https://doi.org/10.37939/jrmc.v27i2.2239

# Stringent Internal Quality Control Procedures in Chemical Pathology Lead To Better Performance In External Proficiency Testing

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## Abstract

**Objective:** To assess the impact of stringent Internal Quality Control (IQC) checks on the performance of proficiency testing
**Material and methods:** This was a Prospective study conducted between September 2020 and April 2021 at the Chemical Pathology lab of Fauji Foundation Hospital Rawalpindi. NEQAPP (National external quality assurance program of Pakistan) cycle 10 round 1 External quality control data (EQC) report received in January 2021 was evaluated. As part of the corrective action plan, IQC checks were enforced, and internal quality control (IQC) data for the month of September 2020 and April 2022 were assessed. Performance characteristics of routine chemistry analytes, coefficient of variance (CV), standard deviations (SD), and Bias were calculated for these months and compared using paired –T-test.
**Results:** Proficiency testing report (NEQAPP) of cycle 10 round 1 showed 11% External Quality Control (EQC) failure among 18 biochemical parameters. Serum creatinine and total protein failed the acceptability criteria with a Z-score of greater than 2. As part of corrective action IQC checks were done, which led to improvement in CV (SD) of these parameters. The next EQC lab report (NEQAPP) for routine chemistry analytes met the acceptability criteria with z-scores of all analytes being less than 2.
**Conclusion:** Precise & accurate IQC results lead to better performance in EQC results
**Keywords:** IQC, EQC, CV, SD

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**Cite this Article:** Atzaz, N., Mehnaz, Zuhra, F. T., Muneer, S., Ali, H., & Saeed, S. (2023). Stringent Internal Quality Control Procedures in Chemical Pathology Lead to Better Performance in External Proficiency Testing. *Journal of Rawalpindi Medical College*, *27*(2). https://doi.org/10.37939/jrmc.v27i2.2239.
**Received January 18, 2023; accepted May 03, 2023; published online June 24, 2023**

## 1. Introduction

Laboratory medicine stands as a unique specialty that imparts key information regarding the health status of any patient. It has undoubtedly emerged as a strong basis on which countless medical decisions are made. However, the impact of these laboratory test results on an individual patient cannot be objectively assessed. [1]

It is incumbent upon medical laboratory professionals to ascertain the reliability and accuracy of the information being shared. This in turn minimizes erroneous diagnosis and treatment by the clinician. The daily work routine of a laboratory not only comprises patients samples assessment but involves an extensive drill on its' quality- the internal quality. [2-7]

The purpose of EQC is to keep the testing process under external surveillance; intending to avoid wrong results that lead to mistreatment of the patient. The earliest example in the history of control run dates back to the 1950s which employed statistical calculations of mean from the same control using a single measure. The control charts showed the time on the x-axis whereas the mean and SD on the y-axis. $\pm$2 SD were set as the control limits from the mean, with 95% of the results expectantly being in control and the remaining 5% highlighting the out-of-control cases. [8, 9]

Almost 20 years later, in 1977, James Westgard suggested different control levels with varying concentrations for each measure, keeping in view the multiple test automated systems.

The $\pm$2 SD limits resulted in a higher number of false rejections which led to the formulation of multiple alternate rules that reduced false rejections and greatly enhanced error detection. The multiple control rules were denoted by short Havel abbreviations. A run was rejected on $1_3$s, which meant a single measurement of the control, exceeding the $\pm$3 SD. The multi-rule system established a set of rules $1_3$s/ $2_2$s/ $R_4$s/ $4_1$s/ $10_{x.}$ [10, 11] Each rule was chosen individually to keep a low probability for false rejection (PFR) and affecting

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positively to increase the probability of error detection (PED). The laboratory professionals could use this multi-role algorithm on automated systems and choose the rules to be applied.

In the 21st century, sigma metrics were introduced- a concept developed on analytical procedure performances. It was expressed as $sigma = (TEa - abs\ SE)/CV$ where (TEa%) was the total analytical error showing the performance that should have been achieved, (abs SE,%) was the systemic error in absolute value and (CV,%) the imprecision. IQC carries a close liaison with EQC performance its accuracy and efficiency need to be authenticated by the external quality.[12]

EQC is done by an accredited body and is an essential requirement for lab accreditation as per ISO 15189 standards. Participants are required to return the results of proficiency testing samples within the allocated time. The data from all the participants is evaluated. Lab test performance (precision and accuracy) is reported in the form of Z-score, SD, and bias. This data is compared with the peer group which comprises the labs sharing the same method and instrument for that particular analyte. This gives a clear picture of the participant's performance in comparison to its peers.[13]

In Pakistan, NEQAPP is run by the Armed Forces Institute of Pathology. It has emerged as a very cost-effective and affordable EQC program. The purpose of NEQAPP is to elevate the proficiency standards of clinical laboratories in Pakistan. It aims to set a benchmark of quality at the national level and minimize errors in the results. NEQAPP runs a 12-month cycle. Laboratories that are registered with NEQAPP receive the proficiency samples quarterly.[14]

Our hospital laboratory, at Fauji Foundation Hospital Rawalpindi, has been affiliated with NEQAPP since 2007 and is a regular participant in this program.

In our study, an analytical error was detected through EQC, so we aimed to improve our IQC procedures to improve our EQC results.

## 2. Materials & Methods

This prospective study was conducted between September 2020 and April 2021, after approval from the institutional review board at Fauji Foundation Hospital Rawalpindi.

External quality control testing NEQAPP results for clinical chemistry tests were evaluated for cycle 10 sample 1.

As part of the corrective action plan after verifying instrument calibration, checking for reagonboardoard stability, technologist error and expiry date of quality control material. The Old preserved EQC sample from round 1 was rerun and indicated analytical error. More stringent measures were taken in the laboratory to bring improvements in the internal quality control program.

1. The frequency of IQC was increased from once every day to twice, once before the morning batch and secondly before the analysis of evening shift samples
2. Daily IQC charting was done by post-graduate trainees in the form of manual L J charts.
3. Previously only conventional QC rules in LJ charts were practiced for rejection as described by Westgard. These were 13s, 22s and R4S.
4. Now 6x, 10x and 7T rule which indicate trends or shifts; a determinant of systematic error were also employed.
5. Each analyte's performance specifications were evaluated from the monthly QC data of September and the results for successive months were compared till the next NEQAPP report.
6. The results were duly verified by a senior technologist and later Chemical Pathologist.

Baselines IQC results for the month of September were recorded on a structured proforma for all the routine chemistry analytes which included SD, CV, and BIAS.

CV was calculated as= SD/MEAN X100

BIAS was calculated as =target value-actual value/actual value x100

These IQC results of September 2020 were compared with the month of April 2021 and the result of performance specification i-e CV and bias were compared using Paired Sample–t-test for variables with normal distribution and Mann Whitney-U test for non-normal distribution.

## 3. Results

The sample summary report for NEQAPP Cycle 10 sample 1 received in January 2021 showed

unacceptable results for a serum creatinine Z score of 2.8 and serum total protein Z score of 3.0. This accounts for an EQC failure of 10 per cent whereas the rest of the analytes (n=18) met the acceptability criteria (z-score less than 2). The individual sample analyte report for creatinine revealed the Z-score to be 2.8 for creatinine and total protein 3.0 respectively. (Table1)

**Table-1** NEQAPP Sample Summary Report of Cycle 10 Round 1.

| Analyte | mean | Result | SD | Z score |
|---|---|---|---|---|
| ALT | 91.08 | 93 | 5.15 | 1.32 |
| AST | 188.89 | 202 | 5.95 | 0.83 |
| Bilirubin | 71.62 | 82 | 6.19 | 1.68 |
| Creatinine | 457.57 | 568 | 60 | 2.8 |
| Glucose | 15.11 | 16.8 | 1 | 1.69 |
| Total Protein | 43.04 | 30 | 13 | 3.0 |
| Urea | 16.68 | 18.1 | 1.58 | 0.9 |

Table 2. Summarizes the performance specifications of level 1 IQC i-e CV, bias for ten routine clinical chemistry analytes for the month of September 2020. Similarly, the performance specifications of level 2 IQC i-e CV, and bias for ten routine chemistry analytes for the month of April 2021 were recorded. (Table2)

**Table-2** NEQAPP Sample Summary Report of Cycle 10 Round 2

| Analyte | mean | Result | SD | Z score |
|---|---|---|---|---|
| ALT | 27.45 | 25 | 2.92 | -0.84 |
| AST | 41.22 | 47 | 3.24 | 1.78 |
| Bilirubin | 19.41 | 22 | 2.91 | 0.89 |
| Creatinine | 183.59 | 192 | 7 | 1.2 |
| Glucose | 4.88 | 5.1 | 0.33 | 0.66 |
| Total Protein | 67.16 | 69 | 2.67 | 0.69 |
| Urea | 5.52 | 5.4 | 0.51 | -0.24 |

When the performance criteria SD, CV, and bias of routine chemistry analytes for the month of September were compared with April using paired T-test, there was a significant reduction in the CV and bias of several analytes, particularly for Creatinine and total protein. Mean ($p$-value$<0.05$) (Table-1).

**Table-3** Performance Specifications of Routine Clinical Chemistry Tests September 2020

| Analyte | IQC LEVEL | Mean | SD | CV% | Target value | BIAS | BIAS% | Problem |
|---|---|---|---|---|---|---|---|---|
| **Glucose** | 1 | 5.59 | 0.47 | 8.37 | 5.52 | 0.07 | 1.27 | |
| | 2 | 13.3 | 0.75 | 5.61 | 13.3 | 0.04 | 0.3 | |
| **Protein** | 1 | 46.15 | 10 | 21 | 36.1 | 10 | 27 | **Imprecision** |
| | 2 | 86.35 | 2.83 | 3.27 | 76.6 | 9.75 | 12.7 | |
| **AST** | 1 | 45.6 | 5.08 | 11.14 | 48 | 2.39 | 4.97 | |
| | 2 | 132.4 | 18.01 | 13.6 | 137 | 4.6 | 3.36 | |
| **Creatinine** | 1 | 100 | 20.65 | 20.65 | 120 | 20 | 17 | **Imprecision** |
| | 2 | 486 | 66.1 | 13.59 | 500 | 13.95 | 2.79 | |
| **ALT** | 1 | 41.7 | 4.39 | 10.53 | 41.6 | 0.1 | 0.24 | |
| | 2 | 126.2 | 15.84 | 12.55 | 124 | 2.2 | 1.77 | |

**Table-4** Performance Specifications Of Routine Clinical Chemistry Tests April 2021

| Analyte | IQC LEVEL | Mean | SD | CV% | Target value | BIAS | BIAS% |
|---|---|---|---|---|---|---|---|
| Glucose | 1 | 5.59 | 0.44 | 7.86 | 5.52 | 0.04 | 0.72 |
| | 2 | 13.3 | 0.77 | 5.78 | 13.3 | 0.08 | 0.6 |
| Protein | 1 | 35.75 | 2.05 | 5.73 | 36.1 | 0.35 | 0.97 |
| | 2 | 74.7 | 4.16 | 5.56 | 76.6 | 1.9 | 2.48 |
| AST | 1 | 46.85 | 3.96 | 8.46 | 48 | 1.15 | 2.4 |
| | 2 | 144.15. | 18.3 | 12.7 | 137 | 7.15 | 5.22 |
| Creatinine | 1 | 117.7 | 12.65 | 10.75 | 120 | 3 | 2.54 |
| | 2 | 501 | 77.5 | 15.42 | 500 | 01 | 0.2 |
| ALT | 1 | 39.7 | 4.37 | 11.0 | 41.6 | 1.9 | 4.57 |
| | 2 | **128.4** | **13.1** | **10.2** | **124** | **4.4** | **3.54** |

The improvement in IQC was vindicated through the next external quality assessment program report in which all routine chemistry analytes met the acceptability criteria (Z-score less than 2)

## 5. Discussion

A large number of modern medical laboratories have adopted automation for reporting results, but it still poses a challenge to the accuracy and precision of their results. This study is therefore used as a measure to improve the IQC in a clinical chemistry lab setup to determine the total errors in it.

The rate of error detection can rise strikingly with a simultaneous reduction in the false rejection rate with appropriate IQC practice.

Clinical laboratories can enhance their performance in proficiency testing results and recognize their precision level of performance by merely IQC data. This can be achieved by monitoring the CVs on a monthly or a long-term basis, calculating and comparing their past CV rates with current ones and allowable imprecision limits. A correct selection of the IQC rules should be made to guarantee the acceptability of the test results. Each analyte has to have at least two different levels of concentration of control materials being run by the clinical laboratory.

EQC stands as an evaluation of the accuracy standards of the test results. It can efficiently pinpoint the under or over-reporting of individual parameters, hence formulating a corrective action plan for IQC improvement.[13]

As per ISO15139, quality indicators are defined as a "measure of the degree to which a set of inherent characteristics fulfil requirements".[15]

As one of the quality indicators in the analysis phase, CV was used as an indicator of quality requirement/performance.

Our Proficiency testing report of cycle 10 round 1 showed 11% EQC failure among 18 biochemical parameters. Serum Creatinine and Total Protein failed the acceptability criteria with a Z-score of greater than 2.

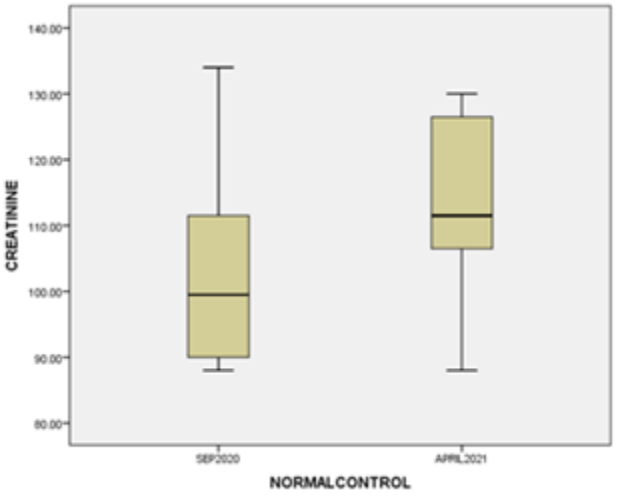


**Figure-1** Distribution of normal Control Value of Creatinine for The Months of September 2020 and April 2021**.**

The CV & Bias of total Protein was initially 21.0% &10.0% for L1 and 3.27 & 9.75% for L2 which

reduced significantly to 5.73% & 0.35% for L1 and 5.5 & 2.4% for L2 (p-value <0.05) and Serum Creatinine the CV & Bias was 20.65% & 20.0% for level L1 and 66.1% & 13.95% for L2 which reduced to 10.75% & 3.0% for L1 and 15.42% & 1.0% for L2 (p-value <0.05) after stringent IQC checks proving IQC closely linked to EQC performance.[12]

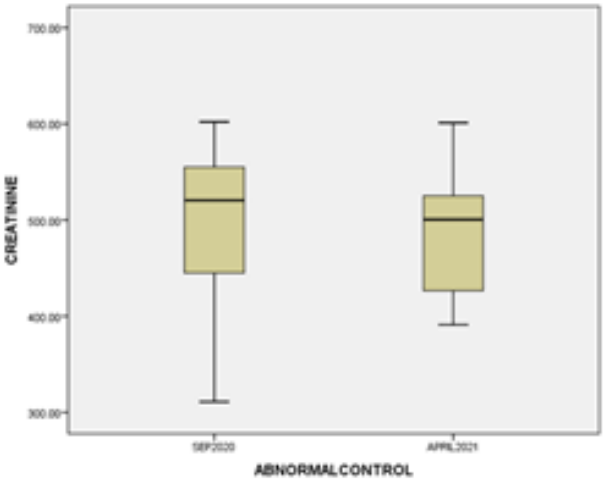


**Figure-2** Distribution of abnormal control value of creatinine for the month of September 2020 and April 2021.

When the corrective action plan for EQC was executed, an analytical error was confirmed. A retrospective check on IQC during the period the proficiency sample was received revealed that IQC material was not run for two days before EQC testing. The previous LJ charts for Creatinine showed rule violation 2 2s and 4 1s for protein. This accounted for the EQC sample's unacceptable results for Creatinine and Protein.

IQC checks included a run of two control levels every day for every analyte regularly, calibration of our instruments, daily plotting of Levey Jennings charts and application of Westgard rules for error detection along with training of our staff. When the corrective action plan for EQC was executed, an analytical error was confirmed.

Our results were by studies done by Jafri L et al in 2015 & Teshome et al in 2021 with Proficiency testing failure of 5.4% and 23.1% respectively.[16, 17]

Similar studies were carried out in China by Zhang S et al. in 2016 and Sun H et al. in 2018 in which they proved that improving IQC leads to a reduction in imprecision, CV and Bias and more accurate EQC results.[15, 18]

IQC and EQC are key to ensuring the quality of measurements in laboratory medicine. The laboratory should affiliate with monthly EQC testing, and internationally accredited programs like CAP (College of American Pathologists), RIQAS, and EQAS. The latest EQC schemes besides having an inter-lab comparison of EQC data are also incorporating IQC data of registered analytes of participating labs. This practice can lead to further improvement in the lab results, reduction in CV and Bias (Total error)and improvement in the sigma value of analytes by comparison of both IQC & EQC of the registered labs.

## 5. Conclusion

Stringent internal quality control measures implemented in pathology laboratories leads to improved performance in external quality control programs.

**CONFLICTS OF INTEREST-** None

**Financial support:** None to report.
**Potential competing interests:** None to report
**Contributions:**
N.A, M, F.T.Z, S.M, H.A, S.S - Conception of study
N.A, M, F.T.Z, S.M, H.A, S.S - Experimentation/Study conduction
N.A, M, F.T.Z, S.M, H.A, S.S - Analysis/Interpretation/Discussion
N.A, M, F.T.Z, S.M, H.A, S.S - Manuscript Writing
N.A, M, F.T.Z, S.M, H.A, S.S - Critical Review
N.A, M, F.T.Z, S.M, H.A, S.S - Facilitation and Material analysis

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