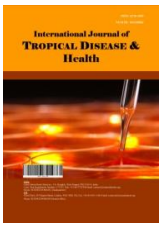

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Analysis of Reported Critical Values and Their Associated Clinical Conditions in a Clinical Chemistry Laboratory of a Tertiary Health Institution in Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. Author TOO wrote the first draft of the manuscript. All authors managed the analyses of the study. All authors read and approved the final manuscript.

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ABSTRACT

Studies involving critical values in recent time have mainly dwelt on compliance to timely reporting as well as the volumes of the individual reported critical analytes. There is paucity of data however, especially in this environment, on the relationships that exist between reported critical biochemical analytes and the presenting clinical conditions of the patients as at the time of the laboratory investigation. This study therefore sought to investigate such relationships.

This study is a retrospective study of data obtained in the year 2018 from the critical value register of the Department of Chemical Pathology, Babcock University Teaching Hospital Ilisan-Remo, Ogun state, Nigeria. Data obtained was analyzed using Statistical Package for Social Sciences (SPSS) version 21.0. Level of statistical significance was set at $p < 0.05$. Relationship between variables was determined using Chi-square Test.

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In the year under review, a total of 270 critical values from various biochemical analytes were obtained; out of which 34.0% was potassium, representing the highest occurrence. Calcium had the highest proportion of its tests from the year having critical outcomes (2.2%) compared to other biochemical parameters. Kidney disease was the most frequently reported clinical condition (25.1%) with critical values of biochemical analytes. This study also showed a strong statistical association (p = 0.000) between diabetic ketoacidosis and critical levels of hyperkalemia, critical outcomes of hypocalcaemia and infection/sepsis as well as critical level of azotemia and pregnancy related complications.

This study has shown potassium as the most reported critical biochemical analyte which occurred mostly as cases of critical hyperkalemia. This was associated with a high burden of kidney diseases among the study population. The study has also drawn attention to the need for immediate and constant check of blood calcium and urea levels in patients that have sepsis and pregnancy related complications respectively.

Keywords: Critical value; diabetic ketoacidosis; azotemia; hyperkalemia.

1. INTRODUCTION

Laboratory diagnostics plays a very important role in both clinical decision making and the managed care of the vast majority of human disorders. Over the past decade or two there has been an ever-increasing level of engagement with the obvious truth that the clinical value of patient-sample testing depends as much on the quality of practice during the pre- and post analytical phases as on the quality of the measurements made during the analytical phase [1]. An essential component of these practices is the identification and timely communication of "highly pathological" values to end users for immediate action [1].

Lundberg [2] was the first to use the term critical (panic) values (CVs) for results, representing a pathophysiological state at such variance with normal as to be life-threatening unless something is done promptly, and for which some corrective action could be taken. Laboratory critical results have been shown to affect several clinical decisions, and in some cases, change the course of treatments of the patient. Howanitz, et al. [3] in their study involving 623 institutions, showed that a change in therapy resulted from 65% of reported CVs, with 94.9% of physicians indicating that critical results are valuable for patient care.

Studies involving critical values in recent time have mainly dwelt on compliance to timely reporting as well as the volumes of the individual reported critical analytes. There is paucity of data, especially in this environment, on the relationships that exist between reported critical biochemical analytes and the presenting clinical conditions of the patients as at the time of the laboratory investigation. This approach may be useful to determine any pattern that exists between any clinical condition and critical outcomes of biochemical analytes which may in turn help clinicians and care givers determine necessary investigations and immediate clinical decisions to make when faced with such conditions. This study evaluated the critical values obtained in the year 2018 from the biochemical investigations made in the Department of Chemical Pathology of Babcock University Teaching Hospital, Ogun state, Nigeria in order to achieve this purpose.

2. METHODOLOGY

2.1 Setting

Babcock University Teaching Hospital is a 204 bedded hospital located in Ogun state; one of the southwestern states of Nigeria. Although a non government owned tertiary health institution, the hospital has over the years become a referral centre to numerous health institutions in it's environ. This is owing to its wide range of approach to health care services including specialized services related to orthopedic, pediatric, obstetric/gynecologic, gastro-enterologic, as well as hearts and vascular medical care (it is one of the few institutions providing cardiovascular related surgeries in the country).

2.2 Data Collection

This study is a retrospective study of data obtained in the year 2018. Data for patients that have had critical results were obtained from the critical value register of the Department of Chemical Pathology, Babcock University

Teaching Hospital. All information accessed was synchronized with what is obtainable in the main laboratory register of the department.

2.3 Data Analysis

Data from this study was analyzed using Statistical Package for Social Sciences (SPSS) version 21.0. Level of statistical significance was set at $p < 0.05$. Relationship between variables was determined using Chi-square Test.

3. RESULTS

Table 1 gives an account of the demographic characteristics of patients with critical results in this study. Of the total population, patients in the adult age category were the most populated with a percentage of 37.4 and closely followed by those in the pediatric age group representing 31.3% of the patient population with critical results. There were only 7 teenagers in this study. Males were higher in number (135) compared to the females (76).

In Fig. 1 it is revealed that patients from the pediatric ward represented the highest population of patients with critical outcome of biochemical tests with a percentage of 23. This is followed by patients admitted to the accident and emergency unit (21%), male medical ward (12%), general outpatient department (10%) as well as the children emergency unit and the female medical ward representing 9% of the study population each.

Several clinical conditions were reported for patients that had critical levels of biochemical tests in this study as shown in Table 2. Of these clinical conditions, kidney disease was the most frequently reported case accounting for 25.1% of the patient population. Other clinical cases reported include neonatal jaundice (14.2%), respiratory/pulmonary disorders (8.5%), diabetes mellitus (6.6%), infection/sepsis (6.2), and other minor cases such as febrile illnesses and vomiting representing 7.6% of the population.

In Fig. 2 it is revealed that potassium was the most reoccurring biochemical analyte having a critical outcome in this study. This is followed by sodium and urea respectively. On the other hand, calcium was the least reported biochemical parameter with critical outcome.

In Table 3 it is shown that potassium had the highest percentage occurrence (34.0%) among the biochemical parameters with critical result. This is followed by sodium with a percentage of 16.7. On the other hand, calcium had the highest proportion of its total test from the year having critical outcomes (2.2%) compared to other biochemical parameters.

In Table 4, parameters were redistributed according to the kind critical level obtained i.e. whether high or low. 100% of patients with critical levels of Bilirubin and urea were on the high side while same percentage had critically low level of bicarbonate. However, this only represented 13.7%, 19.0% and 7.1% of the total population respectively. This table also revealed that hyperkalaemia was the most reported critical case in this study accounting for 24.6% of the total population. This is followed by cases of hypokalaemia (19.0%) and azotemia (19.0%). The table further revealed that hypocalcaemia (92.3%) was twelve times more likely to occur in a critical case with respect to calcium than hypercalcaemia (7.7%). The reverse is however the case with glucose.

Table 5 is an outline of the relationship between reported clinical conditions of the patients with critical results in the period of study and the potassium levels reported. In this table, it is observed that all the patients that had diabetic ketoacidosis and blood related disorders with critical biochemical results were cases of hyperkalemia. Similarly, 100% of the patients

Table 1. Demographic characteristics of patients with critical results

Parameter	Frequency	Percentage
Age category (Years)		
Pediatrics (<1 - 12)	66	31.3
Teenage (13 - 19)	7	3.3
Adult (20 - 59)	79	37.4
Geriatric (>60)	56	26.5
Sex		
Male	135	64.0
Female	76	36.0

Table 2. Reported clinical conditions of patients with critical results

Clinical conditions	Frequency	Percentage
Diabetic ketoacidosis	2	0.9
Blood related disorder	4	1.9
Infection/sepsis	13	6.2
Pregnancy related complication	2	0.9
Gastrointestinal disorder	2	0.9
Stroke	1	0.5
Neonatal jaundice	30	14.2
Cancer	7	3.3
Diabetes mellitus	14	6.6
Kidney disease	53	25.1
Respiratory/pulmonary disorder	18	8.5
Surgical cases	11	5.2
Hyperosmolar hyperglycemic state	2	0.9
Hypertension/heart disease	10	4.7
Routine evaluation	7	3.3
Others	16	7.6

Table 3. Proportion of critical values of biochemical parameters within the total number of tests carried out in the year under review

Biochemical parameter	Test volume for the year	No. of critical values	Percentage of test volume with critical result	Percentage of all critical test results
Potassium	5827	92	1.6	34.0
Sodium	5827	45	0.8	16.7
Chloride	5827	20	0.35	7.4
Bicarbonate	5827	15	0.26	5.6
Urea	5827	40	0.7	14.8
Glucose	2960	16	0.54	5.9
Calcium	594	13	2.2	4.8
Bilirubin	2844	29	1.02	10.8
Total	35,533	270	---	100

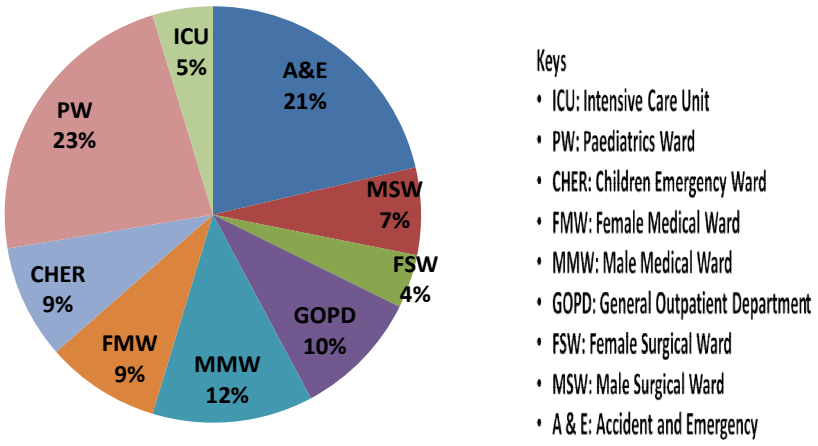

Fig. 1. Wards with patients that had critical results

Table 4. Levels of biochemical parameters with reported critical values

Levels of parameters	Frequency	% of population with parameter	% of total population
Potassium level			
Hyperkalemia	52	56.5	24.6
Hypokalemia	40	43.5	19.0
Bicarbonate level			
High level	0	0	0
Low level	15	100	7.1
Glucoe level			
Hyperglycemia	15	93.8	7.1
hypoglycemia	1	6.2	0.5
Urea level			
High level	40	100	19.0
Low level	0	0	0
Sodium level			
Hypernatremia	15	33.3	7.1
Hyponatremia	30	66.7	14.2
Chloride level			
Hyperchloremia	9	45.0	4.3
Hypochloremia	11	55.0	5.2
Bilirubin level			
Hyperbilirubinaemia	29	100	13.7
Hypobilirubinaemia	0	0	0
Calcium level			
Hypercalcaemia	1	7.7	0.5
Hypocacaemia	12	92.3	5.7

Table 5. Relationship between reported clinical conditions and critical levels of potassium (chi-square test)

Clinical conditions	Hyperkalaemia N (%)**	Hypokalaemia N (%)**	χ^2	p-value
Diabetic ketoacidosis	2 (100)	0 (0)		
Blood related disorder	4 (100)	0 (0)		
Infection/sepsis	3 (23.1)	1 (7.7)		
Pregnancy related complication	0 (0)	0 (0)		
Gastrointestinal disorder	0 (0)	2 (100)		
Stroke	0 (0)	0 (0)		
Neonatal jaundice	1 (3.3)	0 (0)		
Cancer	0 (0)	7 (100)	122.2	0.000*
Diabetes mellitus	1 (7.1)	0 (0)		
Kidney disease	18 (34.0)	10 (18.9)		
Respiratory/pulmonary disorder	3 (16.7)	1 (5.6)		
Surgical cases	4 (36.4)	4 (36.4)		
Hyperosmolar hyperglycemic state	0 (0)	0 (0)		
Hypertension/heart disease	6 (60)	2 (20)		
Routine evaluation	3 (42.9)	2 (28.6)		
Others	2 (12.5)	6 (37.5)		

**statistically significant at $p < 0.05$*

***% = percentage of population with particular clinical condition*

with gastrointestinal disorder and cancer with critical biochemical outcomes had critical hypokalemia. Worthy of note as well, 60% of the population with hypertension/heart disease also had hyperkalemia. However, patients with pregnancy related complications, as well as stroke and hyperosmolar hyperglycemic state had no particular critical changes in their potassium levels. These relationships were statistically significant ($p = 0.000$).

Relationships that exist between reported clinical conditions and critical levels of sodium are reported in Table 6 where it is observed that the only patient with stroke in the study population had just a case of critical hypernatraemia. No critical outcomes were observed in cases of diabetic ketoacidosis (DKA), blood related disorders, pregnancy related and gastrointestinal disorders among others. These relationships were statistically significant (p = 0.000).

In Table 7 it is shown that critical cases of Azotemia were seen in all cases of pregnancy related complications and hyperosmolar hyperglycemic state (HHS), while 50% of patients with blood related disorders reported to

Table 6. Relationship between reported clinical conditions and critical levels of sodium (chi-square test)

Clinical conditions	Hypernatraemia N (%)**	Hyponatraemia N (%)**	χ^2	p-value
Diabetic ketoacidosis	0 (0)	0 (0)		
Blood related disorder	0 (0)	0 (0)		
Infection/sepsis	5 (38.5)	3 (23.1)		
Pregnancy related complication	0 (0)	0 (0)		
Gastrointestinal disorder	0 (0)	0 (0)		
Stroke	1 (100)	0 (0)		
Neonatal jaundice	0 (0)	0 (0)	72.163	0.000*
Cancer	0 (0)	0 (0)		
Diabetes mellitus	2 (14.3)	3 (21.4)		
Kidney disease	2 (3.8)	7 (13.2)		
Respiratory/pulmonary disorder	0 (0)	5 (27.8)		
Surgical cases	0 (0)	1 (9.1)		
Hyperosmolar hyperglycemic state	0 (0)	0 (0)		
Hypertension/heart disease	0 (0)	1 (10.0)		
Routine evaluation	0 (0)	1 (14.3)		
Others	1 (6.2)	6 (37.5)		

**statistically significant at p < 0.05*

***% = percentage of population with particular clinical condition*

Table 7. Relationship between reported clinical conditions and critical levels of urea (chi-square test)

Clinical conditions	High urea level N (%)**	χ^2	p-value
Diabetic ketoacidosis	0 (0)		
Blood related disorder	2 (50)		
Infection/sepsis	2 (15.4)		
Pregnancy related complication	2 (100)		
Gastrointestinal disorder	0 (0)		
Stroke	0 (0)		
Neonatal jaundice	0 (0)		
Cancer	0 (0)	53.083	0.000
Diabetes mellitus	0 (0)		
Kidney disease	20 (37.7)		
Respiratory/pulmonary disorder	2 (11.1)		
Surgical cases	4 (36.4)		
Hyperosmolar hyperglycemic state	2 (100)		
Hypertension/heart disease	2 (20)		
Routine evaluation	2 (28.6)		
Others	0 (0)		

**statistically significant at p < 0.05*

***% = percentage of population with particular clinical condition*

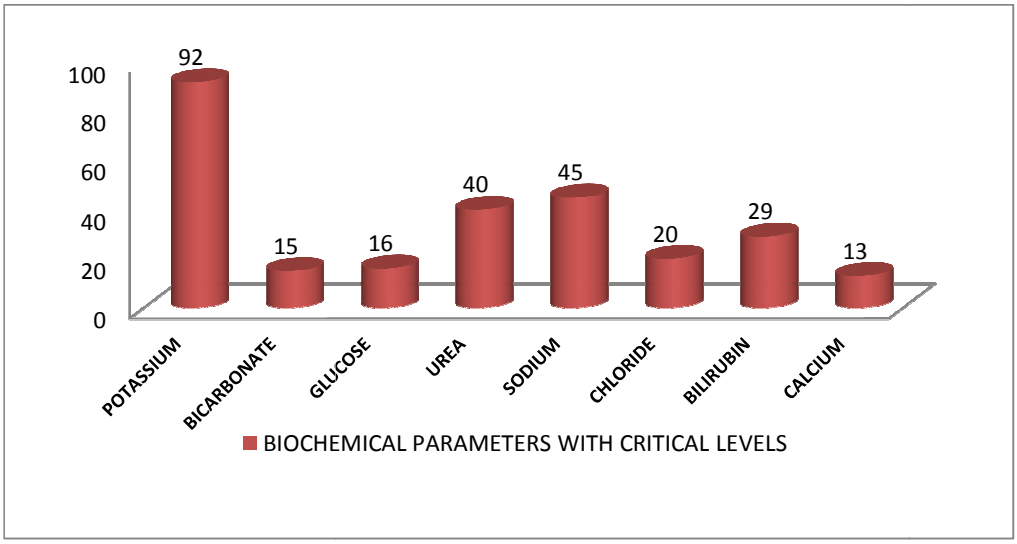

Fig. 2. Biochemical parameters with reported critical levels

Table 8. Relationship between reported clinical conditions and critical levels of calcium (chi-square test)

Clinical conditions	Hypercalcaemia N (%)**	Hypocalcaemia N (%)**	χ^2	p-value
Diabetic ketoacidosis	0 (0)	0 (0)		
Blood related disorder	0 (0)	0 (0)		
Infection/sepsis	0 (0)	6 (46.2)		
Pregnancy related complication	0 (0)	0 (0)		
Gastrointestinal disorder	0 (0)	0 (0)		
Stroke	0 (0)	0 (0)		
Neonatal jaundice	0 (0)	0 (0)		
Cancer	0 (0)	0 (0)		
Diabetes mellitus	0 (0)	0 (0)	72.549	0.000
Kidney disease	0 (0)	0 (0)		
Respiratory/pulmonary disorder	0 (0)	4 (22.2)		
Surgical cases	0 (0)	0 (0)		
Hyperosmolar hyperglycemic state	0 (0)	0 (0)		
Hypertension/heart disease	0 (0)	0 (0)		
Routine evaluation	0 (0)	0 (0)		
Others	1 (6.2)	2 (12.5)		

**statistically significant at p < 0.05*

***% = percentage of population with particular clinical condition*

have critical biochemical results, also had high levels of urea. These relationships were statistically significant.

In Table 8 it is revealed that hypocalcaemia was the most common form of critical outcome of calcium. Most of these cases of critical hypocalcaemia occurred in infection/sepsis (46.2%) while the only form of critical hypercalcaemia obtained was in other minor clinical conditions. These relationships were statistically significant (p = 0.000). There were no critical changes in most of the other outlined clinical conditions.

4. DISCUSSION

Critical values of biochemical analytes can be associated with many clinical conditions with changes seen sometimes when interventions are

carried out. Hence there is a need to see any pattern that may exist between these analytes and the accompanying clinical conditions.

In this study, it was established that potassium had the highest percentage occurrence among the biochemical parameters with critical results. This finding is similar to a 2006 analysis of critical-value reporting at Massachussets General Hospital (MGH), Boston, where Clinical chemistry testing accounted for 68.6% of critical values reported among which the most frequently reported critical values were plasma potassium (7,955; 21.2% of all critical values reported) [4]. Observations on the distribution of the critical potassium level in this study is however different from what was obtained in Beilun People's Hospital of Ningbo, China where critical hypokalaemia was seen to be more frequently encountered and hyperkalaemia rare [5]. This study showed critical hyperkalaemia as a more common condition than hypokalaemia; although both are potentially life-threatening emergencies.

Hypokalemia and hyperkalemia are common electrolyte disorders caused by changes in potassium intake, altered excretion, or transcellular shifts. Diuretic use and gastrointestinal losses are common causes of hypokalemia, whereas kidney disease, hyperglycemia, and medication use are common causes of hyperkalemia [6]. There was a high burden of kidney disease among the study population representing a quarter of the reported clinical conditions. This could have accounted for the higher level of hyperkalemia observed in this study. The high incidence of kidney disease observed in this study supports the report of a cross-sectional observation study by Oluyombo, et al. [7] from 10 semi-urban communities in South-West Nigeria where a reported 14.2% prevalence of kidney disease was observed.

In the same vein, a strong association was also observed between diabetic ketoacidosis and critical level of hyperkalemia among the study population. In DKA, lack of insulin action does not produce hyperglycemia alone but also causes potassium to shift from the intracellular to extracellular space by reducing $Na^{+,}$ K^{+}-ATPase activity [8].

Furthermore, this study revealed that although potassium had the highest occurrence of all the critical test results (34.0%), calcium is however more likely to have a critical outcome compared to other biochemical parameters with majority of it being cases of hypocalcaemia. These cases of critical hypocalcaemia were seen to be strongly associated with reported conditions of sepsis/infection. A study conducted by Zaloga and Chernow [9] observed that hypocalcemia during sepsis occurred in previously normocalcemic patients and was multifactorial in origin, resulting from acquired parathyroid gland insufficiency, renal 1α-hydroxylase insufficiency, vitamin D deficiency, and acquired calcitriol resistance. The study concluded that the hypocalcemia of sepsis is associated with a high mortality rate and usually occurs in previously normocalcemic patients who acquire a defect in the parathyroid-vitamin D axis. Since hypocalcaemia is asymptomatic in these patients, its deficiency is not detected on time in most cases [10]. This shows the need therefore for immediate and continuous check of blood calcium level in patients with this clinical condition so that corrections may be made when necessary.

This study also showed a significant relationship between critical levels of high urea and pregnancy related complications. Studies have shown that while the incidence of pregnancy-related acute renal failure (ARF) in the developed countries is as low as 1-2%, it is a lot higher in developing countries, mostly due to late referral of pregnancy-related complications [11]. Based on the stage of pregnancy, pregnancy-related ARF is divided into three groups, viz, first half, second half and postpartum ARF. Unskilled and septic abortions are the most common causes of ARF during the first half of pregnancy. During the second half, ARF is most commonly associated with preeclampsia or abruptio placentae. Postpartum renal failure is a specific entity and may be considered as a form of hemolytic-uremic syndrome occurring in the postpartum period [12]. At the same time, Obstetric complications are the most common (50-70%) cause of renal cortical necrosis; abruptio placentae, septic abortion, preeclampsia, postpartum hemorrhage and puerperal sepsis are the conditions associated with pregnancy, and are responsible for renal cortical necrosis [13]. It is therefore essential to assess the kidney function of individuals with these forms of pregnancy related complications.

5. CONCLUSION

This study has shown potassium as the most reported critical biochemical analyte which occurred mostly as cases of critical

hyperkalemia. This was associated with a high burden of kidney diseases among the study population. The study has also drawn attention to the need for immediate and constant check of blood calcium and urea levels in patients that have sepsis and pregnancy related complications respectively.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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