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Evaluation of sample rejection rate in clinical biochemistry laboratory before and after implementation of six-sigma methodology

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ABSTRACT

Background: In pre-analytical phase of Clinical Biochemistry Laboratory, sample rejection is a very frequent and important source of error. It affects the overall quality of laboratory services and patient care by increasing cost and turnaround time. It leads to test abandonment and causes inconvenience to patients and staff. **Aims and Objectives:** The aim of the study was to implement the define, measure, analyze, improve, and control (DMAIC) method of six-sigma to decrease the rate of sample rejection in Clinical Biochemistry Laboratory. **Materials and Methods:** In this prospective study, sample rejection rates were analyzed in a clinical Biochemistry Laboratory before and after implementation of DMAIC method of six-sigma. Baseline rejection rates were calculated for a year and classified based on cause of rejection and patient location. Current defects per million opportunities and six sigma values were calculated. This was followed by root cause analysis and implementation of corrective and preventive measures. Reanalysis of the baseline measures was done to observe the impact of these measures. **Results:** After implementation of DMAIC, the overall rejection rate fell from 1.07% to 0.49% with an increase in sigma value from 3.8 to 4.1. **Conclusion:** Six-sigma tool like DMAIC can be successfully implemented to improve sample rejection rates ultimately improving the quality of laboratory services in resource limited setting with minimal financial implications.

Key words: Biochemistry laboratory; Six-sigma; Sample rejection

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INTRODUCTION

Clinical laboratory is at the cornerstones for optimum patient care which mandates regular and continued improvement in the quality of laboratory services. Pre-analytical area still constitutes the source of major errors in a laboratory despite all the measures that have been taken in the past years to improve it.[1] Sample rejection is one of the major pre-analytical errors commonly encountered in laboratory practice. There are various causes of sample rejection. Causes such as clerical errors, illegible handwriting, and incomplete patient information have decreased due to introduction of automation and bar coding; however, other factors such as hemolysis, insufficient quantity, lipemia, and sample in wrong vial still remain a major concern.

The sample rejection rates vary widely from 0.1% to 3.49% described in international studies[2-5] to 1.9–28% in laboratories in developing countries.[6-9] This stark difference emphasizes the need for more stringent measures for quality improvement in the latter group. Lack of resources and awareness is one of the most important factors leading to this disparity.

The term six-sigma originally coined by Motorola engineer Bill smith in 1980's is now considerably well known. It was initially implemented in manufacturing industries but following some scepticism, it has been increasingly incorporated in the health industry. In the recent years, six-sigma has been successfully employed to evaluate the quality of different phases of clinical laboratory from pre-analytical and analytical to post-analytical areas.[10-14]

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Studies have been done to evaluate the rate of sample rejection in biochemistry laboratory, but few discuss the improvement after implementation of corrective measures and fewer have used six-sigma as a process improvement tool.

Aims and objectives

The aim of our study was to follow define, measure, analyze, improve, and control (DMAIC) methodology of six-sigma to evaluate the rate of sample rejection in a year in a tertiary care hospital in North India and initiate corrective and preventive measures to improve the rejection rates.

The objectives were (1) to calculate the rate of sample rejection in clinical Biochemistry Lab in a year, (2) to identify the causes of sample rejection, (3) to initiate corrective and preventive measures to decrease the rate of rejection, and (4) reassess the rejection rate after implementation of corrective measures.

MATERIALS AND METHODS

This was a prospective before and after analysis of sample rejection rates in clinical Biochemistry Laboratory of a tertiary care hospital in North India after implementation of DMAIC method of six-sigma. Sample rejection rate for the year 2020 was calculated followed by implementation of measures to improve rejection rates. Reanalysis was done to check for improvements in the baseline measures. Ethical clearance for the study was taken from the Institutional Ethics Review Board.

Define phase

The samples rejected were classified based on the cause of rejection (hemolysis, lipemia, wrong vacutainer, insufficient quantity, missing patient details, wrong patient ID, and clotted sample) and patient location, through the manual entry log for rejected samples. The laboratory staff is trained to follow the pre-defined criteria of sample rejection.

The tests included blood and urine samples for routine biochemistry, glycated hemoglobin, hormones, tumor markers, immunoassays, drugs of abuse, and therapeutic drug monitoring.

Measure phase

The baseline measures of the current rejection rates were recorded.

The rejection rate (Defects %) was calculated as number of samples rejected/Total number of samples * 100.

The defects per million opportunities (DPMO) were calculated as number of defects/total number of opportunities * 10,00,000.

The yield and the sigma values were calculated using online calculator.[15]

Analyze phase

After looking at the causes of sample rejection obtained in the measure phase, meetings were arranged with Clinical Biochemistry Laboratory staff to go into the depth of causes. The following observations were made

1. Majority of the samples rejected were from the inpatient department (IPD)
2. A list of departments with maximum samples rejected was made in the decreasing order. It was observed that among the IPD, samples from the emergency department (ED) were most frequently rejected followed by medicine unit
3. Further, within each department, the subunits with more samples rejected were identified
4. At the laboratory level, it was found that the rejection log had missing entries. Furthermore, different abbreviations for different locations were used by different staff.

Improve phase

After the discussions, a multifaceted approach was followed to circumvent the issues found in the analyze phase (Figure 1).

Control phase

After the implementation of the said recommendations, few months were given for the measures to take affect and reanalysis of the baseline measures was done from September 2021 to April 2022 to look for changes.

Descriptive statistics were done using Microsoft Excel.

RESULTS

During the period of 1 year from January 2020 to December 2020, a total of 407,845 samples were received in the clinical biochemistry laboratory. Out of these, 4345 samples were rejected. The monthly sample no, samples rejected, and the rejection rates are shown in Figure 2. The average defects % for the year 2020 was 1.07% with a sigma value of 3.8. The average DPMO was 10653.55 and yield was 98.93 (Table 1).

The most common cause of sample rejection was found to be hemolysis (4010) followed by clotted samples (257). Thirty-three samples were wrongly labeled. For 18 samples, the test request was there in the Hospital information system, but sample was not received by the laboratory

Table 1: Monthly defects %, DPMO, yield, and sigma value for the year 2020, pre-DMAIC intervention

Month	No of samples	Samples rejected	Defects %	Defects per million opportunity DPMO	Sigma value	Yield
January	52,085	473	0.91	9081.30	3.86	99.09
February	52,153	470	0.90	9011.94	3.87	99.10
March	40,119	352	0.88	8773.89	3.88	99.12
April	16,486	134	0.81	8128.10	3.90	99.19
May	22,252	192	0.86	8628.43	3.88	99.14
June	27,837	206	0.74	7400.22	3.94	99.26
July	29,444	357	1.21	12124.73	3.75	98.79
August	25,692	318	1.24	12377.39	3.75	98.76
September	29,987	406	1.35	13539.20	3.71	98.65
October	36,591	456	1.25	12462.08	3.74	98.75
November	36,843	502	1.36	13625.38	3.71	98.64
December	38,356	479	1.25	12488.26	3.74	98.75
Total	407,845	4345	1.07	10653.55	3.80	98.93

DMAIC: Define, measure, analyze, improve, and control, DPMO: Defects per million opportunities

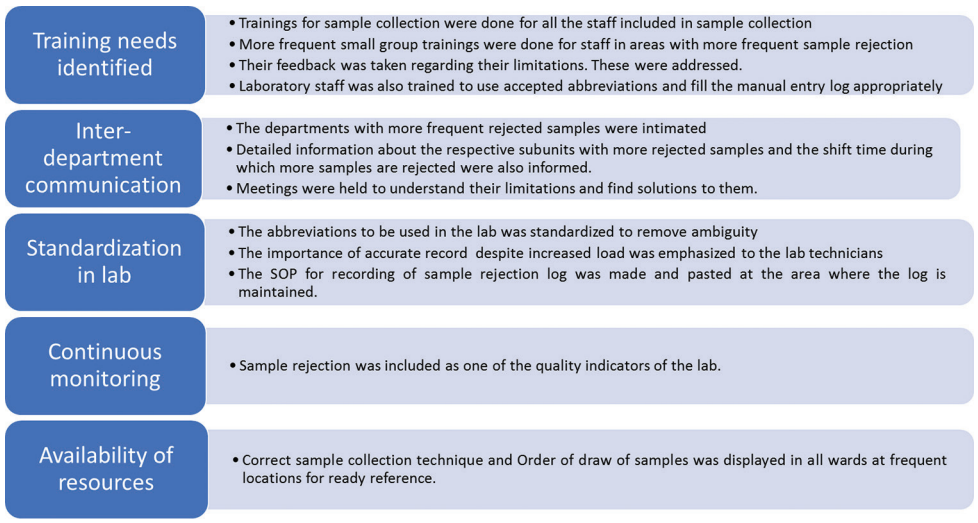

Figure 1: Steps taken to decrease sample rejection in improve phase of define, measure, analyze, improve, and control (DMAIC)

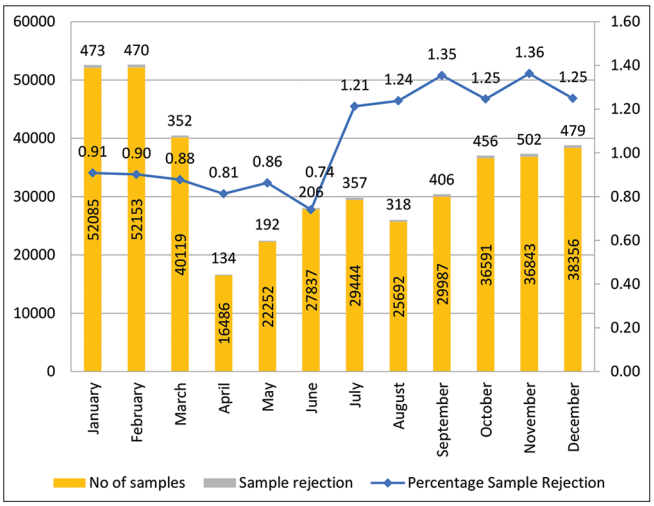

Figure 2: Total number of monthly samples received, samples rejected, and the percentage of monthly sample rejection for the year 2020 pre-DMAIC intervention

(lost in transportation). For 10 samples, the cause of rejection was missing in the sample rejection data entry log, 10 samples were quantity not sufficient, four samples were too thick to be analyzed, and one sample was sent twice as depicted in Table 2.

Rejected samples were received from all the departments; however, maximum samples that got rejected were from the ED (34%) followed by medicine unit (8.7%). In all the departments, the main cause of rejection remained hemolysis. The ED also had the maximum number of clotted samples.

For departments with multiple subunits, further scrutinization was done within departments to see which areas had more frequency of rejected samples. Within departments, most of the rejected samples came from corresponding intensive care unit (ICU)'s.

Following the recommendations decided on in the improve phase, reanalysis of sample rejection rates was done for the period between September 2021 and April 2022 as depicted in Figure 3.

It was observed that the sample rejection rates remained below 1% for all the months following intervention and the average rejection rate fell from 1.07% pre-DMAIC intervention to 0.49% post-intervention. The sigma value increased from 3.8 to 4.1 resulting in a fall of DPMO from 10653.55 to 4864.49. Table 3 describes the changes in these parameters for the months post-DMAIC.

The rejected samples were decreased among almost all categories of rejection as shown in table. QNS sample % was more than baseline measure. In addition, the manual rejection log was being maintained with uniform abbreviations and data were not missing in most cases as shown in Table 4.

Table 2: Frequency of *causes of sample rejection* pre-DMAIC intervention

Cause of rejection	Samples rejected	Percentage (total No 4345) (%)
Hemolyzed	4010	92.29
Clot	257	5.91
Wrong label	33	0.76
Not received	18	0.41
No data	10	0.23
QNS	10	0.23
Thick fluid	4	0.09
Wrong vial	2	0.05
Double sample	1	0.02

DMAIC: Define, measure, analyze, improve, and control

DISCUSSION

Quality laboratory services are the need of the hour in today's time when most of the clinical decisions are dependent on accurate and timely laboratory results. Maintenance of quality services requires frequent auditing of the various processes (pre-analytical, analytical, and post-analytical). In this study, we focused on improving the rate of sample rejection using six-sigma methodology.

Sample rejection was chosen as the area of focus as it increases the cost due to repeated use of consumables and causes delay in getting patient results as well as delay in reporting of critical values thus severely affecting patient management. In addition, it also causes inconvenience to the staff as well as patients as the samples must be drawn again. It causes increase in the turnaround time affecting the quality of laboratory services. Some studies have also reported test abandonment rates of 48.3%[16] and 11.2%[17] following sample rejection.

At the baseline, the overall sample rejection rate in our laboratory was found to be 1.07% for the year 2020 with

Table 3: Rejection rates, DPMO, sigma value, and yield post-DMAIC intervention

Month	No of samples	Sample rejection	Defects %	Defects per million opportunity DPMO	Sigma value	Yield
September	46,417	294	0.63	6333.89	4.0	99.37
October	49,149	237	0.48	4822.07	4.1	99.52
November	47,919	304	0.63	6344.04	4.0	99.37
December	44,900	199	0.44	4432.07	4.1	99.56
January	37,927	181	0.47	4772.33	4.1	99.53
February	41,632	193	0.46	4635.86	4.1	99.54
March	47,048	164	0.34	3485.80	4.2	99.66
April	44,347	176	0.39	3968.70	4.2	99.61
Total	359,339	1748	0.49	4864.49	4.1	99.51

DMAIC: Define, measure, analyze, improve, and control, DPMO: Defects per million opportunities

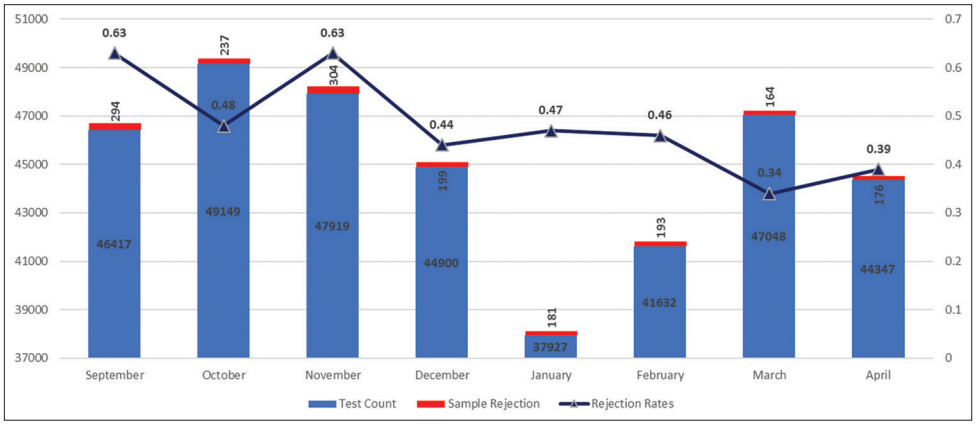

Figure 3: Total number of monthly samples received, samples rejected, and the percentage of monthly sample rejection between September 2021 and April 2022, post-DMAIC intervention

Table 4: Causes of sample rejection post-DMAIC intervention

Cause of rejection	Samples rejected	Percentage (total no. 4345)
Hemolyzed	1606	91.88
Clot	102	5.84
Wrong Label	13	0.74
Not received	7	0.40
No data	3	0.17
QNS	14	0.80
Thick fluid	2	0.11
Wrong Vial	1	0.06
Double sample	0	0.00

DMAIC: Define, measure, analyze, improve, and control

an average sigma value of 3.8 and DPMO of 10653.55. Our rejection rates were closer to that seen in international studies (0.1–3.49%)[2-5] and some studies in developing countries with rejection rate of 1.5%.[9,12]

The most common cause of sample rejection was found to be hemolysis (92.29%). *In vitro* hemolysis can be a result of various causes associated with sample collection, handling, or transportation such as incorrect needle size, improper sample mixing, incorrect filling of vacutainers, prolonged tourniquet, jarring transportation, extreme temperatures, delayed processing, or prolonged storage.[18,19] Several studies have shown that hemolysis interferes with various analytical parameters.[20-22] Other studies have also found hemolysis to be the primary cause of sample rejection in their laboratories.[4,23,24] Yet others have mentioned sample clot to be the more frequent cause of sample rejection.[5,16,25] We found clotted samples to be much less in frequency than hemolysis (5.91%). Since a major bulk of our rejected samples were due to hemolysis and it is also corroborated by various other studies, we sensitized and trained the staff involved in sample collection regarding the various causes of *in vitro* hemolysis and methods to avoid these errors.

Although in small number, we also came across other causes of rejection such as wrong label (0.76%), QNS (0.23%), and wrong vial (0.05%). Insufficient sample was found to be the most common cause of sample rejection by Kulkarni et al. The causes could be pediatric samples, untrained phlebotomists, or too many investigations ordered from one sample.[12] These are avoidable if staff is adequately sensitized. The charts for "order of draw of samples" were displayed in all wards and ED for ready reference.

In our study, maximum samples that were rejected were from the IPD especially the ED rather than outpatient department (OPD). Other studies have also reported higher rejection rates from IPD and EDs compared to OPD.[4,5,25-28] The reason for this could be that OPD samples are usually collected at dedicated sample collection centers; however, the staff employed in IPD and ED works in shifts and keeps changing. Hence, more frequent training sessions in sample collection and transport were organized for IPD and emergency staff.

The departments with multiple sub-units were looked at to specifically target the areas that needed more supervision. We found that respective ICUs had more incidence of rejected samples. Dikmen et al.,[25] also discusses more prevalence of rejected samples within respective ICUs. We organized small group training sessions in these areas for a more focused approach.

Apart from the rejection rates, we found some disparities in the way the record was being maintained as the laboratory staff used different abbreviations for the different patient locations and some fields were missing in the manual data entry log (0.23%) in certain cases making patient location difficult to identify and thus increase delay in reporting. Hence, DMAIC gave us a chance to look at the lacunae in our record keeping for sample rejection as well which has a direct bearing on the quality of lab services. We standardized and documented the abbreviations to be used in laboratory and sensitized the laboratory staff regarding the same in keeping with good clinical laboratory practices.

After implementation of all these corrective and preventive measures, we re-evaluated the baseline characteristics. The average rate of sample rejection fell to 0.49% from the previous 1.07%. The sigma value increased from 3.8 to 4.1 and the average DPMO fell from 10653.55 to 4864.49. The errors with a sigma value of ≥4 in pre-analytical area indicate a well-controlled process.[12] All categories of sample rejection showed a decline post-DMAIC except QNS (increased from 0.23% to 0.8%). The reason was found to be a greater number of pediatric samples during this time increasing the overall percentage.

Much has been studied about six-sigma and its role in healthcare in recent years. More than half of these studies have been done in the US.[29] Very few hospitals in India have implemented six-sigma tools due to lack of knowledge and availability of resources.[30]

Limitations of the study

This was a single center study from a private tertiary care hospital in North India. Medical and Laboratory facilities vary widely in our country. A multi-center study will provide a better insight into applicability of DMAIC six-sigma for improving rejection rates in different hospital settings.

CONCLUSION

The results show that with some innovation, six-sigma can be an appropriate tool that can be beneficial in improving quality of laboratory services in the still troublesome pre-analytical area even in a resource limited setting like India.

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REFERENCES

1. Cornes M, Atherton J, Pourmahram G, Borthwick H, Kyle B, West J, et al. Monitoring and reporting of preanalytical errors in laboratory medicine: The UK situation. Ann Clin Biochem. 2016;53(Pt 2):279-284.
   https://doi:10.1177/0004563215599561
2. Alsine MJ, Alvarez V, Barba N, Bullich S, Cortes M, Escoda L, et al. Preanalytical quality control program-an overview of results (2001-2005 summary). Clin Chem Lab Med. 2008;46:849-854.
   https://doi:10.1515/CCLM.2008.168
3. Bonini P, Plebani M, Ceriotti F and Rubboli F. Errors in laboratory medicine. Clin Chem. 2002;48:691-698.
4. Stark A, Jones BA, Chapman D, Well K, Krajenta R, Meier F, et al. Clinical laboratory specimen rejection-association with the site of patient care and patients characteristics: Finding from a single health care organization. Arch Pathol Lab Med. 2007;131(4):588-592.
   https://doi.org/10.5858/2007-131-588-CLSRWT
5. Atay A, Demir L, Cuhadar S, Saglam G, Unal H, Aksun S, et al. Clinical biochemistry laboratory rejection rates due to various types of preanalytical errors. Biochem Med. 2014;24:376-382.
   https://doi.org/10.11613/BM.2014.040
6. Chhilar N, Khurana S, Agarwal R and Singh N. Effect of pre-analytical errors on quality of laboratory medicine at a neuropsychiatry institute in north India. Indian J Clin Biochem. 2011;26(1):46-49.
   https://doi.org/10.1007/s12291-010-0082-2
7. Agarwal R, Chaturvedi S, Chillar N, Pant I, Kaushik S, Tripathi C, et al. A trend analysis of quality indicators of patient safety in the clinical laboratory over 21 months. Lab Med. 2012;43:300-306.
8. Agarwal R, Chaturvedi S, Chillar N, Goyal R, Pant I and Tripathi CB. Role of intervention on laboratory performance: Evaluation of quality indicators in a tertiary care hospital. Indian J Clin Biochem. 2012;27(1):61-68.
   https://doi.org/10.1007/s12291-011-0182-7
9. Chawala R, Goswami B, Tayal B and Mallika B. Identification of the types of Pre-analytical errors in clinical chemistry laboratory: 1-year study at G.B pant hospital. Lab Med. 2010;41:89-92.
10. Inal T, Goruroglu Ozturk O, Kibar F, Cetiner S, Matyar S, Daglioglu G, et al. Lean six sigma methodologies improve clinical laboratory efficiency and reduce turnaround times. J Clin Lab Anal. 2018;32(1):e22180.
    https://doi.org/10.1002/jcla.22180
11. Letelier P, Guzman N, Medina G, Calcumil L, Huencho P, Mora J, et al. Workflow optimization in a clinical laboratory using Lean management principles in the pre-analytical phase. J Med Biochem. 2021;40(1):26-32.
    https://doi.org/10.5937/jomb0-26055
12. Kulkarni S, Ramesh R, Srinivasan AR and Silvia CR. Evaluation of preanalytical quality indicators by six sigma and pareto's principle. Indian J Clin Biochem. 2018;33(1):102-107.
    https://doi.org/10.1007/s12291-017-0654-5
13. Zhou B, Wu Y, He H, Li C, Tan L and Cao Y. Practical application of six sigma management in analytical biochemistry processes in clinical settings. J Clin Lab Anal. 2020;34(1):e23126.
    https://doi.org/10.1002/jcla.23126
14. Mao X, Shao J, Zhang B and Wang Y. Evaluating analytical quality in clinical biochemistry laboratory using six sigma. Biochem Med. 2018;28(2):020904.
    https://doi.org/10.11613/BM.2018.020904
15. Process Sigma Calculator Assumptions. Available from: https://www.isixsigma.com/process-sigma-calculator/process-sigma-calculator-assumptions [Last accessed on 2022 Mar].
16. Jacobsz LA, Zemlin AE, Roos MJ and Erasmus RT. Chemistry and haematology sample rejection and clinical impact in a tertiary laboratory in Cape Town. Clin Chem Lab Med. 2011;49(12):2047-2050.
    https://doi.org/10.1515/CCLM.2011.743
17. Karcher DS and Lehman CM. Clinical consequences of specimen Rejection: A college of American pathologists Q-Probes analysis of 78 clinical laboratories. Arch Patho Lab Med. 2014;138(8):1003-1008.
    https://doi.org/10.5858/arpa.2013-0331-CP
18. Azman WN, Omar J, Koon TS and Ismail TS. Hemolyzed specimens: Major challenge for identifying and rejecting specimens in clinical laboratories. Oman Med J. 2019;34(2):94-98.
    https://doi.org/10.5001/omj.2019.19
19. Tolan N, Kaleta E, Fang J, Colby CE, Carey WA, Karon BS, et al. Neonatal intensive care unit quality initiative: Identifying preanalytical variables contributing to specimen hemolysis and measuring the impact of evidence-based practice interventions. Am J Clin Pathol. 2016;146(1):113-118.
    https://doi.org/10.1093/ajcp/aqw086
20. Grafmeyer D, Bondon M, Bondon M and Levillain P. The influence of bilirubin, haemolysis and turbidity on 20 analytical tests performed on automatic analysers. Results of an interlaboratory study. Eur J Clin Chem Clin Biochem. 1995;33:31-52.
    https://doi.org/10.1515/cclm.1995.33.1.31
21. Sonntag O. Haemolysis as an interference factor in clinical chemistry. J Clin Chem Clin Biochem. 1986;24(2):127-139.
22. Koseoglu M, Hur A, Atay A and Cuhadar S. Effects of hemolysis interferences on routine biochemistry parameters. Biochem Med (Zagreb). 2011;21(1):79-85.
    https://doi.org/10.11613/bm.2011.015
23. Chawla R, Goswami B, Singh B, Chawla A, Gupta VK and Mallika V. Evaluating laboratory performance with quality indicators. Labmedicine. 2010;41:297-300.
24. Mukhopadhyay T, Shekhar S, Dagar VK and Mukhopadhyay AK. Characterization of pre-analytical errors using six sigma metrics and process capability index in a clinical biochemistry laboratory. Int J Health Sci Res. 2021;11:171-176.
25. Dikmen ZG, Pinar A and Akbiyik F. Specimen rejection in laboratory medicine: Necessary for patient safety? Biochem Med (Zagreb). 2015;25(3):377-385.
    https://doi:10.11613/BM.2015.037
26. Jones BA, Meier F and Howanitz PJ. Complete blood count

specimen acceptability: A college of American pathologists Q-probes study of 703 laboratories. Arch Pathol Lab Med. 1995;119(3):203-208.

27. Jones BA, Calam RR and Howanitz PJ. Chemistry specimen acceptability: A college of American pathologists Q-Probes study of 453 laboratories. Arch Pathol Lab Med. 1997;121(1):19-26.
28. Zarbo RJ, Jones B, Friedberg R, Valenstein PN, Renner SW, Schifman RB, et al. Q-Tracks: A college of American pathologists program of continuous laboratory monitoring and longitudinal performance tracking. Arch Pathol Lab Med. 2002;126(9): 1036-1044.

    https://doi:10.5858/2002-126-1036-QT
29. Zimmermann G, Siqueira L and Bohomol E. Lean six sigma methodology application in health care settings: An integrative review. Rev Bras Enferm. 2020;73:e20190861.

    https://doi:10.1590/0034-7167-2019-0861
30. Suman G and Prajapati DR. Utilization of lean & six sigma quality initiatives in Indian healthcare sector. PLoS One. 2021;16(12):e0261747.

    https://doi.org/10.1371/journal.pone.0261747

Authors' Contributions:
NMJ- Prepared the concept and design of the study, interpreted the results, and prepared the first draft of manuscript; **NKB and EB**- Supervised the entire study; **AG-** Helped with coordination and statistical analysis; All the authors edited and reviewed the manuscript.

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