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Comparison of Acid Base Status and Electrolytes in Individuals with Prediabetes, Diabetes and Normoglycemia

Asma Khan, Naveed Asif*, Taimoor Ashraf Khan*, Azadi Khan*, Sana Iqbal, Mehreen Aftab Khan**

Department of Pathology, Combined Military Hospital Multan/National University of Medical Sciences (NUMS) Pakistan, *Department of Pathology, Combined Military Hospital, Quetta/National University of Medical Sciences (NUMS) Pakistan, **Department of Pathology, Armed Forces Institute of Pathology/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To determine the acid-base status and electrolytes in individuals with pre-diabetes, diabetes and normoglycemia.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Chemical Pathology, Combined Military Hospital, Quetta Pakistan, from Jan 2020 to Jun 2020.

Methodology: Two hundred study participants were part of this cross-sectional study. Study participants were divided into 3 groups based on plasma glucose levels normoglycemics, prediabetics, and patients with diabetes. Sample for serum electrolytes, plasma glucose, and venous blood gases was taken and analyzed. Results were calculated statistically by using SPSS 21.

Results: Mean age of study participants as 40.11+/-13.93 years. Out of these, 130(65%) study participants were males and 70(35%) were females. Out of these 200study participants, 105(52.5%) had sodium level <135mmol/L and serum potassium <3.5mmol/L, 90(45%) had serum sodium level between 135-145mmol/L and serum potassium level between 3.5-5.5mmol/L and only 5(2.5%) had serum sodium level >145mmol/Land serum potassium >5.5mmol/L. Similarly, 5(2.5%) study participants had serum chloride level <98mmol/L, 84(42%) between 98-108 mmol/L and 111(55.5%) ad >108mmol/L with a mean of 106±5 mmol/L. Regarding acid base disturbance, metabolic acidosis was observed in patients with diabetes as compared to normoglycemic and prediabetics.

Conclusion: Patients with different stages of hyperglycemia have a different pattern of electrolytes and acid-base status which can be used as surrogate markers of normoglycemia, prediabetes, and diabetes.

Keywords: Acid-base status, Diabetes melitus, Electrolytes, Hypernatremia, Hyperglycemia, Prediabetes.

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INTRODUCTION

Electrolytes have an indispensable contribution in different functioning of a body, acid-base balance (pH), blood clotting, fluid levels, conduction of impulse and muscle contraction.[1] Appropriate electrolyte balance requires potassium, sodium, and chloride. One of the recommended contributing factors towards complications observed in diabetes and other endocrine disorders is electrolyte imbalance resulting from kidney failure, vomiting, dehydration, and fever.[2]

A divergent category of metabolic disorder specified by hyperglycemia with is diabetes mellitus (DM) which from results from either a defect in insulin secretion and/or action.[3] Diabetes progresses over various stages, such as normoglycemia, prediabetes and overt diabetes mellitus.[4] These are a few major symptoms of DM which include polyuria(excessive urination) polydipsia (excessive thirst), weight reduction, fatigue, increased hunger, obscure vision and diabetic dermatome.[5] Confirmation with a second measurement is required for any screening used to diagnose DM excepting that clear symptoms of diabetes exist.[6]

Interruption of each acid and base status induces mechanized compensatory mechanisms that restore the blood pH toward the physiological position. Normally, respiratory system compensates formetabolic distortion and the metabolic mechanism is compensated by respiratory system.[7] At start, the compensating mechanism may rehabilitate pH near to standard value. Consequently, if the pH of blood has been changed remarkably, this is the sign that the body's capability of restoration is declining. In these circumstances, immediate intervention for the fundamental disorder of the acid-base disruption is necessary. Metabolic acidosis is known as the most harmful metabolic disorder of DM.[8] Increased production and presence of β-hydroxybutyric acid, acetate or lactate is

Correspondence: Dr Asma Khan, Department of Pathology, Combined Military Hospital, Multan Pakistan

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the main reason for metabolic acidosis with a high anion gap.

Currently, about 1.3% of the world's total population which is approximately 100 million people is victim ofDM and this tendency is still on the rise with the progression of DM and the sufferers are prone to develop complications like coronary artery disease. The Internal environment has been set by hyperglycemia for osmotic diuresis while effecting the dilutional consequence on electrolyte concentrations.[9] Due to diminished blood quantity and shifting of solution from intracellular spaces, cellular desiccationis provoked as an outcome of the osmotic effect of glucose. Acid base status, sodium, potassium and chloride have been chosen by us because these are the most prevailing macro electrolytes and interacted with distinct stages of DM.[10] Theaim of this study was to detect the acid base status and electrolytes distribution in various stages, normoglycemia, prediabetes, & diabetes mellitus.

METHODOLOGY

The cross-sectional study was conducted at the Departments of Pathology, Combined Military Hospital, Quetta Pakistan, from January 2020 to June 2020. Approval for this studywas acquired from the Ethical Review Committee (Ltr no. IRB#044). Written informed consent of all the participants was taken. Sample size of 200 was calculated using WHO calculator, keeping in view a confidence level of 95% proportion of cases as 70.5% and 5% as a margin of error. Out of these 350 individuals, 200 met inclusion and exclusion criteria. Prediabetes, diabetes and normoglycemia were diagnosed on basis of American diabetes association criteria with prediabetics with Fasting plasma glucose (IPG:5.6-6.9mmol/l) and glycated hemoglobin (HbA1c: 5.7-6.4%), diabetics with FPG >7mmol/l and HbA1c: >6.5%, & normoglycemic with FPG: <5.7 mmol/l and HbA1c <5.7%.[11]

Inclusion Criteria: Patients reporting to Outpatient Clinic, of either gender with prediabetes, diabetes and normoglycemic levels were included in study.

Exclusion Criteria: Patients with history of Hypertension, impaired renal function, cancers, history of hormonal disorders like Cushing Syndrome, hyper/ hypothyroidism and acromegaly and pregnant females were excluded from this study.

Sample was collected using non-probability convenient sampling technique after taking informed written consent from each subject, information was handled by a specialized proforma prepared for the study. After considering each subject, relatable history like polyuria, hyperphagia and polydipsia were inquired. Venous blood sample from each patient was obtained and sent to the same hospital's laboratory for analysis of serum electrolytes, serum urea and creatinine (to rule out complications) in clot activator tube. For plasma glucose, sodium fluoride tube was used,and venous sample was taken for venous blood gases (VBGs) in lithium heparin syringe and the results were adjusted to arterial blood gases (ABGs). We used a pH of 7.40 as a cut-off point so apH of 7.37 is categorized as acidosis and a pH of 7.42 is categorized as alkalosis. Next, we evaluated the respiratory and metabolic components of the ABG result with PaCO2 and HCO3, respectively. The PaCO2 indicates whether the acidosis or alkalosis is primarily from a respiratory or metabolic acidosis/alkalosis. Paco2>40 with a pH<7.4, indicates a respiratory acidosis, and <40 and pH<7.4 indicates a respiratory alkalosis. Next, we assessed for evidence of compensation for the primary acidosis or alkalosis by looking for the value (PaCO2 or HCO3) that is not consistent with the pH. Lastly, we assessed the PaO2 for any abnormalities in oxygenation.

SPSS version 21.0 was used for data analysis. Frequencies and percentages were recorded for gender. Estimation of mean and standard deviation was recorded regarding age, serum sodium, potassium, chloride, and plasma glucose. Tests like Chi-square and ANOVA were applied to compare variables while p-value <0.05was taken as statistically noteworthy and significant.

RESULT

In this study, two hundred patients who met the inclusion criteria of different ages were included. Patients were divided intofour different groups based on their ages. There were only 9(4.5%) Subjects in the group of 1-12 years, 12(6%) belonged to 13-18 years while 154(77 %) Subjects were of 19-45 years and 25(12.5%) were above 45 years.Mean age with SD of patients was 40.11±13.93 years. Out of these, 130(65%) subjects were males and 70(35%) were females.

Out of 200 patients, 105(52.5%) patients had sodium level <135mmol/L and serum potassium <3.5 mmol/L, 90(45%) had serum sodium level between 135-145 mmol/L and serum potassium level between 3.5-5.5 mmol/L and only 5(2.5%) had serum sodium level >145mmol/L. & serum potassium >5.5mmol/L. Similarly, 5(2.5%) had serum chloride level <98 mmol/L, 84(42%) between 98-108 mmol/L and 111 (55.5%) had >108mmol/L with 106±5 mmol/L Mean± SD (as shown in Table-I). On the testimony of plasma glucose level, patients were divided into three main groups normoglycemic, prediabetics and overt diabetes. Frequency of individuals in each group and their relationship with serum electrolytes and acid base status is shown in Table-II.

Non-parametric data was observed after applying KolmogorovSmirnov test. Chi- square applied between plasma glucose and acid base status, and plasma glucose and serum electrolytes showed *p*-value <0.05. ANOVA test was also used to compare plasma glucose, acid base status and electrolytes which also showed *p*-value <0.05 (as shown in Table-III).

interesting thing is that no serum sodium level abnormality was observed in normoglycemia patients but only three patients had hyponatremia and four patients presented with hypernatremia that might be due to dehydration or medication like diuretics. Similar to our study Al-Hassan *et al*. also reported hyponatremia in diabetic patients while serum potassium and serum chloride were raised compared to the control group.[12] Similarly,Jiskani *et al* also reported hyponatremia in diabetic patients while no effect on potassium and chloride was observed inpatients with diabetes.[13]

Table-I: Comparison of different variables among Normoglycemic, Prediabetics and Diabetics (n=200)

Variables	Normoglycemics (n=29)	Prediabetics (n=59)	Patients with Diabetes(n=112)
	Mean±SD	Mean±SD	Mean±SD
Age (years)	26±15	40±12	43±12
Fasting Plasma Glucose (mmol/L)	4.9±0.47	8.4±1.16	14.31±2.29
Serum Sodium (mmol/L)	141±6.3	143±6.1	130±6.4
Serum Potassium (mmol/L)	4.4±0.57	4.2±0.69	3.3±0.68
Serum Chloride (mmol/L)	103.6±2.8	103.2±4.5	108.6±0.45

Table-II: Comparison of electrolytes among subjects with Normoglycemia, Prediabetes AND Diabetes Mellitus (n=200)

Variables	Number of Individuals			Total	*p*-value
Serum of sodium mmol/L	**<135**	**136-145**	**>145**		
Normoglycemia	1	28	0	29(14.5%)	<0.001
Prediabetes	3	52	4	59(29.5%)	<0.001
Diabetes	101	10	1	112(56%)	<0.001
Total	105(52.5%)	90(45%)	05(2.5%)		
Serum Potassium mmol/L	**<3.5**	**3.5-5.5**	**> 5.5**		
Normoglycemia	1	28	0	29(14.5%)	<0.001
Prediabetes	3	52	4	59(29.5%)	<0.001
Diabetes	101	10	1	112(56%)	<0.001
Total	105(52.5%)	90(45%)	05(2.5%)		
Serum Chloride mmol/L	**<98**	**99-108**	**>108**		
Normoglycemia	0	24	5	29(14.5%)	<0.001
Prediabetes	4	51	4	59(29.5%)	<0.001
Diabetes	1	09	102	112(56%)	<0.001
Total	05(2.5%)	84(42%)	111(55.5%)		

Table-III: Comparison of acid base status in subjects with Normoglycemia, Prediabetes and Diabetes Mellitus (n=200)

	Number of Individuals					*p*-value
	Acid Base Status					
	Metabolic Acidosis	Metabolic Alkalosis	Respiratory Acidosis	Respiratory Alkalosis	No Acid Base disorder	
Normoglycemia	0	0	0	0	29(14.5)	<0.001
Prediabetes	0	14(7%)	13(6.5)	03(1.5%)	29(14.5)	<0.001
Diabetes	80(40%)	02(1%)	06(3%)	19(9.5)	05(2.5)	<0.001

DISCUSSION

In present study, the ubiquity of electrolyte abnormalities inpatients with diabetes was quite immense. It was observed during the evaluation of serum electrolytes in our study that the most frequent abnormality found inpatients with diabeteswas hyponatremia or low serum sodium concentration. Another

In literature, hypokalemia is also linked with DM. Another electrolyte inequality observed inpatients with diabeteswas Hypokalemia or extremely low blood potassium level.[13] Other research also pointed out abnormally low serum levels of potassium in diabetic patient.[14-15] Similarly, a study by Hasona *et al.* reported a low potassium levels in diabetic patients in addition to low sodium and deranged lipid profile.[16] In our studies, the level of serum potassium is very similar to serum sodium such as hypokalemia in the diabetic group.

Tertiary abnormal serum identified in this learning was a high serum chloride ion or diabetic hyperchloremia. Electrolyte abnormality is common in diabetics and may be associated with uncontrolled hyperglycemia and the vast Variety of drug regimen that diabetics receive especially diuretics which may cause electrolyte imbalance.[17]

In our study, the development of metabolic acidosis was linked with diabetes. While metabolic alkalosis and respiratory acidosis are noticed in prediabetes and no acid base abnormality was observed in normoglycemia. It is a general belief that acid bade disturbance is observed in diabetics when they are suffering from diabetic ketoacidosis while our study points that many diabetics had metabolic acidosis even when they had a normal renal function and no diabetic ketoacidosis. Similar to our study, Sotirakopoulous *et al*. aim to study acid base disturbance in diabetics who did not have ketoacidosis and had a normal renal function test, the study points that patient with long standing diabetes had metabolic alkalosis and with the deterioration of renal functions patients develop metabolic acidosis while most common electrolyte abnormality observed in long-standing diabetes were hypernatremia and hypokalemia.[18] Estifan *et al*. referred to hypernatremia in Diabetes as Salty diabetes. The limitation of our study is that we did not take into consideration the lifestyle, dietary habits and drugs or treatment taken by diabetic patients which might affectthe electrolyte disturbance and acid base status.

CONCLUSION

The study suggests the patients with diabetes have varied acid base status and electrolyte leve lseven with normal renal function tests. Patients with different stages of hyperglycemia have a different pattern of electrolytes and acid base status which can be used as surrogate markers of normoglycemia, prediabetes and diabetes. A multicenter prospective study should be initiated to strengthen causality between the acid base status and electrolytes with normoglycemia, prediabetes and diabetes.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

AK & NA & TAK: Conception, study design, drafting the manuscript, approval of the final version to be published.

AK & SI & MAK: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Han TS, Correa E, Lean ME, Lee DM, O'Neill TW, Bartfai G, et al. Changes in prevalence of obesity and high waist circumference over four years across European regions the European male ageing study (EMAS). Endocr. 201; 55(2): 456-469.
2. Heymsfield SB, Wadden TA. Mechanisms, pathophysiology, and management of obesity. N Engl J Med 2017; 376(3):254-266. https://doi: 10.1056/NEJMra1514009.
3. Crujeiras AB, Cabia B, Carreira MC. Secreted factors derived from obese visceral adipose tissue regulate the expression of breast malignant transformation genes. Int J Obes (Lond) 2016; 40(3): 514-523.
4. Van Gaal LF, Maggioni AP. Overweight, obesity, and outcomes: fat mass and beyond. Lancet. 2014; 383(9921): 935-936.
5. Gomez-Arbelaez D, Bellido D, Castro AI. Body Composition Changes After Very-Low-Calorie Ketogenic Diet in Obesity Evaluated by 3 Standardized Methods. J Clin Endocr Metab. 2017;102(2):488-498. https://doi: 10.1210/jc.2016-2385.
6. Merra G, Gratteri S, De Lorenzo A, Barrucco S. Effects of very-low-calorie diet on body composi-tion, metabolic state, and genes expression: a randomized double-blind placebo-controlled trial. Eur. Rev. Med. Pharmacol 2017; 21(2): 329–345.
7. Berghe G, Wilmer A, Hermans G. Intensive insulin therapy in the medical ICU. N Engl J Med 2006; 354(5): 449-461.
8. Nguyen MK, Kurtz I. Quantitative interrelationship between Gibbs-Donnan equilibrium, osmolality of body fluid compartments, and plasma water sodium concentration. J Appl Physiol 2006; 100(4): 1293-300.
9. Mcpherson RA, Pincus MR. HENRY S Clinical Diagnosis and Management by Laboratory Methods. New York: Elsevier 2011. [Internet] available at: https://www.elsevier.com/books/henrys-clinical-diagnosis-and-management-by-laboratory-methods/mcpherson/978-0-323-41315-2] Cited 15 Oct 2020.
10. Bhave G, Neilson EG. Volume depletion versus dehydration: how understanding the difference can guide therapy. Am J Kidney Dis 2011; 58(2): 302-309.
11. American Diabetes Association. "2. Classification and diagnosis of diabetes." Diabetes Care 2017; 40(1): S11-S24. https://doi: 10.2337/dc17-S005.
12. Al-Hassan AM, Hatif RA, Dhari RH, Edan EH. Study on Diabetes Mellitus and the Balance of Electrolytes. J Babylon Uni 2016; 24(7): 1947-53.
13. Jiskani SA, Khawaja SI, Talpur RA. Disturbances in Serum Electrolytes in Type 2 Diabetes Mellitus. Natl J 2018; 3(4): 129.
14. Tzamaloukas AH, Ing TS, Siamopoulos KC, Patho-physiology and management of fluid and electrolyte disturbances in patients on chronic dialysis with severe hyperglycemia.Semin Dial 2008; 21(5): 431–439.
15. Lin J, Cheng Z, Ding X, Qian Q. Acid base and electrolyte managements in chronic kidney disease and endstage renal disease: case-based discussion. Blood Purif 2018; 45(1-3): 179–186. https://doi: 10.1159/000485155.
16. Hasona NA, Elasbali A. Evaluation of electrolytes imbalance and dyslipidemia in diabetic patients. Med Sci(Basel) 2016; 4(2): 7.
17. Liamis G, Liberopoulos E, Barkas F. Diabetes mellitus and electrolyte disorders. World J Clin Cases (WJCC) 2014; 2(10): 488.
18. Sotirakopoulos N, Kalogiannidou I, Tersi M, Armentzioiou K, Sivridis D, Mavromatidis K et al. Acid-base and electrolyte disorders in patients with diabetes mellitus. Saudi J Kidney Dis Transpl 2012; 23(1):58-62.