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QUALITY CONTROL IN CLINICAL BIOCHEMISTRY LABORATORY: A GLIMPSE

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Abstract

Quality is defined as the conformance to satisfying the needs and expectations of the customers. Quality control is one of the components of quality assurance program. In Clinical Biochemistry it refers to maintenance of quality of the laboratory tests during analysis.Two types of quality control are practiced in clinical biochemistry: Internal and external quality controls. The purpose of Quality control is to ensure the reliability of each measurement performed on a sample. This mini review summarizes the utmost importance of quality control in clinical biochemistry.

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Introduction:

"Quality is never an accident; it is always the result of high intention, sincere effort, intelligent direction and skillful execution; it represents the wise choice of many alternatives**"**[1].The principles of quality management, assurance and control have become the foundation by which the clinical laboratories are managed and operated. Today`s health care system is dependent on

laboratory reports for clinical diagnosis, in this context laboratory diagnosis and quality control has gained tremendous importance.

What is Quality control?

Total laboratory automation has replaced manual testing of parameters but still laboratory errors like preexamination /preanalytical, examination/ analytical and post examination/ post analytical errors are in the rise. The only way to keep a check on laboratory errors is by quality control at all phases of testing. Quality control in the medical laboratory is a statistical process used to monitor and evaluate the analytical process that produces patient results and establishing conditions such that the quality of all tests performed in the medical lab assists clinicians in practicing good medicine. When a diagnostic test is performed in the medical laboratory, the outcome of the test is a result. The result may be a patient result or it may be a quality control (QC) result. The result may be quantitative (a number) or qualitative (positive or negative) or semi-quantitative (limited to a few different values). QC results are used to validate whether the instrument is operating within pre-defined specifications, inferring that patient test results are reliable. Once the test system is validated, patient results can then be used for diagnosis, prognosis, or treatment planning. The question of reliability for most testing can be resolved by regular use of quality control materials and statistical process control [2].

QC Material

Quality control material is a pool of specific biological fluid and contain analytes which are determined by the laboratory ideally in concentration close to the decision limits where medical decision is required. Control samples with same analytes but different concentrations are called levels.

Two levels of QC should be run at least once on the day of performing the test irrespective of the size of the laboratory. If the laboratory is operational 24X7, two level controls should be run in the peak hour subsequently one level every 8 hours.[3] Laboratory quality control material is also run after an instrument is serviced, when reagent lots are changed, after calibration, and whenever patient results seem inappropriate.

Quality control materials should have the following characteristics. They should have the same matrix as patient specimens, including viscosity, turbidity, composition, and color. Both freeze-dried and liquid stabilized control materials are subject to inherent errors. There may be instability in certain analytes (for example Creatine kinase,

bicarbonate) after reconstitution (freeze-dried) or thawing (liquid stable). The act of reconstitution can introduce an error far greater than the inherent error of the rest of the analytical process and there may be contamination from the diluent. [4]

Each laboratory should perform stability testing for control material after reconstitution or thawing and for material in long term storage. This should be supported by manufacturer's documentation.[4]

Types of Quality control programs:

Internal and external quality control programmes are the two different monitoring procedures and complementary to each other. Internal QC checks for day to day variation in laboratory in the form of precision and external quality control is for accuracy of the result given by the laboratory by comparing the results with peer group and by analyzing proficiency testing material.

1. **INTERNAL QUALITY CONTROL**

This is based on monitoring the biochemistry test procedure that is performed in the laboratory. It includes measurement on specially prepared materials and repeated measurements on routine specimens, as well as statistical analysis day-by-day of date obtained from the test which has been routinely carried out. There is thus continuous evaluation of the reliability of the work of the laboratory. Hence IQC primarily checks the precision of lab work. Each laboratory should establish its own mean and control limits for daily monitoring of IQC. The mean for each parameter should be calculated by taking into consideration values for at least twenty days then standard deviation and Coefficient of variation should be calculated. [5,6]

- **Allowable Error Limit** (AEL) for each analytes:

This can be calculated as %AEL= [0.25xReference Interval/Mean of normal range] x 100

For eg: Glucose the normal range is 70-110mg/dl.

Hence, %AEL =[0.25x110-70/70+110/2] x 100 = 10/90x100=11.11%

If the result fall outside this limit it should be rejected. [7]

Analysis and monitoring Developing data for Levey– Jennings chart:

- SD is a measurement of variation in a set of results. It is very useful to the laboratory in analyzing QC results. The

formula for calculating standard deviation is:

$$s = \sqrt{\frac{\sum(x_i - \bar{x})^2}{(n - 1)}}$$

Where **S** represents the standard deviation, Σ means summation of all the $(x_i - \bar{x})^2$ values, x_i is n individual control result, $\bar{x}$ is the mean of the control results, the number of independent data points (values) in a data set are represented by "n". Calculating the mean reduces the number of independent data points to n – 1. Dividing by n –1 reduces bias. The values of the mean, as well as the values of + 1, 2 and 3 SDs are needed to develop the chart used to plot the daily control values. To calculate 2 SDs, multiply the SD by 2 then add and subtract each result from the mean. To calculate 3 SDs, multiply the SD by 3, then add and subtract each result from the mean.[7]

Once the appropriate range of control values have been established, the laboratory will find it very useful to represent the range graphically for the purpose of daily monitoring. The common method for this graphing is the use of Levey–Jennings charts. In order to develop Levey–Jennings charts for daily use in the laboratory, the first step is the calculation of the mean and SD of a set of 20 control values. A Levey–Jennings chart can then be drawn, showing the mean value as well as + 1, 2, and 3 SD. The mean is shown by drawing a line horizontally in the middle of the graph and the SD are marked off at appropriate intervals and lines drawn horizontally on the graph, as shown below. In order to use the Levey–Jennings chart to record and monitor daily control values, label the x-axis with days, runs or other intervals used to run QC. Label the chart with the name of the test and the lot number of the control being used.[8]

Interpreting quality control data

For example in the below Levey–Jennings chart,the value which fall around the mean 190.5 is within 1SD and 193.5 which is between 1SD & 2 SD are acceptable. The mean value 185.6 which is in between 2SD and 3 SD is considered as warning sign. The mean value beyond 3SD should be rejected.

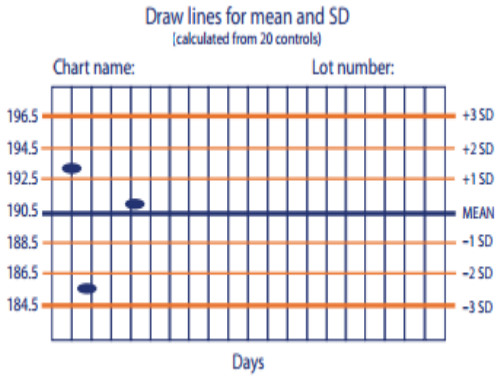

Fig 1: Quality control data

Westgard Rules: [9]

The following control rules are used to interpret the control data:

1. 1_{2s} – One control observation exceeding the mean ±2SD used only as a "warning" rule that initiates testing of the control data by the other control rules

2. 1_{3s}- One control observation exceeding the mean ±3SD primarily sensitive to random error.

3. 2_{2s} – Two consecutive control observations exceeding the same mean +2SD or mean

-2SD primarily sensitive to systematic error.

4. R_{4s} – One observation exceeding the mean +2SD and another exceeding the mean

-2SD is primarily sensitive to random error.

5. 4_{1s}– Four consecutive observations exceeding the mean +1SD or the mean

-1SD primarily sensitive to systematic error.

6. 10_x– 10 consecutive control observations falling on one side of the mean(above or below, with no other requirement on size of the deviations) - sensitive to systematic error.

Shifts & Trends:

A shift is when the QC values move suddenly upword or downword from the mean and continue the same way mathematically changing the mean. Common causes are when new reagent or quality control material has been used, change in the internal temperature or dirty cuvettes and when the calibration not accurate.

A trend is when the QC value slowly moves up or down from the mean and continue moving the same direction overtime. Trends can be caused by calibration that is failing, deterioration of reagents, tubing, or light sources.

Shifts and trends can occur without loss of precision and can occur together or independently. The occurrence of shifts and trends on the Levey Jennings control chart is the results of either proportional or constant error. [10]

Important steps to follow in case of quality control failure

- Stop testing samples/release of reports
- Search for recent events that could have caused the changes
- Examine environmental conditions
- Follow manufacturer's troubleshooting guide

- Root cause analysis (RCA), corrective and preventive actions (CAPA) should be taken

Determine the type of error

- Random error may be due to:
    a. Bubbles in the reagents
    b. Inadequately mixed reagents
    c. Unstable temperature and incubation
    d. Unstable electrical supply
    e. Fibrin /clot in the sample/ probe
- Systematic error may be due to – A trend or shift away from the laboratory established mean
    a. Change in reagent lot and calibrator lot
    b. Improperly prepared reagents
    c. Deterioration of reagents/calibrators/ control material
    d. Inadequate storage of reagents/calibrators
    e. Change in sample or reagent volume due to pipette maladjustment
    f. Change in temperature of incubators and reaction blocks
    g. Deterioration of a photometric light source
    h. Change in procedure from one operator to another
    i. Gradual accumulation of debris in sample and/or reagent probe

2. EXTERNAL QUALITY CONTROL

A system designed to objectively assess the quality of results obtained by laboratories, by means of an external agency. The objectives of External Quality Assurance Scheme (EQAS) are to provide a measure for individual laboratory quality. To supplement internal quality control procedures, provide a measure of the "state of the art" for a test. To obtain consensus values when true values are unknown. To investigate factors in performance (methods, staff etc). To act as an educational stimulus to improvement in performance IFCC 1977

EQAS report should show laboratory performance, comparison with target value, comparison with all results, comparison with method group and performance over time, Scientific reliability and validity, accredited proficiency testing scheme provider, international accreditation, Conformity Assessment – General Requirements for Proficiency Testing assures that the EQA provider itself has a quality policy. EQAS educates us about Frequency of methods used, Performance of methods used, accuracy and precision, Susceptibility of methods to

interference including other analytes and matrix and Interpretation of results.[11]

Several external quality control programmes are available. The participating laboratory is sent vials of controls without reference ranges.

Statistical Analysis includes:

- **Homogeneity Testing**

Homogeneity test is performed to check for the presence of vial-to-vial variations using the IUPAC Protocol (2006). 10 % of the control sample for each level are randomly selected and analyzed in duplicates. The results must be subjected to Cochran's *t* test for outliers and compared with critical values at 95 % confidence interval**.** [12]

- **Stability Testing**

In order to study the stability of lyophilized serum, a single level control sample must be stored at two different temperatures, 4–8 °C and −20 °C and are analyzed in 3, 5, 7 and 8 months. Results are statistically analyzed using SPSS program and tested for equality of variance by Levene's test and *t* test.[12]

- **Setting Assigned Values**

Samples of each level must be analyzed for 3 days in duplicate at the three ISO certified laboratories and the appropriate values must be assigned with reference to ±2 SD

- **Performance Evaluation**

Performance is evaluated by calculating VIS(Variance Index Score) :

$$VIS = [(X_{lab} - AV)/AV \times 100]/CCV \times 100$$

Where X_{lab} is the result from the participants, *AV* the assigned values from reference laboratory value/peer group value and *CCV* is the chosen coefficient of variation. When the (i) VIS is lying between 0 and 50 the performance is graded as excellent, (ii) VIS 51–100 as very good (iii) VIS 101–150 as good performance, (vi) VIS 151–200 as acceptable performance, (v) VIS 200–250 as performance needs improvement (vi) VIS >250 as unacceptable. The maximum VIS is up to 400 and the sign is ignored**.** [12]

Evaluation of Cause of Errors in EQAS

1. Clerical error may be due to Transcription error (Typing/Calculation) & Wrong method registered for analysis
2. To rule out methodological errors: Check for instrument function, daily instrument maintenance, instrument calibration , reagents/

sample reconstitution details, storage temperature after sample receipt/reconstitution, alignment of instrument probe, pipette calibration and environomental conditions

3. To rule out technical errors: Check for delayed testing after reconstitution, QC material run within expiry date, Acceptability of QC result on the day of run, QC data showing a specific trend, Manual pipetting/dilution proper, labeling of Secondary tubes and sample processed correctly
4. Proficiency testing materials error may be due to: Incorrect volume/sample received, hemolysed sample.
5. Error due to evaluation of results by PT provider may be due to: Inappropriate target value and Incorrect data entry by PT provider

The purpose of Quality Control

Is to monitor the accuracy and precision of laboratory assays before releasing patient results. The reliability of a method is judged in terms of accuracy and precision.[8] **Laboratory quality control** is designed to detect, reduce, and correct deficiencies in a laboratory's internal analytical process prior to the release of patient results, in order to improve the quality of the results reported by the laboratory.

CONCLUSION:

Reliability of Clinical Biochemistry laboratory performance relies on day-to-day monitoring of QC data. Application of these techniques will help to reduce errors, achieve quality goals and thus release of quality reports and give both the laboratory and the clinician confidence in the results.

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CONFLICT OF INTEREST

Authors have no conflict of interest to declare.

REFERENCES:

1. Behterin Rehnuma, Mohammad Ibrahim, Tareak Al Nasir. Quality Assurance and Quality Control in Clinical Laboratories;Pulse. 2015; 8: 62-5.
2. http://www.qcnet.com/Portals/50/PDFs/QCWorkbook2008_Jun08.pdf.
   Basic Lessons inLaboratory Quality Control accessed on 17/06/2017

3. NABL 112 Specific Criteria for Accreditation for Medical Laboratories. May 2016.
4. Hens and Koen. "Sigma metrics used to assess analytical quality of clinical chemistry assays: importance of the allowable total error (TEa) target." Clinical Chemistry and Laboratory Medicine (CCLM) 2014; 52 (7): 973-80.
5. Kanagasabapathy AS, Swaminathan S. and Selvakumar R. Quality control in Clinical Chemistry Indian J Clin Biochem 1996; 11: 17
6. Quality Control Charting for the Analytical Laboratory Part 1. Univariate methods. A review. R. J. Howarth, Analyst, 1995, 120, 1851.
7. http://clinchem.aaccjnls.org/content/35/4/630. Allowable Limit of Error in Clinical Chemistry Quality Control. CLIN. CHEM. 35/4, 1989;630-31 accessed on 17/06/2017
8. Daneshkohan and Abbas. "Factors affecting job motivation among health workers: A study from Iran." Global journal of health . 2015;7(3): 153
9. Westgard, J.O., P.L. Barry, and M.R. Hunt ."A Multi-rule Shewhart Chart for Quality Control in Clinical Chemistry."Clinical Chemistry. 1981; 27: 493-501.
10. http://www.clinlabnavigator.com/quality-control.html. Quality Control. Accessed on 01/07/2017
11. LN Sandle. The management of externl quality assurance. J Clin Pathol 2005; 58: 141 -4.
12. Rixin Jamtsho, Wilairat Nuchpramool.Implementation of external quality assessment scheme in clinical chemistryfor district lboaratories in Bhutan. Indian J Clin Biochem. 2012; 27(3): 300-5.