INTRODUCTION

Reference intervals refer to the range of values for a laboratory test typically described by upper and lower reference limits. It serves as means for physicians to compare results of patients to the expected values in their clinical settings ***(Sundaram et al., 2008***), as it includes most of the subjects with characteristics similar to the reference group and excludes the others ***(Katayev et al., 2010).*** The reference values of complete blood count (CBC) currently used in Africa are derived from data collected for populations living in industrialized countries. The few small studies with African populations that have been reported indicate differences in normal values compared with those for populations in industrialized countries. Ethnic origin, genetics, gender, altitude, and environmental factors, especially pathogens, may influence some values of hematologic indices, suggesting that the development of locally derived reference values for the African population is mandatory ***(Eric et al., 2004).***

Recent published literature has confirmed that many of the reference values obtained from the developed countries differ significantly from what pertains in most African localities; thus making it necessary to establish locally relevant values. The Clinical and Laboratory Standards Institute (CLSI) and the International Federation for Clinical Chemistry (IFCC)

recommend that each laboratory establishes its own reference values ***(Dosso et al., 2012).***

Prior to assessment of laboratory reference intervals of CBC, standardization of procedures and devices used in the haematology laboratories should be achieved according to international standards. According to the international standardization organization (ISO) 15189 for laboratory requirement, standardization of procedures and inter-laboratory comparison between different laboratories are essential requirements for certification and accreditation ***(National Accreditation Board for Testing and Calibration Laboratories, 2012).***

AIM OF THE WORK

This work aims to monitor standardization of procedures and devices used in the haematology laboratories, prior to establishment of national complete blood picture (CBC) reference values in Egyptian healthy individuals.

QUALITY ASSURANCE OF PRE ANALYTICAL, ANALYTICAL AND POST ANALYTICAL PHASES OF CBC ANALYSIS

For accurate assessment of reference interval for complete blood count (CBC), it is essential first to ensure reliable test results with the necessary degree of precision and accuracy. Quality assurance (QA) is defined as the overall program for achieving these objectives ***(Sele Sylvester Ebisine, 2014).***

A quality assurance program includes internal quality control, external quality control, standardization of tests and instrumentation in order to achieve acceptable levels of precision and accuracy. It must also ensure adequate control of the pre-analytical, analytical and post-analytical stages. These objectives represent good laboratory practice (GLP); the mechanism for achieving GLP is encompassed in Total Quality Management (TQM) ***(Shareefa Asam Manik NSCL, 2013).***

QUALITY ASSURANCE PROCEDURES

The procedures that should be included in a quality assurance programme vary with the *tests* undertaken, the *instruments* used (especially if these include a fully automatic counting system) and the *size of the laboratory* and the *numbers of specimens* handled. At least some form of internal quality

control must be undertaken and there must be participation in an external quality assessment scheme where one is available. Some control procedures should be performed daily and other performance checks should be done at appropriate intervals, the latter is particularly important when there is a change in staff and after maintenance service or repair has been carried out on equipment ***(West and Corrons.2011)***

Terms and Definitions Related to Quality Assurance in Clinical Laboratory Practice

Some Terms are related to quality assurance in clinical laboratory practice, which are applied on daily basis in every step of quality assurance procedures according to ***West and Corrons (2011):***

Precision (Reproducibility /Repeatability)

The degree to which repeated measurements show the same results under unchanged conditions. Figure (1) it can be controlled by replicate tests and by repeated tests on previously measured specimens ***(West and Corrons, 2011).***

Accuracy

The degree of closeness of measurements of a quantity to that quantity's actual (true) value. It can be checked only by the use of reference materials that have been assayed by reference methods ***(West and Corrons, 2011).***

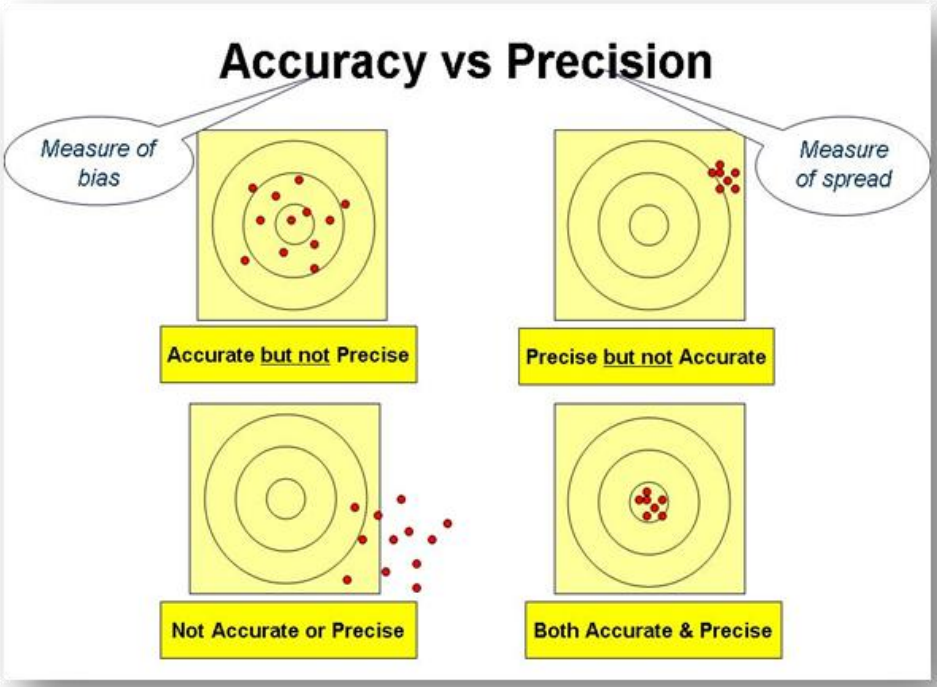

Figure (1): Accuracy versus Precision ***(Pal Bela Szecsi et al., 2009).***

Standardization:

Encompasses both materials and methods. Standard materials are used to calibrate analytical instruments and to assign quantitative values to calibrators. Where possible they must be traceable to defined physical or chemical measurement based on the metrological units of length (metre), mass (kilogram), amount of substance (mole) and time (seconds) ***(West and Corrons, 2011).***

Reference method:

Is an exactly defined technique that is used in association with a reference preparation, when available, to *provide sufficiently precise and accurate data for scientific purposes and for assessing the validity of other methods* ***(West and Corrons, 2011).***

Selected method:

Is one that is directly comparable with and traceable to the international reference method; *it serves as an alternative to the reference method when an international reference material is not available*; it should be used for evaluation and validation of a proposed routine ***(CAP, 2000).***

Working method/Recommended method:

Is intended for use in routine practice, taking account of economy of labour and materials and ease of performance and having been shown by a validation study with a reference method to be sufficiently reliable for its intended purpose ***(CAP, 2000).***

Controls:

Are preparations that are used for either internal quality control or external quality assessment. Some control preparations have assigned values but they should not be used

as standards because the assigned values are usually only approximations and they are often stable for a limited time only ***(CAP, 2000).***

LABORATORY TESTING CYCLE

The "laboratory testing cycle" *consists of all steps between the time when a clinician thinks about and orders a laboratory test , the time the appropriate patient's sample for testing is obtained (for example a blood specimen taken from an antecubital vein) and the results of the testing are returned to the clinician.* This is often called it "*vein-to-brain"* turnaround time (TAT) of test results ***(Plebani and Lippi, 2011).***

These are days of increased pressure to reduce costs and increase efficiency, productivity and quality for laboratory operations all over the world, from large enterprise facilities to small analytical services centers. It's a multifaceted challenge that demands many diverse and sometimes conflicting needs to be fulfilled, such as: *maximizing throughput, reducing waste, saving energy, shortening turnaround times, efficiently allocating laboratory staff and resources, quickly delivering analytical results, timely reporting of relevant information, adhering to quality standards, increasing regulatory compliance* ***(Plebani and Lippi, 2011).***

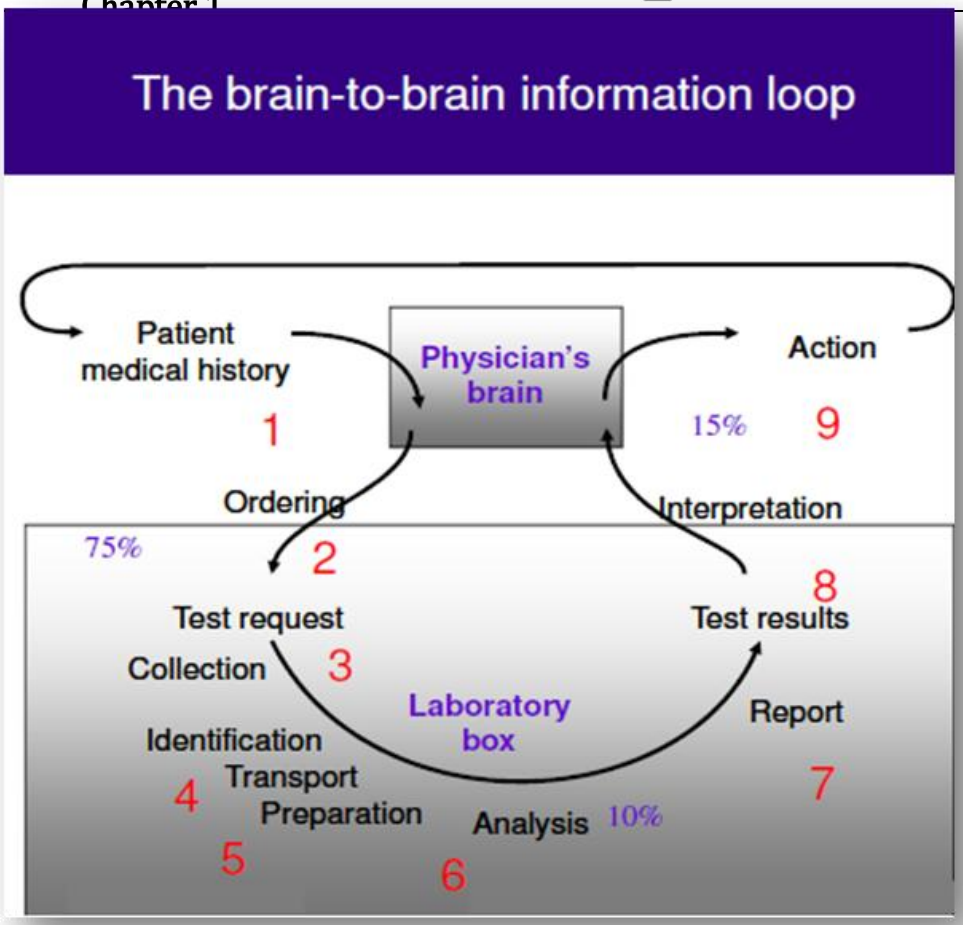

Figure (2): The brain to brain information loop ***(Plebani and Lippi, 2011).***

According to the hierarchical approach of the brain to brain information loop to classify strategies to set analytical quality specifications, the "assessment of the effect of analytical performance on specific clinical decision-making" is comprehensively at the top and therefore should be applied as much as possible to address analytical efforts towards effective goals (Fig. 2). In addition, an increasing number of laboratories worldwide are adopting risk management strategies such as Six Sigma since these techniques allow the identification of the most critical steps in the total testing process, and to reduce the patient-related risk of error. As a matter of fact, an increasing

number of laboratory professionals recognize the importance of understanding and monitoring any step in the total testing process, including the appropriateness of the test request as well as the appropriate interpretation and utilization of test results ***(Plebani and Lippi, 2011).***

This cycle consists of 3 phases

I-Pre-Analytical Phase

The pre-analytical phase is an important component of total laboratory quality. Errors in this phase represent about 75% of total lab errors (Fig. 3). A wide range of variables and errors can affect the result for a patient from whom a specimen of blood has been collected. These variables include*: the procedure for collection, handling and processing before analysis. Physiological variables, such as life style, age, sex and conditions such as pregnancy and menstruation are some of the pre-analytical phase factors* ***(Naryanan, 2000)***.

Procedures for monitoring pre-analytical phase

1-Proper patient preparation:

Proper patient preparation is essential for the test results to be meaningful. The laboratory must define the instructions and procedures for patient preparation in both oral and written instructions ***(Lewis and Bradshaw, 2011).***

2-Correct identification of patients and samples:

The specimen label should include full patient name, lab or hospital number, date and time of sample collection. It should be identical to the identification or the requisition form ***(Favaloro et al., 2012).***

3-Specimen collection and transport:

Specimen collection should be done by specialized and well trained team. Individuals who process the specimen should be trained to look for any document collection problems ***(Favaloro et al., 2012).***

4-Turn around time (TAT):

TAT is one of the most noticeable signs of laboratory service and is often used as *a key performance indicator of laboratory performance*. This is done by recording the actual times of registration, specimen collection, delivery to the laboratory, verification and reporting of test results. A 90% completion time (sample registration to result reporting) of <60 minutes for common laboratory tests is suggested as an initial goal for acceptable TAT ***(Hawkins, 2007).***

Errors associated with the collection and storage of blood samples

A reasonable definition for laboratory errors acknowledged by the International Organization for Standardization (ISO) is ‘‘*any*

defect from ordering tests to reporting results and appropriately interpreting and reacting on these" .In the pre-analytical phase many sources may contribute to erroneous results (Fig. 3) ***(Lippi et al., 2006).***

Favaloro et al. (2012) stated that these errors are associated with:

1. Collecting blood from the wrong patient which can easily occur when there is no check for the *patient's identification.*
2. Collecting blood without removing the needle from a syringe before dispensing the blood resulting in *hemolysis*.
3. Collecting blood from an arm into which an intravenous infusion is being given resulting in a *diluted sample*.
4. Applying a *tourniquet too tightly or for too long period* leading to venous stasis and false increase in the concentration of hemoglobin and other substances in the blood.
5. Dispensing venous blood into a container with insufficient anticoagulant or inadequate mixing of the blood with the anticoagulant, resulting in *clots in the sample*. Difficulty in obtaining blood can also cause clot formation.
6. Allowing *too long a delay* before testing the blood.

7. Leaving the blood at *high ambient temperature (24□) or in direct sunlight* before testing it resulting in physical, chemical and morphological blood cell changes.
8. Incorrect technique *when collecting capillary blood*, particularly excessive squeezing of a finger or infant's heel, resulting in the sample being diluted with tissue fluid.

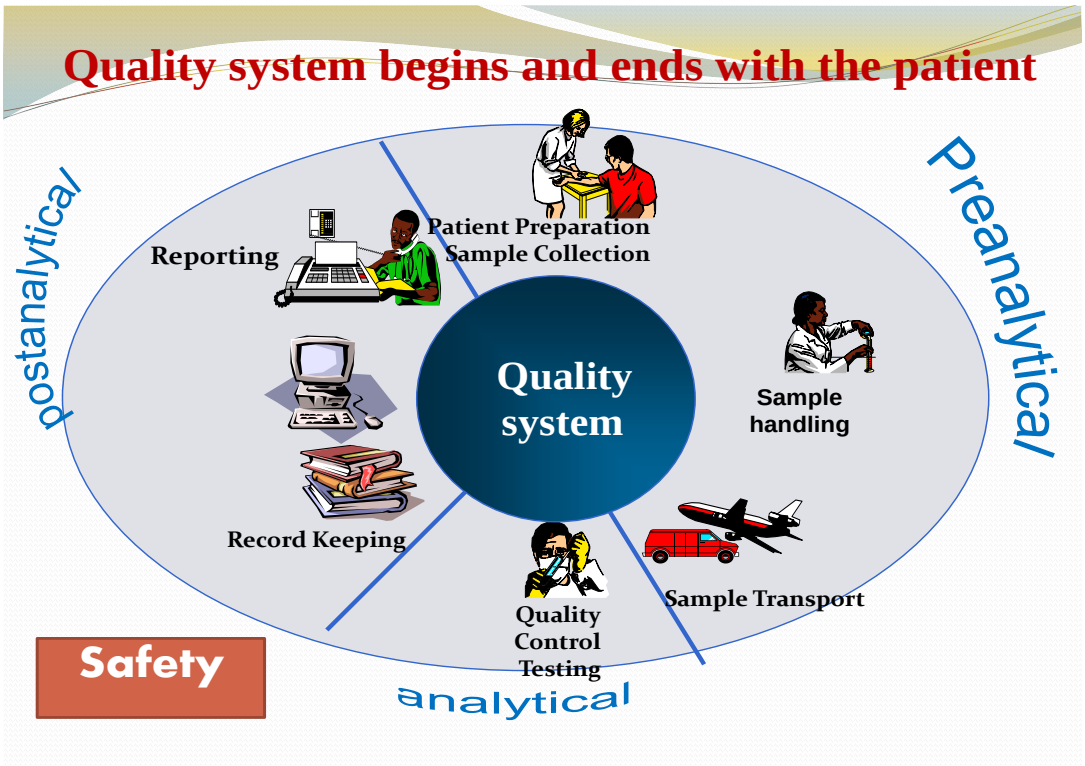

Figure (3): Phases of cell cycle ***(Wians, 2009).***

II-Analytical Phase