Original Research Paper

Biochemistry

AN OBSERVATIONAL STUDY OF PROCALCITONIN LEVELS AMONG TYPE 2 DIABETES MELLITUS PATIENTS WITH INFECTIONS

Dr. S. Manimekalai*	Professor And Head Department Of Biochemistry Coimbatore Medical College And Hospital Coimbatore * Corresponding Author
Dr. Lakshmi. C.	I Year Post Graduate Department Of Biochemistry Coimbatore Medical College And Hospital Coimbatore

ABSTRACT **OBJECTIVE:** To ascertain high PCT levels in Type 2 DM patients among respiratory infections, urinary tract infections and diabetic foot ulcers.
METHODS: An observational study was done among Type 2 DM patients with three groups namely GRP-1 (respiratory infections), GRP-2 (urinary tract infections) and GRP-3 (diabetic foot ulcer).
RESULTS: Among the three groups it was found that the sensitivity (true positive rate) was 0.93 for GRP-1, 0.96 for GRP-2, 0.95 for GRP-3; specificity (true negative rate) was 0.83 for GRP-1, 0.71 for GRP-2, 0.89 for GRP-3 and accuracy was 0.90 for GRP1 and GRP2, 0.93 for GRP-3.
CONCLUSION: PCT showed significant correlation with each of the three infections that were taken for study. Further, studies with larger number of samples when done along with other sepsis biomarkers can give more significant diagnostic results.

KEYWORDS : Procalcitonin, Bio Marker, Diabetes Mellitus, Elisa, Respiratory Infection, Urinary Tract Infection, Foot Ulcer, Skin And Soft Tissue Infection.

1. INTRODUCTION

Patients with Diabetes Mellitus are more prone for infections. Certain possible infections include Urinary Tract Infection, Respiratory Infection, Infection of Foot possibly due to Ulcer and many more. Patients are usually asymptomatic in early stages of infection. It is possibly diagnosed using laboratory investigations like blood test which includes fasting plasma glucose, two-hour plasma glucose, HBA1C, complete blood count, renal function test, urine routine, X ray imaging and culture tests (when required).   Hence blood investigations play a vital role for detection of DM as well as infections. Total leucocyte count as well as high sensitivity C- reactive protein (CRP) which is produced by the liver in response to inflammation are the two routine tests widely used in the detection of infections. A high level of CRP possibly will predict variety of conditions from infections to cancer. Even with the existence of minor infections CRP will increase. Hence it is excluded from this study. Also it is to be noted that as an alternative to CRP, Procalcitonin (PCT) marker is taken for this study. Procalcitonin (PCT) has found to be a valuable marker in identifying bacterial sepsis. In recent clinical investigations, PCT attracted the medical practitioners. It is a fact that contemporaneous infections among DM patients does not provide symptomatic value of PCT. On the other hand, there are also studies that have proved serum PCT levels which tends to increase within three to four hour of infections among DM patients. The increase ranges to its peak within six to twelve hour of infections and it is mentioned in the study [1]. In another study [2], PCT protein maintains its stability in the serum which is the most important factor that marks PCT as an applicable inflammatory marker in laboratory investigations. From various studies it is found that Procalcitonin has been proved to be a marker of sepsis and also its early detection has proven its diagnostic importance [3] – [9]. Also it is inferred that, the cut-off value of serum PCT level in DM patients with infections is not yet known. To conduct this study, patients with DM ≥ 55 years old are chosen. Among them those with respiratory infection, urinary infections and infected diabetic foot ulcers are targeted. These patients were taken as test subjects and their values are aimed to compare with the differences in terms of sensitivity and specificity between PCT and White Blood Cells (WBC) in detecting infections.

2. MATERIALS

2.1. SPECIMEN COLLECTION AND MARKER EXAMINATION

The patients are divided into three groups namely GRP-1, GRP-2 and GRP-3. GRP-1 denotes patients with respiratory infections, GRP-2 denotes patients with UTI and GRP-3 denotes patients with infected diabetic foot ulcer. Each patient is collected with the history (which includes additional information like age of the patient, gender, present history, past history, family history, personal history, lifestyle [regarding food habits, occupation, any previous medications and treatment taken]). Peripheral venous blood is taken and sent to the laboratory for PCT and WBC levels. The PCT is performed using

double anti-body sandwich enzyme – linked immunosorbent one step process assay ELISA. The technical specification of the ELISA kit is portrayed in Table-1.

Table-1. Technical Specification of the ELISA Kit

Reagents(store at 2-8°C)	1×96Wells	Pre-coated
96 wells	8*12strip	Ready to use
Standard（300ng/ml)	0.6ml	Dilute according to instructions
Standard diluent	6.0ml	Could be used as blank controls
Special diluent	6.0ml	Ready-to-use
HRP-Conjugate reagent	6.0ml	Ready-to-use
20X Wash solution	25ml	Dilute according to instructions
Chromogen Solution A	6.0ml	Ready-to-use
Chromogen Solution B	6.0ml	Ready-to-use
Stop Solution	6.0ml	Ready-to-use
Microplate Sealers	2	Ready-to-use
User manual	1	Ready-to-use
Sealed bags	1	Ready-to-use

3. PATIENTS AND METHODS

3.1. RESEARCH SUBJECTS

On the whole, 80 type 2 DM patients (≥ 55 years old) are involved in this study. The inclusion criteria of the patients are:

1. More than 55 years of age
2. Patients with Type 2 Diabetes Mellitus diagnosed according to the 2019 ADA guideline
3. Patients with urinary tract infections (UTI), respiratory and skin and soft tissue infections (SSTI)

The exclusion criteria of the patients are

1. Patients with severe comorbid conditions, existing severe dysfunction in vital organs
2. Patients with heart failure and also those admitted with intensive coronary care unit
3. Severe pre-existing infections
4. Malignancies
5. Post-operative patients
6. Trauma

3.2. STATISTICAL ANALYSIS

Data analysis was done using Microsoft Excel 2000. The diagnostic results that were assessed are true positive, true negative, false positive, false negative, sensitivity, specificity and accuracy.

4. RESULTS AND DISCUSSIONS

As already stated, the chosen patients were classified as GRP-1, GRP-2

and GRP-3. The diagnostic value of serum PCT measurements in detecting the 3 different infections were found to be higher. As far as respiratory infection is concerned, the total samples taken were 20. Among that, 14 were found to have severe respiratory infections and 6 were found to have mild to moderate infections. After performing the ELISA it was found that 13 out of 14 patients showed severe positivity, and among the 6, 5 of the test reports gave minimal negativity. Remaining 2 patients were those with inconsiderable reports. Taking into account of urinary tract infection, the total samples taken were 30. Among that, 22 were found to have infections with high severity and 8 were found to have moderate UTI. After ELISA was done, it was found that all 22 showed positivity, and among the 8, 5 found to have minimal

negativity. Remaining 3 patients were those with minimal or nil positivity. Finally, adding on to diabetic foot ulcer patients, the total samples taken were 30. Among that, 20 were found to have severe infection and 10 were found to have mild to moderate infections. After performing the ELISA it is concluded that all 20 showed high positivity and out of the 10 remaining, 8 showed minimal negativity. Remaining 2 patients were those with minimal positivity. From the overall analysis, more than 90% accuracy is attained while performing test using ELISA for PCT assessment. The statistical analysis of the three groups with infections are presented in Table -1, Table -2 and Table – 3. The performance chart are also presented in Fig.1., Fig.2., Fig.3., and Fig.4.

**Table 1. Statistical analysis of PCT in Respiratory infections among Type 2 DM patients**

|	Respiratory Infection (n=20)						
	True Positive	True Negative	False Positive	False Negative	True Positive Rate / Sensitivity	True Negative Rate / Specificity	Accuracy
PCT (ng/mL)	13	5	1	1	0.93	0.83	0.90

Table 2. Statistical analysis of PCT in UTI among Type 2 DM patients

	UTI (n=30)						
	True Positive	True Negative	False Positive	False Negative	True Positive Rate / Sensitivity	True Negative Rate / Specificity	Accuracy
PCT (ng/mL)	22	5	2	1	0.96	0.71	0.90

Table 3. Statistical analysis of PCT in diabetic foot ulcer among Type 2 DM patients

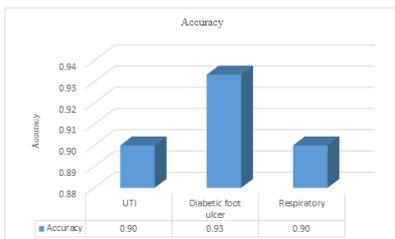|	Diabetic foot ulcer (n=30)						
	True Positive	True Negative	False Positive	False Negative	True Positive Rate / Sensitivity	True Negative Rate / Specificity	Accuracy
PCT (ng/mL)	20	8	1	1	0.95	0.89	0.93
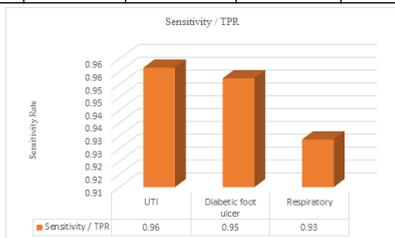
Fig.1. Sensitivity / true positive analysis
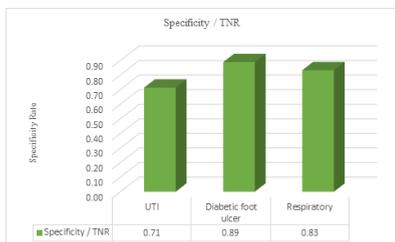
Fig.2. Specificity / true negative analysis

Fig.3. Accuracy analysis

Fig.4. Overall analysis of PCT among Type 2 DM patients with

infections

5. CONCLUSION AND FUTURE SCOPE
To summarize, the aim of this study was to demonstrate high Procalcitonin values in DM patients with severe infection. Our study proved 90% to 95% accuracy among the samples that were chosen. In elderly patients a strong positive correlation was demonstrated among type 2 DM patients with GRP-1, GRP-2 and GRP-3. Even though it showed high positivity, a future study with large sample population and correlation with other sepsis biomarkers could provide with 98 – 100 % accurate results which would help in treatment modalities.

REFERENCES
1. Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012;54:e132–73.
2. Brownrigg JR, Davey J, Holt PJ, Davis WA, Thompson MM, Ray KK, et al. The association of ulceration of the foot with cardiovascular and all-cause mortality in patients with diabetes: A meta-analysis. Diabetologia. 2012;55:2906–12.
3. Jeandrot A, Richard JL, Combescure C, Jourdan N, Finge S, Rodier M, et al. Serum procalcitonin and C-reactive protein concentrations to distinguish mildly infected from non-infected diabetic foot ulcers: A pilot study. Diabetologia. 2008;51:347–52.
4. Jonaidi Jafari N, Safaee Firouzabadi M, Izadi M, Safaee Firouzabadi MS, Saburi A. Can procalcitonin be an accurate diagnostic marker for the classification of diabetic foot ulcers? Int J Endocrinol Metab. 2014;12:e13376.
5. Christ-Crain M, Müller B. Procalcitonin in bacterial infections – Hype, hope, more or less? Swiss Med Wkly. 2005;135:451–60.
6. Assicot M, Gendrel D, Carsin H, Raymond J, Guilbaud J, Bohuon C. High serum procalcitonin concentrations in patients with sepsis and infection. Lancet. 1993;341:515–8.
7. Schmiemann G, Kniehl E, Gebhardt K, Matejczyk MM, Hummers-Pradier E, The diagnosis of urinary tract infection: a systematic review, Dtsch. Arztebl. Int. 2010: 361-367.
8. Lee H, Procalcitonin as a biomarker of infectious diseases, Korean J. Intern. Med. 2013:28:285-291.
9. Bharath MS, Hiremath RS, Basu A, Role of procalcitonin and C-reactive protein in urinary tract infection diagnosis in adults, Int. J. Adv. Med. 2017:4:417-419.