J. Fac. Pharm. Ankara/ Ankara Ecz. Fak. Derg., 48(4): 1293-1302, 2024
Doi: 10.33483/jfpau.1443744

ORIGINAL ARTICLE / ÖZGÜN MAKALE

CRITICAL POINTS OF INTERFERENCE AND PROBABLE INFLUENCE ON THE VALIDITY OF RESULTS OF A BIOCHEMICAL MEDICAL ANALYSIS: STATISTICAL APPROACH

BİYOKİMYASAL TIBBİ ANALİZ SONUÇLARININ GEÇERLİLİĞİ ÜZERİNDEKİ KRİTİK MÜDAHALE NOKTALARI VE OLASI ETKİLERİ: İSTATİSTİKSEL YAKLAŞIM

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ABSTRACT

Objective: *The manipulator must be aware that some results obtained by the various biochemical analysis methods may be erroneous and don't represent reality. For this, the biochemist is asked to identify the critical points responsible for the aberration of the results obtained and it is imperative that he be aware of all the factors that can induce the modification of the results obtained. The influencing factors listed are the results of long practical experience within a biochemical analysis laboratory supplemented by bibliographic research that we have brought together in an educational document in the form of a guide and of which the statistical study is reported by the present study.*
Material and Method: *Through this study, we used the Ichikawa diagram of Hazard Analysis Critical Control Point to list and organize all the factors of influence and probable interference on the results of a biochemical medical analysis, subsequently, we determined the influence rates of each factor as well as all the factors linked to it. The statistical study carried out relates to the pre-analytical, analytical and post-analytical stages of a biochemical analysis. The rates obtained represent the influence of an isolated factor or a common set of factors in relation to all the factors determined.*
Result and Discussion: *The critical points of interference and influence on the validity of the results obtained have been listed through all the steps of a biochemical analysis with variable rates of 60.26%, 28.75% and 07.84% respectively for the pre- analytical stage, analytical and post analytical stage; The highest rate for the pre--analytical stage was represented by factors related to patient with a rate of 35.29%,concerning the analytical stage, the materials used presented a rate of 11.11% for the post-analytical stage, factors that could interfere with the measurement presented a rate of 05.58%.*
Keywords: *Analysis, biochemical, HACCP, influence, interference*

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Submitted / Gönderilme : 03.03.2024
Accepted / Kabul : 27.05.2024
Published / Yayınlanma : 25.11.2024

Presented at the 1st International Conference on Trends Methods in Analytical Chemistry (CTMAC 2023), 06-08 March 2023, Bechar, Algeria.

ÖZ

Amaç: *Manipülatör, çeşitli biyokimyasal analiz yöntemleriyle elde edilen bazı sonuçların hatalı olabileceğinin ve gerçeği temsil etmediğinin farkında olmalıdır. Bunun için, biyokimyacıdan elde edilen sonuçların sapmasından sorumlu kritik noktaları belirlemesi istenir ve elde edilen sonuçların değişmesine neden olabilecek tüm faktörlerin farkında olması zorunludur. Listelenen etkileyici faktörler, bir biyokimyasal analiz laboratuvarındaki uzun pratik deneyimin sonuçları olup, bir rehber şeklinde bir eğitim belgesinde bir araya getirdiğimiz ve istatistiksel çalışması bu çalışma tarafından rapor edilen bibliyografik araştırmalarla desteklenmiştir.*

Gereç ve Yöntem: *Bu çalışmada, bir biyokimyasal tıbbi analizin sonuçları üzerindeki tüm etki faktörlerini ve olası girişimleri listelemek ve düzenlemek için Tehlike Analizi Kritik Kontrol Noktasının Ichikawa diyagramını kullandık, ardından her bir faktörün etki oranlarını ve bununla bağlantılı tüm faktörleri belirledik. Yürütülen istatistiksel çalışma, bir biyokimyasal analizin analiz öncesi, analitik ve analitik sonrası aşamalarıyla ilgilidir. Elde edilen oranlar, belirlenen tüm faktörlerle ilişkili olarak izole bir faktörün veya ortak bir faktör kümesinin etkisini temsil etmektedir.*

Sonuç ve Tartışma: *Elde edilen sonuçların geçerliliği üzerindeki kritik müdahale ve etki noktaları, biyokimyasal bir analizin tüm aşamaları boyunca %60.26, %28.75 ve %07.84 gibi değişken oranlarla listelenmiştir. En yüksek oran analitik öncesi aşamada %35.29 ile hastaya ait faktörlerde, analitik aşamada kullanılan malzemeler %11.11 oranında, analiz sonrası aşama için ölçümü etkileyebilecek faktörler %05.58 oranında ortaya çıkmıştır.*

Anahtar Kelimeler: *Analiz, biyokimyasal, HACCP, girişim, etki*

INTRODUCTION

The human body is governed by a panoply of devices themselves made up of organs, which are structured by tissues and cells whose functioning is orchestrated by a set of chemical molecules participating in cellular anabolism and catabolism. These chemical molecules are found in the blood and other bodily fluids, with a remarkable divine balance expressing unequivocal homeostasis, with varying serum levels. The detection and measurement of the levels of these molecules are carried out by qualitative and quantitative biochemical analysis methods. The smooth running of the detection and measurement of the levels of these molecules is the major objective of the present study.

In order to provide correct results to patients, the biochemist is called upon to follow a panoply of recommendations and directives and to avoid prohibitions relating to factors and critical points that may interfere with or influence the validity of the result of the analysis at the level of the pre-analytical stage, the analytical stage, and the post-analytical stage.

Indeed, such simple gestures as bringing the reagent used to room temperature before implementing the "sample-reagent" reaction and handling the micropipette may involve a set of interfering and influencing factors that can induce the modification of results of the biochemical medical analysis.

The objectives of the present study are to list all the factors of interference and influence, realize a statistical study of the factors listed, and help the biochemist become aware of interfering and influencing factors in order to avoid them.

All the factors listed through the study conducted were exposed through a practical guide entitled "Critical points of interference and probable influence on the validity of the results of a biochemical analysis" [1], which we present in this follows the overall statistical study obtained.

MATERIAL AND METHOD

Means of Study

Through this study, we exposed all the factors that we have listed through the Ichikawa diagram, which allowed us to organize the factors revealed in the form of a multitude of axes, each consisting of several levels presenting certain correlations.

The Ishikawa diagram is a method of brainstorming that is used to find and represent the different causes of a problem. The Ishikawa diagram is particularly well suited to the risk management. We have adapted it to our study, in order to identify the problems encountered during a biochemical analysis.

The statistical study carried out relates to the pre-analytical, analytical and post-analytical stages of a biochemical analysis. The rates obtained represent the influence of an isolated factor or a common set of factors in relation to all the factors determined.

$$RIF\ (\%) = 100 / TNF$$

IRF = Rate of Influencing factor(S)
TNF= Total number of factors determined for a stage or all stages of a biochemical médical analysis.

Through this study we evaluated:
* Rate of interference and influence critical points relative to each stage
** Manipulator interference and influence critical point rate relative to each level.
*** Total rate of critical points of interference and influence relating to the manipulator compared to all the factors listed at the level of all the stages of the analysis.

Stages Investigated

We have investigated the three stages that constitute a biochemical medical analysis, which are: [1,2]

a] -pre-analytical stage

is a stage which concerns all the facts and acts which:
- precede the collection of the sample,
- during sampling
- and the processing of the sample in order to prepare a sample ready for the biochemical analysis to be carried out.

b] - analytical stage

The analytical stage concerns all the acts relating to the implementation of the analysis from a sample ready to be analyzed until the expected result is obtained.

c] - post-analytical stage

Concerns all the acts relating to the processing of the result obtained from the analysis carried out: case of an anomaly or inconsistent results, badreading or bad interpretation of the results obtained.

RESULT AND DISCUSSION

Listed Interfering and Influencing Factors

In this part of the study, we present all listed factors, or critical points, of interference and influence on the validity of the results of a biochemical medical analysis, through the pre-analytical stage, analytical stage and post-analytical stage.

Pre-Analytical Stage [1-12]

We have listed a number of 92 factors relating to the patient, including sampling, we have also listed the factors frequently encountered during a biochemical medical analysis.

a] - Patient Factors
b] - Sample Collection Factors
c] - Frequent factors

a] - Patient Factors

At this level, we have listed a fairly large number of factors that may be the cause of the probable modification of the results expected from the biochemical analysis.

Table 1 presents the results of the investigationof interfering and influencing factors relating to the patient.

A large number of factors relating to the patient have been listed, with a value of 54 factors, among which are age, physiological state, sex, weight and others, factors listed in this stage are mainly represented by factors related to the physiological state of the patient concerned.

b] - Sample Collection Factors

Table 2 presents the results of the investigation of interfering and influencing factors relating to

Sample Collection Factors.

Table 1. Probable interfering and influencing factors relating to the patient [1-12]

Interfering and influencing factors relating to the patient		
Age	New born	
	Teenager	
	Adult	
	Old	
Sex	Female	
	Male	
Weight	Obesity	
Physiological State	Fasting	Mandatory
		Preference
		Prolonged
		Not necessary
	Pregnancy	
	Menstrual cycle	
	Menopause	
	Nychthemeral cycle	
	Circadian rhythm	
	Seasons	Summer
		Winter
	Heat	Prolonged exposure to heat
		Fever
	Underlying disease	Infectious episode
		Diabetes
		Dialysis
		Severe hepatic impairment
	Specific diet	Malnutrition.
		High protein
		Rich in carbohydrates
		High in saturated fat
		High calorie
		Vegetarian diets
		Anorexia nervosa
		Fruit and liquorice
		Rich in iron
	Bad consumption Chronic	Alcohol
		Caffeine
		Tobacco
		Cocaine
Others	Physical exercise / cycling	
	Stress / Black skin color	
	Deficiency / Acidity of the sample	
	Ejaculation / Altitude.	

Table 2. Probable interfering and influencing factors relating to sampling [3-9]

Probable interfering and influencing factors relating to sampling		
Terms of Sampling	Moment	Inadequate
	Position	Standing during collection
		Prolonged standing position before sampling
		Bedridden

Table 2 (*continue*). Probable interfering and influencing factors relating to sampling [3-9]

Probable interfering and influencing factors relating to sampling			
Matérials Used	Vials	Cleanliness	
		Quantity	
	Tubing	Without Anticoagulant / clean	
		With Anticoagulant	Nature
			Quantity
		Additive	Nature
			Quantity
	Laidof gorrate	Extended	
		Prohibited	
	Syringe	Diameter	
		Transposition	Remove the needle
			Transpose slowly
	Catheter	Nature	
		Diameter	
Processing of the sample	Distribution	Order of tubes used	
		Quantity distributed	
	Moderate stir (manual turning 6 to 8 times)		
	Preservation	Séparationserum / plasma	
		Temperature	
		Duration	
	Transportation	Jerks	
		Correct tube position	

We have listed a number of 31 factors relating to sampling at the level of:

- terms of sampling,
- materials used,
- and processing of the sample.

c]- Frequent factors [13]

We have listed a number of 4 frequent factors represented by:

- haemolizedserum:increase/ decrease
- lipimicserum:increase/ decrease
- icteric serum:increase
- drugs: normal dose / high dose

Analytical Stage [1,2,5,14-17]

Regarding the analytical stage, we have listed 44 factors relating to:

- a] Materials used
- b] Technical sheet

a]- Materials used

The materials used for the realization of the biochemical medical analysis can present many critical points of inference and influence on the expected results, in particular if the latter is inadequate, badly used, or not controlled.

Table 3 presents the results of the investigationof interfering and influencing factors relating to the materials used.

The factors listed at this level were 17 factors equivalent to 11.11% relative to all the factors that we listed for the three stages of a biochemical analysis.

The manipulator must relate to the equipment used, because the latter is involved in several factors at this level of analysis.

Table 3. Probable interfering and influencing factors relating to the materials used

Probable interfering and influencing factors relating to the materials used			
Materials and equipment used	Measuring devices	*Starting up	
		Maintenance	
		*Programming	
		Specific reagent	
		*Accessories and consumables	
		Specific fuel	
		Agarose gel	
	Pipette and micropipette	Calibration	
		Tip	*Position
			Change*
		Handling	* 1st Stop
			*2nd Stop
	Tank	Quality	
		*State	
		Thickness	
		*Wear	
		*Insertion	

* Probable influence of the manipulator

b]- Technical sheet

The technical sheet presents all the information necessary to carry out the biochemical medical analysis, the latter may present a large number of critical points of interference and influence on the expected results.

Table 4 presents the results of the investigationof interfering and influencing factors relating to the technical sheet**.**

Table 4. Probable interfering and influencing factors relating to the data sheet

Probable interfering and influencing factors relating to the data sheet		
Method adopted	Understanding and applying guidelines	
	Chronological order	
Reagent used	Quantity	
	Bring the reagents to room temperature 25°C	
	Contamination	
	Stability of stored reagent	Duration
		Temperature
	Stability of reconstituted reagent	Duration
		Temperature
	Stability of reagent-Sample reaction,	Duration
		Temperature
	Incubation of reagent-Sample reaction,	Duration
		Temperature
Sample	Nature	
	Quantity	
	Preservation of samples	
Interfering / Influencing factors Manipulator: Behavioral habits		
Compliance with all the directives of the pré analytical / Analytical and post analytical stages		
Organization Labeling	Labeling	
Organization Labeling	Arrangement of materials	
Good gesture		
Chemicals on fingers		

It is essential for the manipulator to be able to understand and apply the directives given in the technical data sheet of the product used for the analysis because the latter is closely linked to all the factors relating to the technical data sheet.

The technical data sheet provides all the information and directives relating to:

- the reagent used,
- the analyzed sample,
-and the method adopted for carrying out the analysis.

The factors relating to the reagent are the most numerous concerning the technical data sheet, the latter presented a rate of 73.33% factors compared to the factors listed for the technical data sheet.

Post-Analytic Stage [18]

At this level, we have listed 12 factors from references and personal experiences:

- during the measurement and after measurement.

The Table 5 presents the results of the investigationof interfering and influencing factors relating to the post-analytic stage.

Table 5. Probable interfering and influencing factors relating to the post- analytical stage

Probable interfering and influencing factors relating to the post- analytical stage	
Errors occurred during measurement	Calibration
	Zero adjustment
	Wave length
	Programming
	Accuracy
	Maintenance
	Aberrant calculation formulas.
Errors occurred after measurement	Results interpretation
	Presentation of the results
	Calculations made
	Confusion between patient A and B
	Reference limit values

We noted that the rate, of critical points of interference and probable influence, at the level of the post-analytical stage, was relatively low compared to the rates highlighted at the level of the pre-analytical and analytical stage and factors listed at this stage of the biochemical analysis are split into factors relating to the measuring device used for the analysis and factors relating to the manipulator.

Results of the Statistical Approach Relating to the Critical Points Which Can Influence the Results of a Biochemical Analysis Manipulator

Regarding to results obtained and Statistical approach realized relating to the critical points that can influence the results of a biochemical analysis a great attention must be paid to the manipulator whose interference and influence factors presented a rate of 40.52% compared to all the factors listed through the present study.

Results of the Statistical Approach of Terfering and Influing Factors Relating to the Manipulator

The rates of interference and influence factors relating to the manipulator are listed in Table 6.

The manipulator is responsible for:

- 77.41% of the factors relating to the –sampling in the pre-analytical stage.
- 58.82% of the factors listed for the material used and 100% of the factors relating to the application of the directives of the technical sheet in the analytical stage.
- 66.66% of the factors that may occur during the measurement and 80% of those that may occur after the measurement in the post- analytical stage.

Therefore, it is imperative for the technician to learn the good practices required for carrying out a biochemical analysis leading to valid results.

Table 6. Interference and influence factors relating to the manipulator [1]

Stages	% *	Manipulator interference level	%**	Total%***
Pre-analytical stage	60.13	Sampling	77.41	40.52
Analytical stage	28.75	Materials used	58.82	
		Data sheet.	100	
		Others	100	
Post-analytical stage	07.84	During measurement	66.66	
		After measurement	80	

* Rate of interference and influence critical points relative to each stage
** Manipulator interference and influence critical point rate relative to each level
*** Total rate of critical points of interference and influence relating to the manipulator compared to all the factors listed at the level of all the stages of the analysis

Results of the Statistical Approach Relating to All Critical Points Which Can Influence the Results of a Biochemical Analysis

The statistical study realized allowed us to evaluate the rates of factors listed using the Ishikawa diagram adopted for the realization of our study, which aims to draw the attention of the manipulator to the most relevant factors that can affect the results expected from a biochemical medical analysis.

The factors listed through our investigation and their rates are recorded in Table 7.

Table 7. Results of the statistical approach relating to the critical points which can influence the results of a biochemical analysis [1]

Stages of biochimical analysis	Critical points of interference/influence	Rate
Pre-analytical stage 92 Factors 60.13%	Patient	35.29%
	Sampling	20.26%
	Common interference factors	04.57%
Analytical stage 44 Factors 28.75%	Materials used	11.11%
	Technical sheet	09.80%
	Manipulator B.H*	03.26%
Post-analytical stage 12 Factors 07.84%%	During measurement	04.57%
	After measurment	03.26%

- The pre-analytical stage revealed a number of 92 points equivalent to a rate of 60.13% presented the highest rate for all the stages investigated.
- Patient-related factors presented the highest rate with a rate of 35.29%,

We have listed at the level of the analytical stage a number of 44 factors equivalent to a rate of 28.75%

- The highest rate was represented by the materials used.
- The post-analytical stage revealed a relatively low number of 12 factors with a value of 07.84%.

Conclusion

Through the Ichikawa diagram of HACCP, we listed all the factors of influence and probable interference on the results of a biochemical medical analysis.

It is very important to bear in mind that some results obtained by the various biochemical analysis methods may be erroneous and don't represent reality. For this, the biochemist is asked to identify the critical points responsible for the aberration of the results obtained and it is imperative that he be aware of all the factors that can induce the modification of the results obtained.

This fact constituted the main objective of the present study, through which we have attempted to list all the critical points from personal experiences and bibliographic datathat must be imperatively known by the manipulator of a biochemical medical analysis, who, alone, presented a rate of factors with a value of 40.52%.

We have the prospect of carrying out other studies and translating them into practice guides for students and technicians.

The educational purpose of these guides is to provide the student with a data base grouping the directives of gestures to follow or to avoid in order to carry out the practice of their specialty under the required conditions.

ACKNOWLEDGMENTS

The authors of this investigation would like to thank anyone who has contributed directly or indirectly to providing useful information, including: Mr Gherdine Ali, Dr Absi Bachir, Dr Benchaib, Dr Talbi Abderrahmane, Mrs Yachir aicha, Mrs Berrached farida, Mrs bouziane djamila, Mrs mehdadi fatiha, Mrs hamida djemaa, Mr Boungabi Ahmed, Mr Zaalan Abd elmadjid, Mr Mamouni aissa, Mr Seddiki hashemi, Mr Zoui abdelwahab, Mr Tasfaout AbdALLAH without forgetting the sampler Mr Moumni Abdeljallil and Miss Hidjazi Daouia; Without forgetting the members of the ENERGARID laboratory of the Tahri Mohamed University of Bechar Algeria. honest thanks to every person who contributed to the enrichment of information related to the present study.

AUTHOR CONTRIBUTIONS

Concept: H.B.; Design: S.A.; Control: H.B., T.B.; Sources; H.B.; Materials: H.B., A.A., S.A.; Data Collection and/or Processing: H.B.; Analysis and/or Interpretation: H.B.; Literature Review: A.A., T.B.; Manuscript Writing: H.B.; Critical Review: T.B.; Other: A.A., S.A.

CONFLICT OF INTEREST

The authors declare that there is no real, potential, or perceived conflict of interest for this article.

ETHICS COMMITTEE APROVAL

The authors declare that the ethics committee approval is not required for this study.

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