ORIGINAL ARTICLE

DEVELOPMENT AND IMPLEMENTATION OF AUTOVERIFICATION ALGORITHM FOR OBSERVED VALUES OF EXAMINATIONS IN CLINICAL CHEMISTRY.

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ABSTRACT: AIMS: Incorporation of autoverification algorithms in the current Laboratory Information System (LIS) for observed values of clinical chemistry examinations performed in the biochemistry department, New Civil Hospital, Surat, Gujarat. **MATERIALS AND METHODS:** Draw Data Flow Diagrams (DFD) based on currently used formal and informal verification algorithms used by technicians for the observed value of examinations. If required make changes in MySQL database data dictionary. Write PHP code modules to execute DFDs and incorporate code in existing LIS code. Perform software testing of LIS to find whether PHP code for autoverification yields intended results. Implement altered LIS code for patient reporting with post-implementation monitoring for errors. Compare turn around time and error done by technical staff between manual verification and Autoverification. **RESULTS:** Autoverification algorithm was successfully developed and implemented for various parameters. 16.75 % errors occurred during manual verification, while no error occurred during autoverification. Average TAT taken for manual verification of 20 dummy cases (reports) was approximately 32 mins verses less than 90 sec for autoverification. **CONCLUSIONS:** Auto-verification, if properly validated for each and every possible outcome, is error proof and fast as compared to manual verification, which results in considerable errors of commission and omission.
KEYWORDS: Autoverification, delta check, Turn Around Time (TAT), middleware

INTRODUCTION: At present all clinical laboratories are continually under pressure to increase productivity in terms of accurate and timely result and shortage of skilled technician. Increased laboratory information related to larger test menu and increase samples adds to the relative shortage of skilled manpower in clinical laboratories. At the same time, laboratories are subject to frequent global budget cuts made in response to pressure from management. These economic constraints have motivated laboratories to work at lower cost leading to continual acceptance of automation. Automation leads to improved quality of results with adequate turnaround times (TAT) at lower costs[1, 2].

AUTOMATION IN CLINICAL BIOCHEMISTRY LABORATORY: As shown in Table-1, Automation of pre-analytical, analytical and reporting procedure is highly advanced, while that of post-analytical procedure is still in the process of development.

Verification of laboratory results by computer is the answer to low efficiency of manual verification of laboratory results by technicians.

As per IS/ISO:15189 2007, every test parameters in a patient sample performed by a medical laboratory is to be followed by post-analysis verification procedure[4]. Even the most primitive biochemistry laboratories perform rudimentary verification of test results just before printing a report or delivering it to the patient. The same processes need to be done by a clinical laboratory systematically for all samples and all examinations. All clinical laboratories with IS/ISO:15189 2007 based accreditation have such Standard Operating Procedures (SOPs) in place which systematically look at all aspects of the test results in view of patient demographic data like age, sex, geographic location etc. and other examinations in the same sample, previous results of the same patient, results of other patients and results of quality control samples before releasing a report. Such verification is generally done by a laboratory technician or medical specialist in pathology, microbiology and biochemistry. With the present day need for laboratory tests in almost every patient attending a clinician, the workload of a public tertiary care center clinical chemistry laboratory, like New Civil Hospital, Surat, Gujarat is too high to go through each and every examination done. Systematically verifying and reporting results is a laborious task. It would require one or two experienced laboratory staff continuously verifying examination results. Autoverification is the answer to the problem of verification of a large number of examination results produced by modern day overloaded clinical chemistry laboratory[1, 2]. Autoverification is fast with least error and satisfying IS/ISO: 15189 2007 based accreditation requirements.

Clinical chemistry laboratory at New Civil Hospital is already NABL accredited for common clinical chemistry analytes since 2012. This work is an effort to develop and implement autoverification system suitable for Clinical Chemistry laboratory, New Civil Hospital, Surat.

MATERIALS AND METHODS: The study was undertaken at the clinical chemistry laboratory, New Civil Hospital, Surat, Gujarat.

Basics of writing algorithms, management of Linux operating system, Apache web server, MySQL database, phpMyAdmin and PHP and HTML programming is studied using Internet resources, as all above mentioned open softwares with extensive help available online.

1. **Writing algorithms for verification of observed values of clinical chemistry examinations.**

Flowchart method was used for writing algorithms for auto-verification [5]. Requirements of IS/ISO 15189 2007 and NABL were studied by purchasing the required standards from the respective organizations. Discussion with authorized signatories of the laboratory is used to understand current practice of manual verification of reports before their release.

2. **Change in MySQL database data dictionary used by the laboratory for storing laboratory data to make database suitable for implementation of algorithms developed.**

Based on need for implementation of algorithms developed, new tables were added to the current MySQL database. PhpMyAdmin was used to modify the database.

3. **Programming the algorithms and user interfaces in PHP**

The laboratory uses in-house PHP scripts to manage MySQL database and create web-browser user interfaces. The current scripts were modified and new scripts were added using a simple PHP editor called "Geany" in Linux operating system[6]. A dummy server was used to test new LIS.

4. **Validation of changes in software system.**

Dummy patient samples with various examinations and dummy results were created to test whether the auto-verification yields desired result or not.

5. **Measuring time for manual verification versus autoverification**

20 dummy patient samples were created and reports were printed. The reports were given to 10 laboratory technicians and residents to verify reports manually. They were given work desk instructions and required data for manual verification. Time taken for manual verification of 20 samples and various mistakes made during manual verification were noted in computer spreadsheet and compared with that of auto-verification.

RESULTS AND DISCUSSION: The flow-chart method is used to develop algorithm[7,8].

The algorithm developed is shown in Figure-1.

CHANGES IN MYSQL DATABASE DONE: In order to store 1) normal range, 2) critical range and 3) absurd range

Three tables were added to the MySQL database.

This table is used by algorithms to retrieve normal ranges for a given examination. The table stores examination code and sample type as the primary key because reference ranges differ across various body fluids for the same examination.

This table is used to find which additional examinations need to be performed reflexly when the result of a test is abnormal.

Currently, the table contains following data for various tests done in serum.

ALT abnormal: Perform ALP, Lipase, Amylase, Total protein, Albumin

Total bilirubin abnormal: Perform ALP, Lipase, Amylase, Total protein, Albumin

Creatinine Abnormal: Perform Urea

PROGRAMMING ALGORITHMS AND USER INTERFACES IN PHP: Programming is done in PHP scripting language. Whenever auto-verification fail, user is adviced by software to take certain actions to resolve failed autoverification.

User interface for autoverification was provided at various points in the main menu of LIS software as follows

1. Autoverification while importing results.

This menu is used to verify a batch of results, as soon as they are imported from the automated chemistry analyzer Erba XL-640. The form, opened in a web browser like Mozilla Firefox, asks for a file name to be imported. Once the form is submitted, auto-verification algorithms are run for every result imported.

2. Autoverification for a specific sample(s) based on search form

This menu is used to verify a set of samples based on the search form. The user is asked to give search conditions. On submitting the form, auto-verification is performed and user communicated as in point-1 above.

3. Auto-verification one-by-one

This menu allows the user to view samples and verify them one by one by clicking over next/previous buttons. This menu also shows results of all past samples of the same patient. Past data from same patient allow user to see if there is any gross alteration in results from past, a semi-automated way to delta check.

4. Autoverification before printing a result

All results are autoverified just before printing. The report shows the verification status in bold as "verified" or "verification failed". The LIS allows printing of reports where verification is failed because some reports with failed verification (e.g. Absurd value) need to be reported with appropriate remark.

This is the screen when a dummy sample id 9999 is autoverified. The left-upper part asks user action to be taken for examinations where autoverification has failed. The left-lower part in green background shows past results of each test done in the same patient. The right side of the screen shows a preview of the report of the sample. Note automated insert of critical value reporting template, segregation of past results of Creatinine and ALT for delta check.

VALIDATION OF CHANGES IN SOFTWARE SYSTEM: Dummy cases created for validation of programmed algorithms showed no error. All results of auto-verification were as expected as described below.

All examinations with results in an absurd range showed

- "Low Absurd", "High Absurd" inserted in the report
- Remark for repeat collection of sample inserted
- "Verification failed" in the report
- Instruction to technician for checking sample transposition, sample integrity etc.

All examinations with results in the critical range showed

- "Low Critical", "High Critical" inserted in the report
- Template for critical reporting record inserted
- "Verification failed" in the report till critical reporting remark completed

All examinations with empty results field showed

- Instruction to technician for writing, importing result or adding remark why it was not done

Whenever Indirect Bilirubin is requested

- It is calculated
- If DBIL>TBIL and the difference was <10%, appropriate remark was added
- Autoverification was failed in DBIL>TBIL > 10%
  Whenever ALT, TBIL or CR results are abnormal
- Appropriate reflex testing was added.

COMPARISON OF MANUAL VS. AUTO VERIFICATION: As shown in table-9 for each action required during manual verification there were errors made by technicians and residents. While, for the same samples, autoverification made no mistakes. As verification algorithms become more and more complex, it is simply impossible for human to concentrate on each and every aspect of verification, emphasizing the need for auto-verification.

As shown in table-10, no technician scored better than 95%, with the average being 83%. The table shows that, errors with manual verification are common and universal.

As shown in table-11 on average technicians took 32 minutes for manual verification of 20 cases, approximately 90 seconds for a sample. A laboratory with 500 samples will need minimum 12-13 hours for manual verification of samples, a usual scenario at a tertiary care center like New Civil Hospital Surat.

CONCLUSION: Auto-verification algorithms based on local needs of the laboratory and compliant with IS/ISO 15189 2007 were developed and implemented at Clinical Biochemistry Laboratory of New civil Hospital and Government Medical College Surat.

Free softwares like Linux, Apache, MySQL and PHP were found suitable for development and implementation of autoverification algorithms.

Auto-verification properly integrated into LIS is very quick as compared to manual verification by skilled laboratory technicians.

Auto-verification, if properly validated for each and every possible outcome, is error proof as compared to manual verification, which results in considerable errors of commission and omission.

The present study has not considered for all possible verification requirements (e.g. automated QC check, consistency check across examinations in the sample and verification of lower limits of detection).

ACKNOWLEDGMENT: I am thankful to Dr. Punit Saxena (Associate Professor), Dr. Piyush B. Tailor (Assistant professor), all technical staff and all my colleagues in The Department of Biochemistry, New Civil Hospital, Surat.

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Table-1

Various strategies used for automation of clinical laboratory processes [3]

Pre-analytical process:

2. Specimen identification
    1. Computerized Labeling bearing unique patient identity
    2. Barcoding
    3. Optical character recognition
    4. Magnetic strip and magnetic ink character recognition
    5. Radio frequency identification
    6. Smart card
3. Specimen delivery system
    7. Pneumatic tube system
    8. Electrical track vehicle
    9. Mobile Robots
4. Specimen preparation
    10. Centrifugation
    11. Decapping
    12. Aliquoting
    13. Sorting

Analytical process:

1. Fully Automated Analyzer
2. Automated Pipetting
3. Automated calculated result
4. Reflexive testing
5. Middleware

Post Analytical Process:

1. Specimen archive and retrieval
2. Finished specimen discards
3. Autoverification of result

Reporting process:

1. Transmission of report via HMIS
2. Transmission of report via email, SMS

Table 2: Table structure for table abnormal alert

Column	Type	Description
Code	varchar(20)	Primary key
sample_type	varchar(20)	Primary key Reference ranges differ depending on sample type. E.g. plasma and CSF have different reference ranges for glucose
operator	varchar(20)	'more_than' or 'less_than'
Value	float	
src	varchar(50)	The source from where reference range was obtained, e.g. name of book, paper etc.

Table 3: Current data for table abnormal alert

code	sample type	operator	value	Src
ADA	Blood (Serum, Plasma)	more than	15	Ref_Literature
ADA	CSF	more than	10	clinician_opinion
ALB	Blood (Serum, Plasma)	less than	3.5	Tietz_4th_edition [3]
ALB	Blood (Serum, Plasma)	more than	5.2	Tietz_4th_edition
ALP	Blood (Serum, Plasma)	more than	128	Tietz_4th_edition
ALT	Blood (Serum, Plasma)	more than	45	Tietz_4th_edition
AMY	Blood (Serum, Plasma)	more than	100	Tietz_4th_edition
CAL	Blood (Serum, Plasma)	less than	8.6	Tietz_4th_edition
CAL	Blood (Serum, Plasma)	more than	10.2	Tietz_4th_edition
CCR	Urine	more than	0.2	
CHO	Blood (Serum, Plasma)	more than	200	Tietz_4th_edition
CHOH	Blood (Serum, Plasma)	less than	40	Tietz_4th_edition
CHOL	Blood (Serum, Plasma)	more than	130	Tietz_4th_edition
CHOV	Blood (Serum, Plasma)	more than	30	Tietz_4th_edition
CKMB	Blood (Serum, Plasma)	more than	24	Tietz_4th_edition
CL	Blood (Serum, Plasma)	less than	98	Tietz_4th_edition
CL	Blood (Serum, Plasma)	more than	107	Tietz_4th_edition
CR	Blood (Serum, Plasma)	more than	1.7	Tietz_4th_edition
DBIL	Blood (Serum, Plasma)	more than	0.2	Tietz_4th_edition
FT4	Blood (Serum, Plasma)	less than	0.2	Tietz_4th_edition
FT4	Blood (Serum, Plasma)	more than	2.7	Tietz_4th_edition
GLC	Blood (Serum, Plasma)	less than	74	Tietz_4th_edition
GLC	Blood (Serum, Plasma)	more than	100	Tietz_4th_edition
GLC	CSF	less than	40	Tietz_4th_edition
GLC	CSF	more than	70	Tietz_4th_edition
IBIL	Blood (Serum, Plasma)	more than	2	Tietz_4th_edition
K	Blood (Serum, Plasma)	less than	3.5	Tietz_4th_edition
K	Blood (Serum, Plasma)	more than	5.1	Tietz_4th_edition
LDH	Blood (Serum, Plasma)	more than	360	Tietz_4th_edition
LI	Blood (Serum, Plasma)	more than	1.2	Tietz_4th_edition
LIP	Blood (Serum, Plasma)	more than	120	Ref_Literature
MPR	CSF	less than	15	Tietz_4th_edition

code	sample_type	operator	value	Src
MPR	CSF	more than	25	Tietz_4th_edition
NA	Blood (Serum, Plasma)	less than	136	Tietz_4th_edition
NA	Blood (Serum, Plasma)	more than	145	Tietz_4th_edition
TBIL	Blood (Serum, Plasma)	more than	2	Tietz_4th_edition
TG	Blood (Serum, Plasma)	more than	150	Tietz_4th_edition
TP	Blood (Serum, Plasma)	less than	6.4	Tietz_4th_edition
TP	Blood (Serum, Plasma)	more than	8.3	Tietz_4th_edition
TPO	Blood (Serum, Plasma)	more than	30	Kit literature
TSH	Blood (Serum, Plasma)	less than	0.4	Tietz_4th_edition
TSH	Blood (Serum, Plasma)	more than	4.2	Tietz_4th_edition
UA	Blood (Serum, Plasma)	more than	7.2	Tietz_4th_edition
URE	Blood (Serum, Plasma)	less than	13	Tietz_4th_edition
URE	Blood (Serum, Plasma)	more than	43	Tietz_4th_edition

Units for each examination code are stored in a different table

Table 4: Table structure for table critical alert

Column	Type
code	varchar(20)
sample type	varchar(20)
operator	varchar(20)
value	Float

Table 5: Current data for table critical alert [3]

code	sample type	operator	value
ALB	Blood (Serum, Plasma)	less than	1
ALP	Blood (Serum, Plasma)	more than	1000
AMY	Blood (Serum, Plasma)	more than	400
CAL	Blood (Serum, Plasma)	less than	6.5
CAL	Blood (Serum, Plasma)	more than	13
CR	Blood (Serum, Plasma)	more than	5
GLC	Blood (Serum, Plasma)	less than	55
GLC	Blood (Serum, Plasma)	more than	300
GLC	CSF	less than	30
IBIL	Blood (Serum, Plasma)	more than	15

K	Blood (Serum, Plasma)	less than	3
K	Blood (Serum, Plasma)	more than	6
LI	Blood (Serum, Plasma)	more than	2
NA	Blood (Serum, Plasma)	less than	125
NA	Blood (Serum, Plasma)	more than	160
TBIL	Blood (Serum, Plasma)	more than	15
TG	Blood (Serum, Plasma)	more than	1000
TP	Blood (Serum, Plasma)	less than	3
UA	Blood (Serum, Plasma)	more than	10
URE	Blood (Serum, Plasma)	more than	100

Table 6: Table structure for table reportable alert

Column	Type
code	varchar(20)
sample type	varchar(20)
operator	varchar(20)
value	Float

This table stores absurd values for various examinations.

Table 7: Current data for table reportable_alert [3]

code	sample type	operator	value
ALB	Blood (Serum, Plasma)	less than	0.5
ALB	Blood (Serum, Plasma)	more than	10
ALP	Blood (Serum, Plasma)	more than	3000
AMY	Blood (Serum, Plasma)	more than	5000
CAL	Blood (Serum, Plasma)	less than	3
CAL	Blood (Serum, Plasma)	more than	15
CR	Blood (Serum, Plasma)	less than	0.2
CR	Blood (Serum, Plasma)	more than	40
DBIL	Blood (Serum, Plasma)	more than	50
GLC	Blood (Serum, Plasma)	less than	5
GLC	Blood (Serum, Plasma)	more than	1500
GLC	CSF	less than	5
GLC	CSF	more than	1500
IBIL	Blood (Serum, Plasma)	more than	50

K	Blood (Serum, Plasma)	less than	1
K	Blood (Serum, Plasma)	more than	7.5
LI	Blood (Serum, Plasma)	more than	3
NA	Blood (Serum, Plasma)	less than	80
NA	Blood (Serum, Plasma)	more than	200
TBIL	Blood (Serum, Plasma)	more than	50
TG	Blood (Serum, Plasma)	more than	1500
TP	Blood (Serum, Plasma)	less than	1
TP	Blood (Serum, Plasma)	more than	15
UA	Blood (Serum, Plasma)	more than	20
URE	Blood (Serum, Plasma)	more than	400

Table 8: Table structure for table reflex examination

Column	**Type**
examination	int(11)
reflex	int(11)

Comparison of Manual vs. Auto verification

Table 9: Estimation of errors made by technicians and residents during manual verification

Action required	**Maximum Score**	**Participant score**	**% correct in manual verification**	**% error in manual verification**
critical alert entry in report	80	60	75	25
critical alert record	70	55	79	21
absurd alert entry in report	40	35	87	13
absurd alert remark	30	26	87	13
Reflex test added	110	93	85	15
Empty Result fields filled	20	14	70	30
Empty Result fields remarked	20	17	85	15

Calculated tests reported	60	59	98	2
Average	53.75	44.875	83.20	16.75

Table 10: Manual verification Score Obtained by Individual Technician

Technician ID	Maximum Score	Obtained Score	% Score Obtained
1	43	40	93
2	43	36	84
3	43	41	95
4	43	30	70
5	43	38	88
6	43	38	88
7	43	38	88
8	43	23	53
9	43	37	86
10	43	38	88
Average % Score Obtained			83

Table 11: Time Taken for Manual Verification by Individual Technician

Technician ID	Time taken
1	39 min
2	31 min
3	35 min
4	40 min
5	25 min
6	30 min
7	29 min
8	23 min
9	46 min
10	25 min
Average time taken	32 min

The flow-chart method is used to develop algorithm[7,8].
The algorithm developed is shown in Figure-1.

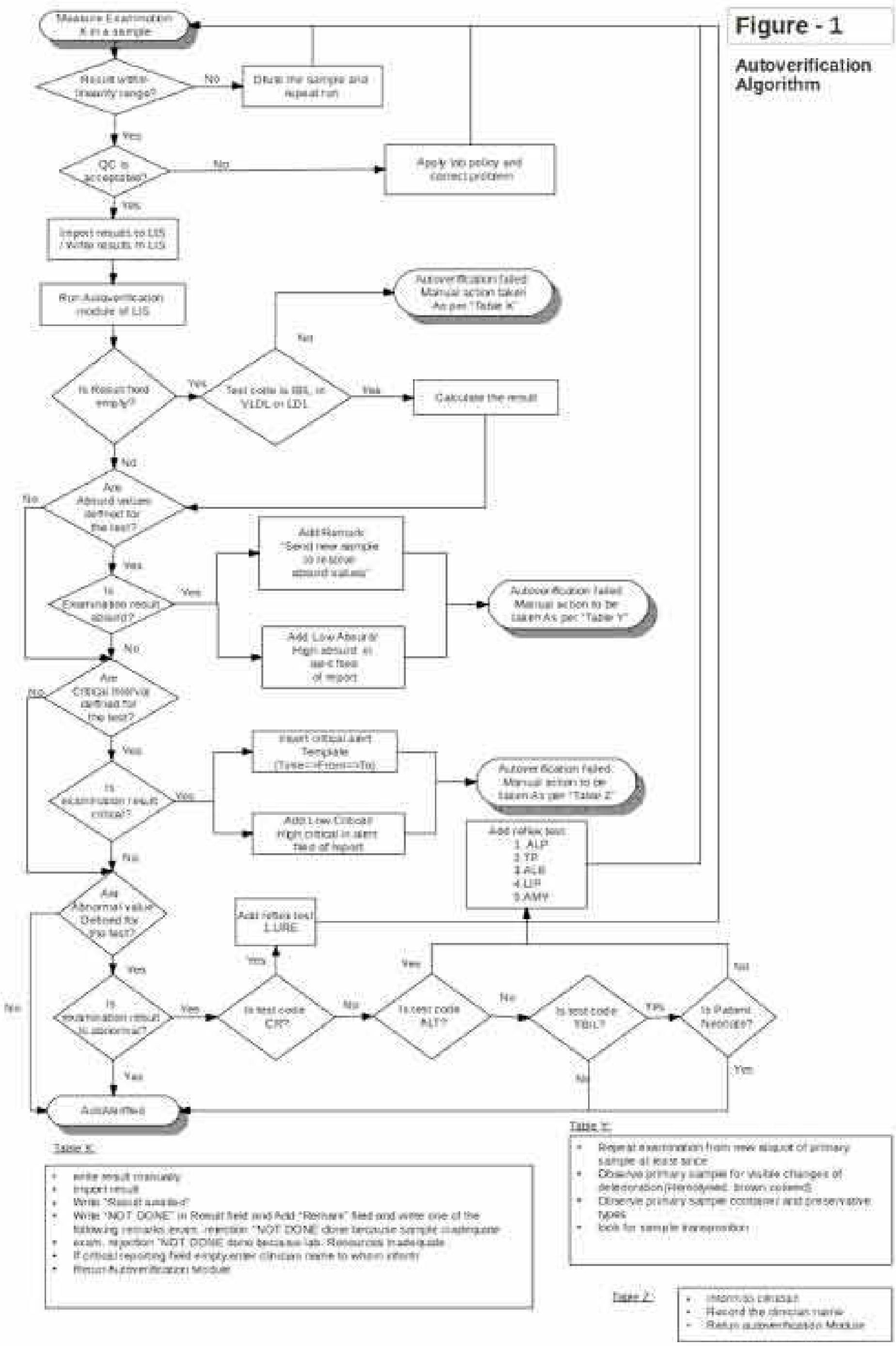

Figure - 1
Autoverification Algorithm

Figure-2 : A screen-shots of the user interface in web-browser.