

## “The Impact of Potassium Test Specimen Rejection on Laboratory Routine Service and Financial Implications for a Laboratory in Najran, Saudi Arabia”

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## Background:

Accurate potassium measurements are crucial for effective clinical management of hyperkalemia. Pre-analytical factors can influence laboratory measurements, leading to inaccurate results and inappropriate patient management. This can have negative implications on the efficiency, finances, and overall functioning of laboratories and hospitals.

## Objective:

This study aimed to evaluate the impact of rejected potassium test requests on laboratory service.

## Methods:

We conducted a retrospective descriptive study to analyze potassium test data from a public laboratory in Najran, South Saudi Arabia. The data included samples collected between January 2023 and December 2023 from an academic hospital, peripheral hospitals, and outpatient clinics.

We examined the relationship between reasons for rejection and the type of health facility, as well as the financial implications for the laboratory.

## Results:

The study examined the rejection rate and reasons for rejecting potassium test results. Among 112,501 tests conducted 91,939 yielded valid outcomes, while 22,741 were rejected. The primary reasons for rejection were old samples (41.4%; n = 9,522) and haemolysed samples (38.2%; n = 8,786). EDTA-K contamination (6.3%; n = 1,449). Labelling errors accounted for 3.5% of rejections (n = 805), while miscellaneous reasons (10.6%; n = 2,179) included leaks, wrong tubes, lost items, insufficient specimens, broken containers, duplicate registrations, and non-receipt of specimens.

## Conclusion:

Peripheral hospitals and outpatient departments accounted for the majority of rejected potassium testing results, potentially due to transportation delays. Improved sample collection, handling, and expedited transportation are recommended to mitigate such issues.

## What this study adds:

This study emphasizes the importance of proper sample collection, handling, and adherence to pre-analytical considerations. It sheds light on the undesirable consequences of disregarding these factors.

**Keywords:** Hyperkalemia, Pseudohyperkalemia, Pre-analytical factors, Result rejection, Sample rejection.

## INTRODUCTION :

Hyperkalemia is defined as potassium levels greater than 5.5 mmol/L [1]. It can occur as a result of dysfunction in the renin-angiotensin-aldosterone system due to kidney failure, adrenal hypofunction, or the use of certain medications, leading to decreased potassium elimination [2][3]. Other common causes of hyperkalemia include increased release of potassium from cells, as observed in diabetic ketoacidosis due to decreased insulin levels, as well as cellular breakdown or necrosis, such as rhabdomyolysis, tumor lysis syndrome, hemolysis, trauma, and burns [4][5]. Patients with thrombocytosis or leukocytosis may also experience hyperkalemia [5][6]. Persistent hyperkalemia can be life-threatening, potentially causing cardiac arrhythmias, cardiac arrest, or respiratory muscle paralysis, even with slight deviations from normal potassium levels (3.5 mmol/L - 5.0mmol/L) [1][6]. Therefore, accurate potassium measurements in the laboratory are essential for clinicians to make appropriate medical decisions.

In the laboratory setting, the quality and reliability of a test result depend on the overall testing process, which includes the pre-analytical, analytical, and post-analytical stages [7][8]. This is particularly crucial as 60% - 70% of medical decisions rely on laboratory investigations [9]. With advancements in laboratory methods, instruments, and quality control and assurance programs, errors during the analytical phase have significantly reduced [8][10]. The pre-analytical phase involves the test requisition, patient identification, sample collection, transportation, and preparation for analysis. It is during this phase that various factors can affect the accuracy and reliability of laboratory results [7].and sample labeling, collection, handling, transport, and processing. This phase accounts for up to 70% - 75% of all laboratory errors reported, most of which

are due to human errors (8,9). These errors can lead to samples that are unsuitable for analysis or unreportable results requiring rejection. Pre-analytical factors that may affect sample quality include hemolyzed, clotted, or icteric samples, as well as samples that are mislabeled, unlabeled, or collected in inappropriate tubes. Insufficient sample volume not only limits the number of tests that can be done from the received sample but can also affect sample quality, as the blood-to-additive ratio may interfere with analysis and produce erroneous results (8,9).

Mild contamination by ethylenediaminetetraacetic acid (EDTA-K), a potassium-containing anticoagulant, may also cause subtle analyte changes that can be missed (11). Prolonged centrifugation of samples during the pre-analytical phase can also interfere with sample quality where, for example, platelets can lyse, resulting in falsely elevated potassium levels (12,13,14). Falsely elevated potassium levels or pseudohyperkalemia occurs when generated results are not consistent with the clinical features of the patient (4,12). Not only can pseudohyperkalemia result in inappropriate patient management, but it can also mask hypokalemia, leading to a missed diagnosis as concentrations may falsely present within a 'normal' reference interval (12). The most commonly occurring source of pseudohyperkalemia is hemolysis, which is reported to cause up to fivefold more rejections than any other reason (7,13). A subset of hemolyzed samples may result from endogenous causes such as hemolytic anemia, immune reactions, toxin exposure, and hemodialysis treatment, or due to direct damage to red blood cells (3,5). In vitro or exogenous hemolysis accounts for most hemolyzed cases. Causes include poor sample acquisition technique, substandard handling and transport, prolonged storage time, and delayed processing (15,16). Sample acquisition techniques that specifically affect potassium include prolonged tourniquet application and patient fist clenching, which can cause a 1 mmol/L - 2 mmol/L increase in potassium levels due to potassium efflux from cells during muscle contraction (12,13,14). The use of needles with unsuitable diameters during sample collection can also result in hemolysis. In addition, cold temperatures can decrease the function of the sodium/potassium-adenosine triphosphatase pump, resulting in the passive movement of potassium down the concentration gradient and out of red blood cells (12).

Rejection of samples or test results inconveniences both patients and healthcare personnel as it delays urgent clinical decision-making. Specimen recollection may be required, leading to prolonged admission for the patient and unnecessary costs to the laboratory and the hospital or clinic (10,17). Although sample and result rejection may appear to be a small and insignificant factor in the total testing process, it is an important quality indicator for laboratories and can have great implications for the patient and health facility. This study thus aimed to assess the frequency and reasons for potassium test request rejection at the National Health Laboratory Service during the period from 01 January 2023 to 31 December 2023 and the financial impact of these rejections on this laboratory.

#### STUDY DESIGN AND SETTING:

A retrospective descriptive observational study was conducted using data for potassium test requests, including both resulted and rejected tests, at the Chemistry laboratory from 01 January 2023 to 31 December 2023. Variables considered were reasons for rejection and the facility where the sample was obtained. Rejected potassium test requests were either for unreported results or samples not tested for potassium, each of which was replaced by a reason for rejection. Potassium requests generally form part of a urea and electrolytes profile.

#### RESULTS:

The rejection rate and reasons for rejection of potassium test results were examined. A total of 112,501 potassium tests were requested during the study period (Table 1). Out of these, 91,939 tests resulted in valid outcomes, while 22,741 tests were rejected. The most common reasons for rejection were old samples (1 day or older), accounting for 41.4% of rejections ( $n = 9,522$ ). Haemolysed samples constituted 38.2% of rejections ( $n = 8,786$ ), followed by EDTA-K contamination (6.3%;  $n = 1,449$ ), which was determined based on reduced magnesium, calcium, and alkaline phosphatase results. Labelling errors accounted for 3.5% of rejections ( $n = 805$ ) and included missing or mismatched information on the sample and the request form (Figure 1). Additional rejection reasons, making up 10.6% of all rejections ( $n = 2,179$ ), were categorized as miscellaneous reasons and encompassed issues such as leaks, wrong tubes, items lost in transit, insufficient specimens, broken specimen containers, duplicate registrations, and non-receipt of specimens.

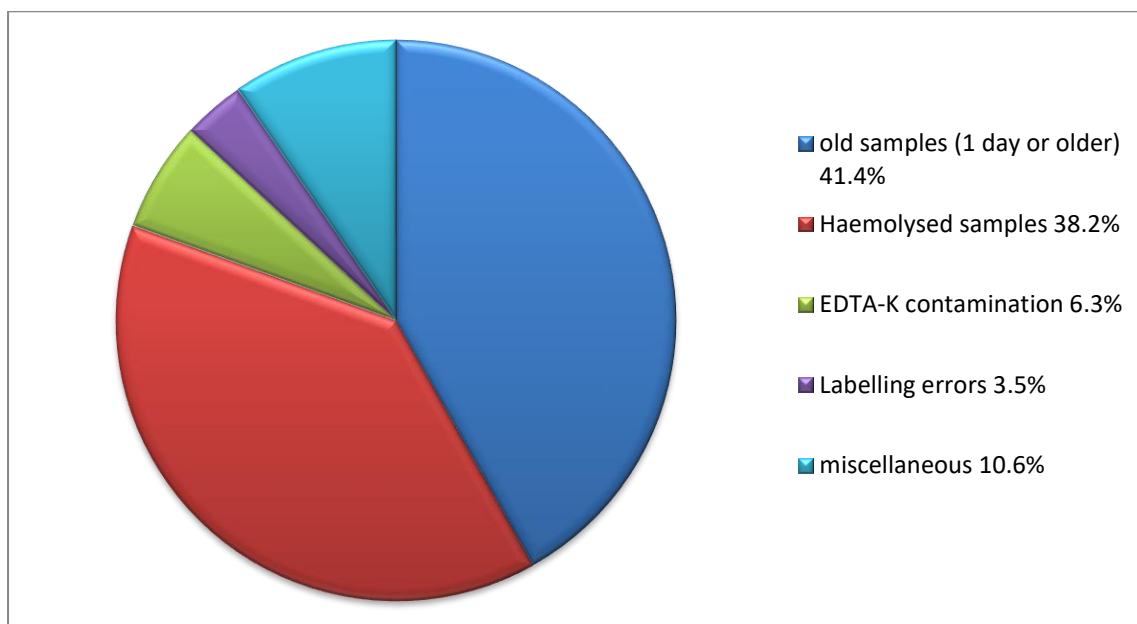


FIGURE 1: Reasons for rejection of potassium test requests at the Laboratory Service

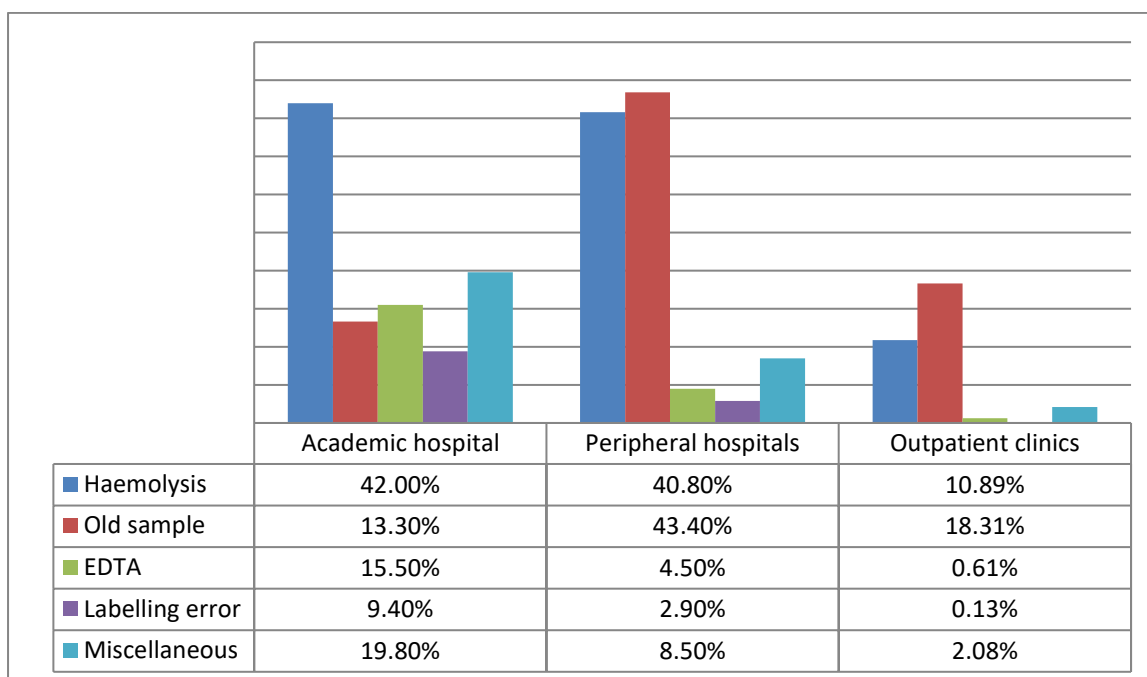


FIGURE 2: Reasons for rejecting requests for potassium testing in the Najran laboratory service from 01 January 2023 to 31 December 2023.

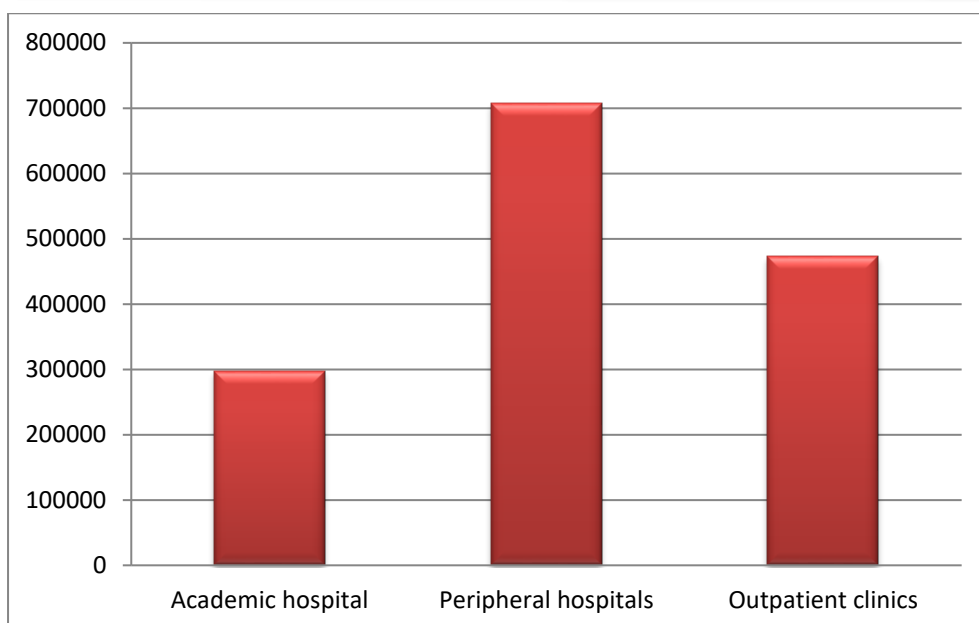


FIGURE 3: Estimated financial loss incurred by the laboratory service in Najran due to rejection of a potassium test request from the academic hospital, peripheral hospitals and outpatient health facilities from 01 January 2023 to 31 December 2023.

#### FINANCIAL IMPACT OF POTASSIUM TEST RESULTS REJECTION :

According to the 2023 price list, the cost per test for potassium testing was estimated to be around \$17.3 USD (equivalent to 65 SR). During the same year, a total of 22,741 potassium test requests were rejected. As a result, the laboratory incurred a cumulative cost of approximately \$393,419 USD (equivalent to 1,475,322 SR) (Figure 3).

#### DISCUSSION

The potassium result rejection rate for the Chemistry laboratory in 2023 was 20.21%, and there was a statistically significant difference between the reasons for potassium result rejection at the different facility types. Old sample was the main reason for rejections, comprising 41.4% of total rejections. This was the most common reason for rejection for both PHs and outpatient facilities. Owing to the location of some of these facilities, it is likely that the reasons for delayed analysis might be multifactorial. These are likely to include distance, long time lapse following collection, storage, and transportation conditions. Other potential reasons for delay in testing may include batch testing or factors related to the testing laboratory itself such as excessive workload, instrument issues, and sample sharing between departments, which may delay sample arrival to the chemistry laboratory as previously described in studies from China and the United States.<sup>16,22</sup>

Old samples are rejected because of biochemical changes that occur as red blood cells break down during long storage, thus leading to erroneous results.<sup>15</sup> Delays in sample analysis can affect accuracy and quality, and, as indicated in a study from the United States, samples stored at temperatures of 2°C–8°C for longer than 24h result in spuriously elevated potassium levels due to cessation of the sodium/potassium-adenosine triphosphatase pump.<sup>12</sup> A study from France has indicated that although potassium levels are stable at room temperature, samples should be analysed within 4 h–6 h for accurate measurements.<sup>23</sup> Moreover, increased potassium levels have been reported in samples stored at room temperature within 1 h of collection in a study done in China in 2017.<sup>16</sup> Another factor to consider when samples are sent to external or distant laboratories for testing is whether the samples were centrifuged at the collection site prior to transportation or only after they arrived at the testing laboratory. Delayed serum separation may cause potassium to leak out of the red blood cells, yielding hyperkalaemia. Ideally, according to a United Kingdom study done in 2003, samples should be centrifuged within 1 h of collection to prevent these falsely increased potassium levels.<sup>24</sup> Additionally, an important aspect to be aware of for potassium measurements is susceptibility to seasonal pseudohyperkalaemia, where potassium levels are elevated in the cooler

winter months owing to the inhibition of the sodium/potassium-adenosine triphosphatase pump activity.<sup>12,24</sup> Interestingly, the main reason for result rejection in this study, old sample, is not the most common cause of rejection reported in previous studies done in Ethiopia, the United States, and Turkey between 2015 and 2016.<sup>10,11,25,26</sup> The major reasons for rejection reported in these studies include haemolysis, insufficient sample, incorrect sample or tube, clotted samples, contamination, and mislabelled or unlabelled samples.<sup>26,27</sup> This difference may, however, be explained by the fact that about 74% of all samples received at this laboratory were referred from off-site facilities, thus making delayed sample analysis a major factor causing rejection. The second most common reason for potassium result rejection in this study was haemolysed samples (38.2%). This was the main reason for potassium result rejection Academic Hospital (42.02%), a facility that makes up a quarter of all samples received by the laboratory. At the peripheral facilities, approximately 50% of rejections were due to haemolysed samples, which is lower than previous reports from Australia and Turkey in 2010, where haemolysed samples account for about 60% of all rejections.<sup>6,28</sup> Findings from previous studies done in Italy in 2008 and Malaysia in 2019 suggest that haemolysis is the main cause of pseudohyperkalaemia.<sup>7,13</sup> Making medical decisions based on these erroneous results can lead to inappropriate patient care. This may occur when there is pseudohyperkalaemia or in instances when hypokalaemia is missed due to false potassium elevation in the sample.<sup>12</sup> A Malaysian study done in 2019 demonstrated that although haemolysis may occur in vivo, this only occurs in about 2% of cases.<sup>7</sup> When in vivo haemolysis is suspected, additional information such as patient history, haptoglobin measurements, bilirubin levels, and red blood cell count are required to arrive at the diagnosis.<sup>7</sup> In 2020, a study in Italy reported that in vitro or exogenous causes are more common and include poor sample collection techniques, poor sample handling and transport, prolonged storage time and inadequate storage temperature.<sup>29</sup> Personnel collecting samples should be trained and educated on the importance of correct collection techniques. A study investigating the impact of educational training among nurses in a hospital in Oman in 2017 showed about 75.9% improvement in sample quality after re-training.<sup>30</sup> The availability of specially trained phlebotomy personnel within a facility is important not just for proper blood sample collection, but also to ease the workload on the already overworked nurses and doctors, who may tend to rush sample collection due to the increased workload.<sup>30</sup> Haemolysed samples certainly pose a serious challenge for clinical laboratories.<sup>7</sup> Contamination by EDTA-K anticoagulant as a cause of pseudohyperkalaemia accounted for 6.3% of the potassium rejections in this study and is common in clinical chemistry laboratories.<sup>31</sup> As reported in studies from Thailand in 2013<sup>32</sup> and India in 2020,<sup>33</sup> EDTA-K contamination may potentially lead to patient mismanagement. Thus, technique and order of draw need to be cautiously considered during sample collection to avoid contamination.<sup>34</sup> Rejection of test results can negatively impact patient care at the health facility and laboratory. Importantly, rejected results can delay critical and potentially life-saving clinical decisions. An additional aspect to consider is the person-hours wasted due to these rejections. Rejection of 22741 potassium test requests over a 12-month period equates to approximately 1895 rejections per month. If the processing time of each of these samples is 10 min, 18950 min or 315 h per month are lost on wasted labour. This equates to approximately 13 days per month. Also, additional time is wasted as laboratory staff remove erroneous results and assign reasons for rejection.

Limitations Access to data was mainly limited to archived data with no knowledge how the samples were collected or stored. The rejection data comprised mostly potassium requests that were either of unreported results or samples not tested for potassium, each of which was replaced by a reason for rejection and could therefore not be reported. The cost of these rejections to the hospitals and the effect on patient management could not be quantified as no clinical information was available for this estimation. The cost could only be estimated for the laboratory and could not be done for the health facilities. Conclusion Findings from this study have shown a high rate of rejection of potassium test requests across all facilities, with PHs and outpatients accounting for most of the rejected potassium test requests. Old sample was the most common reason in facilities located off site due to delays in sample processing. As indicated in the study, test rejections can have significant financial implications for the laboratory

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## ”أثر رفض عينة اختبار البوتاسيوم على الخدمة الروتينية للمختبر والآثار المالية على أحد المختبرات في نجران، المملكة العربية السعودية”

إعداد الباحثين:

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الملخص:

إن قياسات البوتاسيوم الدقيقة ضرورية للإدارة السريرية الفعالة لفرط بوتاسيوم الدم. ويمكن أن تؤثر العوامل التحليلية السابقة على القياسات المعملية، مما يؤدي إلى نتائج غير دقيقة وإدارة غير مناسبة للمريض. وقد يكون لهذا آثار سلبية على كفاءة المختبرات والمستشفيات ومواردها المالية وأدائها العام.