

# The Rising Importance of Pre-Analytical Phase in Medical and Research Laboratory, A New Challenge in the Omics Era

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## Abstract

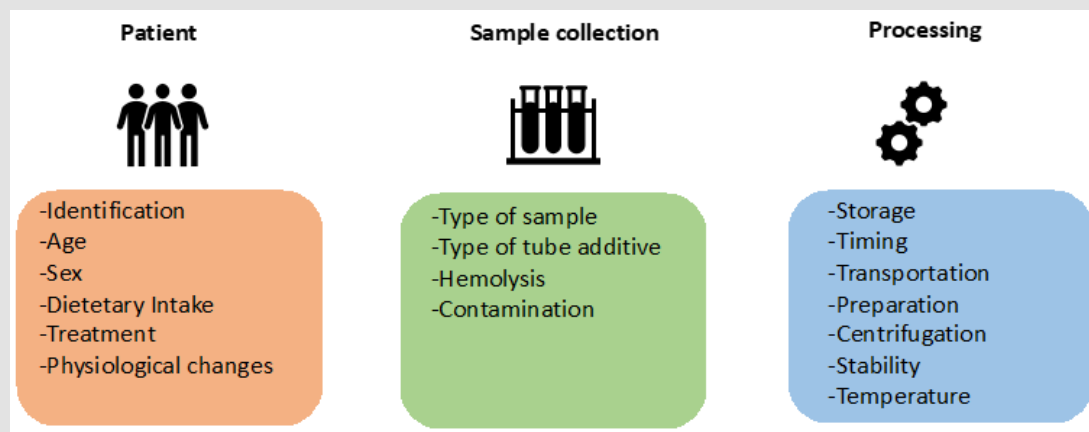
Laboratory analysis involves three main phases: pre-analytical, analytical and post analytical. For a long time, analytical and post-analytical phases were deemed important in medical biology. However, in the last few years, there is growing awareness about pre analytical aspects and issues making it the new major challenge in medical laboratory. Pre analytical phase encompasses a large range of variables that are associated with patient characteristics, sample collection and sample processing. Pre analytical phase is of paramount importance in medical diagnostics, but it continues to be underestimated in research and clinical trials. A paradigm shift in the quality management of pre analytical phase is overdue, especially with the increase of clinical omics application such as metabolomics.

**Keywords:** Pre-Analytical; Medical Laboratory; Clinical Chemistry; Bias; Omics; Metabolomics

## Editorial

Laboratory practice is divided into three broad phases: pre-analytical, analytical and post analytical, that require equal attention towards ensuring overall quality management of laboratory diagnosis. There has been tremendous focus on the establishment of standardized protocols and best practice recommendations for the analytical and post analytical phases. However, there is a dearth of standards for the pre-analytical phase, which is considered the most error-prone and is often underestimated. The primary factors associated with pre analytical errors are linked to patient variables, sample collection and processing (Figure 1). Firstly, patient characteristics may influence pre analytical phase such as feeding state [1] or gender [2]. Physiological changes could promote some pre analytical events such as cell lysis in the form of hemolysis [3,4] or leukocyte lysis that could be related to the type

and levels of blood cells or even some hematological disorders [5-7]. Physiological changes could also modulate other measurements such as calcium influenced by internal pH and albumin concentrations that could complicate medical interpretation and diagnosis [8,9]. Drug intake could also influence measurements of certain parameters by analytical disruption or by physiological modulation [10,11]. Secondly, sample collection method could influence laboratory results. Even the degree of local tissue hypoxia during the application of a tourniquet could be influential [12]. In clinical chemistry, collection tubes contain additives that could influence measurement, choice of serum or plasma [13] and modify numerous variables such as turnaround time [13] and stability [14]. This emphasizes the need for performing validation studies in case of modification of routine additives [15,16].



**Figure 1:** Summary of pre analytical phase and the main variables that may affect laboratory results.

Tube additives can also contaminate the sample. For example, EDTA contamination leads to false elevation of potassium, decrease of calcium and acidification of sample [17,18]. Finally, sample processing comprises other variables such as stability [14,19], sample preparation, centrifugation conditions, transport temperature or storage that must be controlled to avoid false results [20,21]. In summary, measurement of pre analytical errors and subsequent quality management using standardized protocols are currently essential in medical biology but it should also be extended to the field of research given the increase in clinical omics applications [22]. The use of metabolomics particularly warrants more vigilance to pre-analytical issues. Indeed, metabolomics is the study of highly unstable and dynamic biomolecules, metabolites which can be influenced by all the variables described above [23]. In addition to experimental considerations to limiting sources of variation and the choice of instrumentation for analysis, pre analytical issues need to be carefully considered. The most studied metabolite, glucose, presents a classic case where its levels are influenced by physiological changes in the form of cell counts [5] or tube additives that modulate stability [14]. These findings on glucose may be extrapolated to substantial inconsistencies while performing large-scale metabolome analysis. It is imperative that sufficient rigor be applied to ensure robust experimental designs in metabolomics studies that carefully consider patient characteristics to avoid inter-group bias (e.g. drugs, diseases). Ample emphasis must be placed on standardization of sample collection, transport and storage protocols along with downstream sample processing as they could significantly impact pre-analytical errors [12,24,25]. Identification and monitoring of robust quality indicators of the pre analytical phase is necessary for streamlining the quality management process. Continuous tracking and systematic reporting of pre-analytical quality indices will facilitate high quality, reproducible experimentation and data generation. It will also enable efficient harmonization of protocols in large multi-center metabolomics studies and also promote better data sharing and re-use of metabolomics data. To conclude, responsible research

calls for serious efforts towards minimizing pre analytical errors as it can lead to potentially misleading findings and conclusions.

### Competing Interests

The authors declare that they have no competing interests.

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