Research Article

Giray Bozkaya*, Murat Aksit and Merve Zeytinli Aksit

Evaluation of clinical chemistry tests in emergency laboratory by sigma metrics

Acil laboratuvarındaki klinik kimya testlerinin sigma ölçütleri ile değerlendirilmesi

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Abstract

Aim: Emergency department laboratories, besides from giving accurate results, should be quick enough in order not to delay patient care. Giving fast results doesn’t mean to ignore quality, rather it should always be improved to prevent erroneous results. Six sigma is a modern assessment of quality which is used to determine the analytical performance. Our aim was to evaluate the analytical performance of clinical chemistry tests in our emergency department laboratory by using sigma metrics.

Materials and methods: Our study was performed by using the internal and external quality assessment data of 13 clinical chemistry tests of emergency laboratory. Sigma levels were calculated using bias, coefficient of variation and total allowable error (TEa) ratios of CLIA, Ricos, Rilibak and Turkey.

Results: Sigma levels of various tests (CK, amylase, ALT, AST, urea, creatinine, total bilirubin, sodium and chloride) were found to be ≥6 according to different TEa’s, whereas the performance of sodium, potassium and chloride were unsatisfactory, according to TEa’s of CLIA, Ricos, Rilibak and Turkey.

Conclusion: Since most of our sigma values were found to be over 3, the analytical performance of clinical chemistry tests was thought to be acceptable and our laboratory can be regarded as a qualified emergency laboratory.

Keywords: Six sigma; Quality; Emergency; Clinical chemistry.

Özet

Amaç: Acil servis laboratuvarları doğru sonuç vermenin yanında hastanın tedavisinde gecekmek olmaması için yeteneğe hızlı olmalıdır. Hızlı sonuç vermek, kaliteyi göz ardı etmek anlamına gelmez aksine yanlış sonuçları önlemek için kalite süreklı geliştirilmelidir. Altı sigma analitik performansı belirlemek için kullanılan modern bir kalite değerlendirme sistemidir. Amacımız, altı sigma ölçütlerini kullanarak acil servis laboratuvarımızdaki klinik kimya testlerinin analitik performansını değerlendirik.

Materyal metod: Çalışmamız 13 klinik kimya acil laboratuar testinin Temmuz-Aralık 2015 tarihleri arasındaki iç ve dış kalite kontrol verileri kullanarak gerçekleştirilirdi. Sigma düzeyleri bias, varyasyon katsayısı ve CLIA, Ricos, Rilibak ve Türkiye’nin toplam izin verilebilir hata (TEa) oranları kullanılarak hesaplandı.

Sonuç: Farklı TEa’lara göre farklı testlerin (CK, amilaz, ALT, AST, üre, kreatinin, total bilirubin, sodyum ve klor) sigma düzeyleri ≥6 bulunanırken; CLIA, Ricos ve Rilibak’in TEa değerlerine göre sodyum, potasyum ve klorun performansı ıstersizdi.

Tartışma: Sigma değerlerimizin çoğu 3’in üzerinde olduğu için, acil laboratuvarımızda yapılan klinik kimya testlerinin analitik performansının kabul edilebilir ve laboratuvarımızın kaliteli bir acil laboratuarı olarak nitelendirilebileceği düşünüldü.

Anahtar sözcükler: Altı sigma; Kalite; Acil; Klinik kimya.

Introduction

A qualified medical diagnostic laboratory produce test results under the influence of pre-analytical, analytical...
and post-analytical phases. Every phase affects the test results in different ratios which only the analytical phase is under the full control of a clinical biochemist. By the help of a laboratory specialist, quality requirements of a laboratory are determined. Random and systematic errors are minimized by the use of quality indicators because high quality in laboratory testing has a prominent role in high quality health care [1, 2].

Levey and Jennings established internal quality control (IQC) key concepts and Westgard published the essential interpretative rules afterwards for quality control needs of the laboratories [3]. IQC did not contain the clinical biochemists and looked for a complementation to it. External quality assurance programs are born from this need and provided a mechanism for comparison with different laboratories worldwide. A search for a more modern assessment of quality is suggested to be six sigma metrics which combine bias of EQC evaluation, coefficient of variation ratio (CV%) from IQC results and TEa. All of them are converted into the overall assessment of the analytical quality of the test [4]. The tests which are at six sigma level are regarded as defect-free and have world class quality at which no further effort to increase quality needs to be taken [5]. The tests having sigma levels below 3 are considered as undesirable and a warning for applying extreme quality control criteria [6].

In calculation of sigma levels TEa ratios are used but there are different TEa targets of CLIA, Rilibak and Ricos each of which give variable sigma results that makes it difficult to interpret in a routine clinical laboratory [7]. Recently Turkish Ministry of Health published TEa ratios of some clinical chemistry tests. Until that time we had to use TEa of different countries but from now on we are able to take precautions according to our country’s TEa values.

Emergency department laboratories have an important role in the diagnosis and therapy of the disease. Precision, accuracy and short turnaround time are important in effective emergency laboratory services [8]. They should produce accurate results quick enough to delay patient care. The percentage of results which are in reference interval is about 50% and most of the results need immediate clinical evaluation [9]. Like all the medical laboratories, emergency department laboratories should also perform quality control criteria and their analytical performance should be higher in order not to misdiagnose or give harm to the patients.

The present study was undertaken to evaluate the analytical performance of clinical chemistry tests in our emergency department laboratory according to CLIA, Rilibak, Ricos and Turkish TEa% and to determine our tests that have world class analytical performance.

Materials and methods

The IQC and EQC data of 13 clinical chemistry parameters of medical biochemistry laboratory of emergency department between July and December 2015 were used to calculate sigma levels. Olympus AU680 (Beckman Coulter) biochemistry analyzer was used to measure glucose, urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatin kinase (CK), total bilirubin, calcium, amylase, albumin, sodium, potassium and chloride.

Two levels of internal control materials were obtained from Beckman Coulter (Lot no: 00350, 00360). They were assayed twice a day; two levels in the morning at 08:00 a.m. and two levels in the afternoon at 16:00. IQC data of 6 months were used to calculate mean, standart deviation (SD) and CV% of the tests. CV% of test were calculated with “CV%=(SD×100)/mean” formula.

The mean of bias% for 6 months period was used for calculation of sigma levels. Data from EQC, which is performed once a month (Randox International Quality Assessment Scheme (RIQAS) Lot no: RQ9128) was used to obtain bias values with the following formula: “Bias%= (mean of peer group – mean of our lab/mean of peer group) ×100”.

The sigma metrics for 13 tests was calculated by using CV% and Bias% and three different TEa according to “Sigma=(TEa%-Bias%)/CV%” [10]. The different TEa% values were presented in Table 1. Sigma levels of the tests which do not have a TEa% could not be determined in their corresponding groups.

Results

Mean, SD and CV% values of two levels of IQC are presented in Table 2. Bias% values are shown in Table 3 and sigma values according to CLIA, Ricos, Rilibak and Turkish TEa ratios are given in Table 4. The tests were divided into four groups according to their sigma levels. Tests having sigma levels below 3.0 are group 1 tests. Group 2 tests are the ones having sigma values between 3.0 and 3.99. Group 3 tests are the tests which had sigma levels between 4 and 5.99, whereas group 4 had sigma values above 6 meaning world class quality performance. The analytical performance of the tests in group 1 was low whereas the tests in group 4 had world class analytical performance (Table 5).
Table 1: TEa% values of the tests according to CLIA, Ricos, Rilibak and Turkey.

| Tests               | CLIA TEa (%) | Ricos TEa (%) | Rilibak TEa (%) | Turkey TEa (%) |
|---------------------|--------------|---------------|-----------------|---------------|
| Glucose (mg/dL)     | 10           | 6.96          | 11              | 11            |
| Urea (mg/dL)        | 9            | 15.55         | 10.5            | 15            |
| Creatinine (mg/dL)  | 15           | 8.87          | 11.5            | 20            |
| AST (U/L)           | 20           | 16.69         | 11.5            | 20            |
| ALT (U/L)           | 20           | 27.48         | 11.5            | 20            |
| CK (U/L)            | 30           | 30.3          | 11              | c             |
| Total bilirubin (mg/dL) | 20   | 26.94         | 22              | c             |
| Calcium (mg/dL)     | a            | 2.55          | b               | c             |
| Amylase (U/L)       | 30           | 14.6          | c               | c             |
| Sodium (mmol/L)     | 5            | 0.73          | 3               | 9             |
| Potassium (mmol/L)  | 6            | 5.61          | 4.5             | 9             |
| Chloride (mmol/L)   | 5            | 1.5           | 4.5             | 9             |
| Albumin (g/dL)      | 10           | 4.07          | 12.5            | 15            |

aTEa value is not available according to CLIA. bTEa value is not available according to Rilibak. cTEa value is not available according to Turkey.

Table 2: Mean, SD and CV% values calculated from IQC data.

| Tests               | Level 1 | Level 2 |
|---------------------|---------|---------|
|                     | Mean    | SD      | CV (%) | Mean    | SD      | CV (%) |
| Glucose (mg/dL)     | 102.66  | 1.80    | 1.76   | 241.14  | 4.62    | 1.91   |
| Urea (mg/dL)        | 40.00   | 1.63    | 4.10   | 177.80  | 3.67    | 2.06   |
| Creatinine (mg/dL)  | 1.29    | 0.03    | 2.89   | 5.18    | 0.12    | 2.48   |
| AST (U/L)           | 50.12   | 1.75    | 3.50   | 145.23  | 3.12    | 2.14   |
| ALT (U/L)           | 46.13   | 1.67    | 3.63   | 130.63  | 3.61    | 2.75   |
| CK (U/L)            | 160.82  | 6.02    | 3.74   | 401.15  | 11.93   | 2.97   |
| Total bilirubin (mg/dL) | 1.49 | 0.06    | 3.97   | 6.10    | 0.18    | 3.02   |
| Calcium (mg/dL)     | 8.79    | 0.13    | 1.51   | 12.28   | 0.16    | 1.30   |
| Amylase (U/L)       | 92.97   | 2.64    | 2.86   | 240.06  | 4.37    | 3.27   |
| Sodium (mmol/L)     | 120.75  | 1.89    | 1.56   | 151.71  | 1.84    | 1.21   |
| Potassium (mmol/L)  | 3.85    | 0.06    | 1.57   | 6.46    | 0.10    | 1.66   |
| Chloride (mmol/L)   | 88.91   | 1.51    | 1.69   | 109.44  | 1.39    | 1.27   |
| Albumin (g/dL)      | 2.32    | 0.06    | 2.61   | 4.47    | 0.11    | 2.55   |

Table 3: Bias% values calculated from EQC data.

| Tests               | Jul. 2015 | Aug. 2015 | Sep. 2015 | Oct. 2015 | Nov. 2015 | Dec. 2015 | Mean |
|---------------------|-----------|-----------|-----------|-----------|-----------|-----------|------|
| Glucose (mg/dL)     | 3.38      | 0.90      | 1.36      | 0.12      | 1.50      | 0.56      | 1.30 |
| Urea (mg/dL)        | 2.58      | 4.00      | 2.24      | 0.38      | 0.22      | 0.24      | 1.61 |
| Creatinine (mg/dL)  | 9.09      | 1.66      | 3.51      | 1.10      | 0.60      | 2.20      | 3.03 |
| AST (U/L)           | 5.59      | 0.42      | 2.56      | 2.42      | 3.28      | 1.57      | 2.64 |
| ALT (U/L)           | 0.64      | 0.64      | 2.50      | 0.71      | 6.70      | 2.08      | 2.21 |
| CK (U/L)            | 6.70      | 1.66      | 5.89      | 9.37      | 8.86      | 5.17      | 6.28 |
| Total bilirubin (mg/dL) | 3.06 | 1.27      | 1.26      | 2.06      | 2.90      | 0.52      | 1.85 |
| Calcium (mg/dL)     | 1.07      | 0.59      | 1.52      | 0.15      | 0.58      | 1.36      | 0.88 |
| Amylase (U/L)       | 3.42      | 2.55      | 4.88      | 0.30      | 2.78      | 2.94      | 2.81 |
| Sodium (mmol/L)     | 1.44      | 0.07      | 1.12      | 1.41      | 0.89      | 1.34      | 1.05 |
| Potassium (mmol/L)  | 0.77      | 1.67      | 1.37      | 2.75      | 0.71      | 2.57      | 1.64 |
| Chloride (mmol/L)   | 2.32      | 0.87      | 1.16      | 2.63      | 0.31      | 0.16      | 1.24 |
| Albumin (g/dL)      | 0.36      | 1.75      | 1.48      | 0.95      | 2.77      | 0.14      | 1.24 |
Table 4: Sigma levels of the tests.

| Tests                  | CLIA | Ricos | Rilibak | Turkey |
|------------------------|------|-------|---------|--------|
|                        | Level 1 | Level 2 | Level 1 | Level 2 | Level 1 | Level 2 | Level 1 | Level 2 |
| Glucose (mg/dL)        | 4.9   | 4.6   | 3.2     | 3.0     | 5.5     | 5.1     | 5.5     | 5.1     |
| Urea (mg/dL)           | 1.8   | 3.6   | 3.4     | 6.8     | 2.2     | 4.3     | 3.3     | 6.5     |
| Creatinine (mg/dL)     | 4.1   | 4.8   | 2.0     | 2.4     | 2.9     | 3.4     | 5.9     | 6.8     |
| AST (U/L)              | 5.0   | 8.1   | 4.0     | 6.6     | 2.5     | 4.1     | 5.0     | 8.1     |
| ALT (U/L)              | 4.9   | 6.5   | 6.9     | 9.2     | 2.6     | 3.4     | 4.9     | 6.5     |
| CK (U/L)               | 6.3   | 8.0   | 6.4     | 8.1     | 1.3     | 1.6     | c       | c       |
| Total bilirubin (mg/dL)| 4.6   | 6.0   | 6.3     | 8.3     | 5.1     | 6.7     | c       | c       |
| Calcium (mg/dL)        | a     | a     | 1.1     | 1.3     | 3.4     | 3.9     | c       | c       |
| Amylase (U/L)          | 9.5   | 8.3   | 4.1     | 3.6     | b       | b       | c       | c       |
| Sodium (mmol/L)        | 2.5   | 3.3   | 0.2     | 0.3     | 1.3     | 1.6     | 5.1     | 6.6     |
| Potassium (mmol/L)     | 2.8   | 2.6   | 2.5     | 2.4     | 1.8     | 1.7     | 4.7     | 4.4     |
| Chloride (mmol/L)      | 2.2   | 3.0   | 0.2     | 0.2     | 1.9     | 2.6     | 4.6     | 6.1     |
| Albumin (g/dL)         | 3.4   | 3.4   | 1.1     | 1.1     | 4.3     | 4.4     | 5.3     | 5.4     |

*aSigma level could not be calculated because TEa value is not available according to CLIA.*  
*bSigma level could not be calculated because TEa value is not available according to Rilibak.*  
*cSigma level could not be calculated because TEa value is not available according to Turkey.

Table 5: Groups of tests according to sigma levels.

| Groups                  | CLIA                           | Ricos                          | Rilibak                         | Turkey                           |
|-------------------------|--------------------------------|--------------------------------|---------------------------------|----------------------------------|
|                        | Level 1 | Level 2 | Level 1 | Level 2 | Level 1 | Level 2 | Level 1 | Level 2 |
| Group 1 (σ: <3.0)       | Urea    | Potassium | Creatinine | Creatinine | Creatinine | CK    | Sodium | Potassium |
|                         | Sodium  | Chloride | Calcium  | Calcium  | Sodium  | AST    | ALT    | Chloride |
|                         | Chloride| Albumin | Sodium  | Potassium | Chloride | CK    | Sodium | Albumin |
| Group 2 (σ: 3.0–3.99)   | Albumin | Urea    | Glucose  | Glucose  | Calcium | Creatinine | ALT    | Calcium |
|                         | Sodium  | Chlroride | Urea     | Amylase  |         |          |       |         |
| Group 3 (σ: 4.0–5.99)   | Glucose | Creatinine | AST      | Creatinine | Glucose | Glucose | Creatinine | ALT    | Sodium |
|                         | Creatinine | Amylase | Total bilirubin | Albumin | Total bilirubin | Albumin |         | Albumin |
| Group 4 (σ: ≥6.0)       | CK      | AMylase | AST      | ALT      | CK      | Urea    | AST    | Total bilirubin |
|                         | ALT     | CK      | Total bilirubin | CK      | Total bilirubin |        |         |         |
|                         | CK      | Total bilirubin | AMylase | Total bilirubin |        |         |         |         |
Discussion

The clinical laboratories have an important role in the diagnosis of diseases. This role is more important in emergency departments where the physicians race to diagnose and make therapy. The patients applying to emergency departments and the number of urgent tests increase every year. In order to satisfy both the patients and physicians, emergency laboratory should result the test in a short turnaround time (TAT) because the patients and the doctors are waiting laboratory results for prompt diagnostic and therapeutic decision [11].

Although TAT is thought to be a marker of laboratory efficiency, it should not cause an increase in the laboratory’s errors rate [11, 12]. The laboratory technicians should have enough time to make proper controls for analytical performance, in order not to give erroneous test results. In our emergency laboratory two levels of IQC samples are performed two times a day and we use EQC samples every month. The results of both IQC and EQC are in acceptable limits. This meant us that the analytical performance of clinical chemistry tests in emergency department is sufficient. In order to check this, we decided to calculate sigma levels of the tests. Sigma metrics is regarded as “a more modern assessment of quality” which is the combination of bias, imprecision and TEa resulting as an overall analytical quality [4, 6]. Since there are different TEa suggestions from different countries we decided to use 3 of them to make a comparison. Recently Turkish Ministry of Health published TEa ratios of some clinical chemistry tests allowing us to use TEa percentages of our own country.

We were happy to see that some of our tests had nearly defect free performances with sigma levels ≥6 (Table 5). Interestingly while obtaining sigma levels over six for CK in both levels according to CLIA and Ricos, CK test operated below 3 according to Rilibak which is considered as undesirable for routine operation. We evaluated this as the natural consequence of Rilibak’s low TEa% level that is approximately one third of CLIA and Ricos TEa ratios. Since Turkish CK TEa has not been published yet, we do not have a calculation for CK sigma. If we assume that it will be around CLIA and Ricos TEa levels, our sigma level for CK will be in world class, also. We may say that emergency department laboratory serves nearly defect free for the diseases diagnosed by the help of those tests.

Glucose, which is the most widely requested laboratory test, is very important in emergency departments in determination of hyperglycemic or hypoglycemic conditions since many diabetic patients may be brought to the emergency department in coma situation being unconscious. Glucose hardly situates in group 2 tests according to Ricos with a lower TEa level compared to CLIA, Rilibak and Turkish TEa’s (Table 1). Nevertheless glucose had sigma levels between 4.6 and 5.5 according to CLIA, Rilibak and Turkish TEa’s (Table 4). We may say that our emergency department laboratory serves in high analytical performance in diagnosing patients with either hypoglycemia or hyperglycemia. Thus the physicians can reliably deal with diabetic comas.

The main problem seemed to be in sodium, potassium and chloride. Like many laboratories worldwide we had sigma levels below 3 for these analytes [6, 13, 14]. The tests with sigma levels below 3 are considered undesirable for routine operation. In fact it is almost impossible to have a sigma level over three with the TEa’s of CLIA, Rilibak and especially Ricos (Table 1). We think that Turkish authorities realized this fact and published such TEa levels that make it possible to achieve sigma levels which encourage the medical laboratory experts. By using Turkish TEa levels our sigma levels for sodium, potassium and chloride increased and these tests became the members of group 3 for level 1 and groups 3 and 4 for level 2.

The limitations of our study are as follows: (i) We used “bias” calculated from EQC data. There may be negative aspects of this approach. The matrix of the samples, the concentration of the analytes in EQC samples may be different from IQC samples. The bias is obtained only from single measurement and shows the performance according to the peer group. Despite these facts, there are studies using bias calculated from EQC data [1, 5, 7, 10]. (ii) We used Westgard’s formula for the calculation of sigma levels. It is suggested that Westgard’s sigma metric calculation is not correct mathematically since only half of the group is taken into account which always results lower sigma values [15]. Since a small positive change in sigma, although in decimal level, has a favourable effect on defects per million opportunities (DMPO), this helps to obtain results reflecting their real performance in some tests like sodium which have lower performance according to Westgard’s sigma metric calculation [16]. These facts may be the limitations of our study.

For the beginning, although the number of the tests is limited, Turkish TEa levels are encouraging. As a Turkish medical laboratory, we may use the published Turkish Tea’s. Besides, by using lower TEa in calculation of sigma levels from different guides, we may target to increase our analytical performance if needed. At this point we should take extra precautions such as increasing our IQC frequency in order not to decrease our analytical
performance. Thus we can catch a world class analytical performance.

We realized that we should be more careful about our quality control applications because although average CV% and bias% seemed low, some monthly CV% and bias% levels were high causing low sigma levels. We can design our QC procedures for each test according to the needs of emergency department. Our test results should be accurate enough for the physicians waiting laboratory results for prompt therapeutic decision and quick enough without compromising analytical performance. By showing the sigma level of the test and determining the major source of the error, sigma metrics may be useful on achieving this target.

Conflict of interest: Authors have no conflict of interest.

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