoward incidence or sudden inadvertent change, computer programming was also set up and rights shared to the authorized personnel.

Results

The efficacy and the advantage of the AV system was gauged based on the following factors.

- Autoverification passing rate: The AV passing rate was closely examined with the incorporation of additional parameters and with increase in the AV tolerance limits. The AV rate recorded during the initial phase of establishing AV was 53.7% which later was documented as 85.4% with the phase wise inclusion of all the parameters and extension of the tolerance limit. AV passing rate was determined as a percentage of total number of tests autoverified and total number of tests performed in the lab in a day.
- Turnaround Time (TAT): Significant improvement in the TAT (Fig. 2) was noted after implementation of AV for both immunoassay (from 88.28 to 97.32%) and routine chemistry parameters (from 82.7 to 95.68%).
- Decrease in the error rates was observed as determined by the reduction in the number of amended reports prior to implementation and after implementation of AV. However, the error rate could not be quantified due to unstructured data.
- With the decrease in the number of staff required (Fig. 3) for manual verification after AV, optimization of the usage of technical staff for other departmental activities like quality improvement, documentation, research activities, etc. could be implemented.

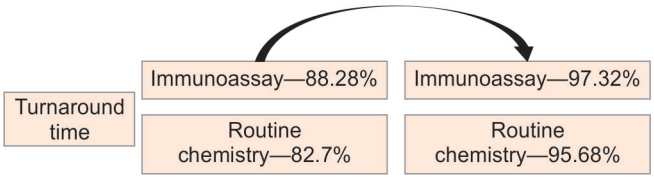

Fig. 2: TAT improvement after AV implementation

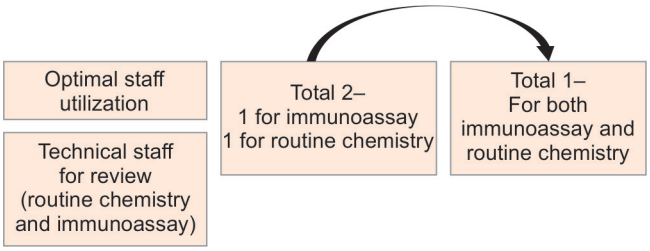

Fig. 3: Reduction in manpower for reports review after AV implementation

Discussion

In the current report, we present our experience with AV in clinical chemistry department of a standalone reference laboratory catering to an average daily load of 4,000 samples. Despite AV of test results being an essential element for increasing efficiency within the clinical laboratories, there are very scant published literatures on its application and degree of its implementation across laboratories. Results of previous surveys describe AV as underutilized in its potential.[8–10] Previous literatures have documented improvements in process efficiency and quality with the use of autoverification based on predefined acceptability criteria. This study evaluates the acceptability of (AV) as a dependable substitute to manual review of laboratory test results.

Autoverification implementation begins with outlining goals. Preparation of the AV rules and compiling the information of each tests (for eg., reference ranges, critical values, delta checks, assay AMR, clinical reportable rangeand instrument flags) into spreadsheets is a crucial initial task for developing a successful AV algorithm.[11] Spreadsheets are used to compile information on reference ranges, critical values, delta checks, assay AMR and clinical reportable range for each test. Involvement of the frontline technical staff in developing the above and addressing errors assures consistency while releasing reports.[12]

Autoverification rules developed prevent the release of incorrect and impractical test results and should be customized to each laboratory's specific requirements based on the sophistication of the LIS, middleware or both.[10] All AV rules after testing should be approved and signed-off by the laboratory/medical director.[13]

Another vital element for successful AV implementation and maintenance is strong informatics support. Team with IT expertise

is essential for translating AV algorithms into computer programs. Completion of the computer programming is followed by extensive UAT wherein the defects are identified, algorithms redesigned and retested till challenges pass.[13]

A back-up or a shadow server for the middleware and/or LIS should be available to prevent periods of system downtime. Laboratories should also have a procedure for risk analysis to identify areas of risks and uncertainties associated with AV system and develop a mitigation plan accordingly. The same has been done by our laboratory as well. The study laboratory also conducts audits at regular intervals to ensure longevity of the quality of the AV system.

Training of the front- line staff before going live with AV is a required prerequisite.[13]

Previous studies have reported the most commonly used criteria in AV algorithms are AMRs, critical values, instrument error codes, serum indices, and delta check values.[5,14] In our study, we included reference ranges, result limit checks, and consistency checks to create a more specific multi-rule algorithm. User acceptance testing was carried out rigorously for a period of six months wherein the algorithms and rules developed were tested, amended where required and again retested.

We gauged the efficacy of AV by evaluating the increase in AV passing rate (53.7–85.4%), significant improvement in TAT (88.28–97.32% for immunoassays and 82.7–95.68% routine chemistry parameters), reduced error rates as evidenced by decreased number of amended reports and reduced need for manual verification. The AV passing rates reported in multiple studies have shown differences[15–17] probably due to using different result limit checks and delta check limits and developments in AV rules over time.

The computer rules also allowed the identification of occasional events through incorporation of consistency checks (for e.g., direct bilirubin > total bilirubin, serum albumin > total protein) that could otherwise elude manual verification by experienced staff as well. For a series of tests ordered for any patient, only the test that falls outside the limits defined are withheld for manual verification, while the remaining are autoverified. Additionally, critical values and AMRs that were not autoverified were subsequently either manually verified or reassayed with dilution. Thus, the results that need more attention genuinely gets extra attention as AV acts as a first filter by omitting its release.

Despite many benefits, the AV system is not free of concerns. Any inadvertent change in the computer programming may cause the release of erroneous results that may go unnoticed by the laboratory staff. Thereby, development of an algorithm for rapid termination of AV is an essential requisite. Additionally, the AV system is incapable of abductive reasoning and functions only within the context of the applied rules.[18] The extent of AV application is limited by the capability of the software used to allow configuration of the rules. The process of autoverification should be reviewed annually. More rules and algorithms can be designed and implemented depending upon the requirement of each laboratory, but should however undergo extensive UAT before implementation.

The benefits of AV outweigh its limitations in terms of its efficiency in reduction of errors and TAT. This ensures overall quality, patient safety and overall staff satisfaction.

Conclusion

Uncertainty for AV implementation arises from a myriad of conditions like lack of robust IT support, limitations of existing software/LIS, opposition by laboratory staff due to fear of attrition on staffing or distrust of the process; uncertainty concerning cost effectiveness, lack of knowledge for implementation of algorithms etc. Through this study, we have attempted to address these issues to a certain extent, though ample work is still needed.

Clinical Significance

Implementation of AV by laboratories will provide efficient and cost-effective work opportunities with scope for continuous growth.

Acknowledgment

The authors would like to acknowledge Mr Santosh Singh Bisht, Section Technical Supervisor, for his significant support in setting up autoverification in the Department of Clinical Chemistry.

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