



## THE RELATIONSHIP OF DERMICIDIN ISOFORM-2 WITH THE OCCURRENCES AND SEVERITY OF DIABETES TYPE 2

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### Abstract

The word diabetes defines a category of metabolic disorders which are described and identified in the absence of treatment by the presence of hyperglycaemia. Stress, on the other hand, defined as a pressure cause, may be a prerequisite for adaptation, being an aggregate of claiming mental, behavioral, neuroendocrine, even immunological course. Similarly as reactions that look like the individual's adjustment to the thing that he perceives alternately likewise a danger (aggressive alternatively not). Alternatively, Dermcidin has an important role in innate immunity it is also considered stress hormone. *The aim of the present study is to evaluate the relationship of dermcidin in occurrence and severity of diabetes type 2.* This study demonstrated that a small, environmentally stress-induced protein 11 kDa called dermcidin isoform-2 (DCN-2) significant with patients of type2 diabetes under stress state, while non- significant with patients under normal condition. But to early considered the dermcidin peptide responsible for the occurrence and severity of diabetes type2.

**Keywords:** Diabetes, stress hormone, Dermcidin, Diabetes with stress.

### Introduction

The word diabetes defines a category of metabolic disorders which are described and identified in the absence of treatment by the presence of hyperglycaemia. The heterogeneous aetiopathology includes abnormalities in insulin production, insulin action or both, and carbohydrate, fat and protein metabolism disorders. Among other risks, the long-term clinical consequences of diabetes include retinopathy, nephropathy and neuropathy. People with diabetes may have an elevated risk of other illnesses, including heart disease, peripheral arterial and cerebrovascular disease, obesity, cataracts, erectile dysfunction and non-alcoholic fatty liver disease. These also pose an elevated risk of other infectious diseases, such as tuberculosis (Organization, 2016). Type 2 diabetes is a multifactorial condition caused by hereditary vulnerability associated with lifestyle factors such as physical inactivity and obesity (Organization, 2019). Insulin resistance associated with a progressive insulin deficiency triggered by defective pancreatic beta-cells is of significant importance in type 2 diabetes. Stress, on the other hand, defined as a pressure cause, may be a prerequisite for adaptation, being an aggregate of claiming mental, behavioral, neuroendocrine, even immunological course. Similarly as reactions that look like the individual's adjustment to the thing that he perceives alternately likewise a danger (aggressive alternatively not). Alternatively, with as much of her integument as homeostasis [3-4]. Stress is considered a contributing factor in diabetes development in persons with predisposition to it (Surwit, 2002). Dermcidine, also known as proteolysis inducing factor (PIF), is a protein encoded by the DCD gene in humans (Chaufan and Saliba, 2019) (Tuomilehto, 2019).

It is an anti-microbial peptide which is secreted on the skin by human eccrine sweat glands as part of the immune system's innate host protection. It also participates in proteolysis (Brauer *et al.*, 2014). Some forms of illness raise the human plasma dermcidin (DCN-2) dramatically. Acute myocardial infarction (AMI) patients have elevated DCN-2

levels in their plasma (Tuomilehto, 2019) (Selvin *et al.*, 2004).

Owing to the fact that diabetes is the main risk factor for the genesis of AMI and atherosclerosis, diabetic patients have a high DCN-2 level in their plasma. Diabetes genesis induced with stress is reported in patients (Badimón, Santos-Gallego and Badimón, 2010). Our laboratory also reports that high-altitude diseases can increase DCN plasma levels due to environmental stress (Bank *et al.*, 2014).

### Material and Method

This case study was conducted at Department of Biochemistry, College of Medicine, University of Baghdad and the National Center for teaching laboratories in Medical City of Baghdad, Iraq. It consisted of 90 men; 30 were patients with type 2 diabetes mellitus, 30 were prediabetes subject and 30 were apparently healthy men their age and BMI were matched with all groups. BMI range between (25–35 kg/m<sup>2</sup>) and aged (35–65 years).

- **Inclusion** criteria of diabetes patients were based on the presence of history of type2 DM, fasting serum glucose and Glycated hemoglobin (HbA1c).
- **Exclusion** criteria of all study groups included those diabetic patients with type 1 DM, aged under 35 years, over 65 years and BMI out of range (25-35 kg/m<sup>2</sup>).

Blood sample was taken from the peripheral vein in a fasting state for all study subjects. Blood samples will be taken after overnight fasting state (8-12 hr.) in serum-separating tube (vacationer gel tube) and (EDTA tube) for HbA1c. The vacationer tube blood sample allows to clot for 30 minutes, centrifuged at 3000 rpm. Fasting serum glucose, using Siemens Dimension RxL Max clinical chemistry system, HbA1c by ARKRAY ADAMS A1c HA-8160 high-performance liquid chromatography (HPLC) Technique, Serum Dermcidin - isoform-2 by using Enzyme-linked immunosorbent assay (ELISA) technique for Biotek company in all subjects.

### Statistical analysis

Data analysis was carried out using the statistical program available from SPSS-21 (Statistical Packages for Social Sciences- version 21) Data were presented in simple frequency, percentage, mean and standard deviation (SD), Differential importance of different means (quantitative data) has been evaluated using Analysis of Variance (ANOVA) test for difference between more than two separate means and Least Significant Difference (LSD) to direct association between mean in two individual groups, Statistical

significance was assessed when the value P was equal to or less than 0.05.

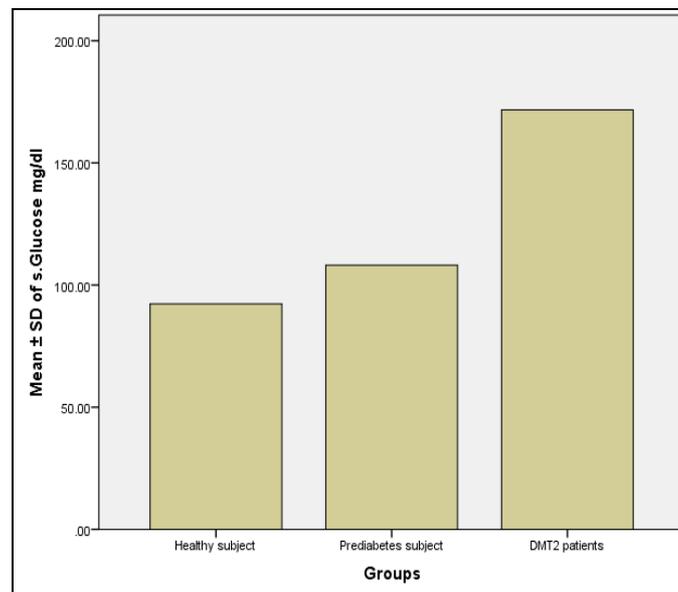
### Results

Successful matching of Age and Body mass index (BMI) achieved by non- significant difference ( $p > 0.05$ ) which was found among and between groups also Successful choice of groups represented by significant difference ( $p \leq 0.05$ ) which was found among and between groups of serum Glucose (Fig. 1) and glycated hemoglobin (HBA1C) (table1),

**Table 1 :** General characterization (mean  $\pm$  SD) of age , BMI , serum glucose and HBA1C in the healthy subject , Prediabetes subject and DMT2 patients

Studied parameters	Studied groups	mean $\pm$ SD	F-Test sig	LSD sig
Age (years)	Healthy subject (a) Prediabetes subject (b) DMT2 patients (c)	43.65 $\pm$ 9.22 48.44 $\pm$ 8.53 45.65 $\pm$ 8.10	$p > 0.05$ N.S	a vs. b $p > 0.05$ N.S a vs. c $p > 0.05$ N.S b vs. c $p > 0.05$ N.S
BMI (kg/m <sup>2</sup> )	Healthy subject (a) Prediabetes subject (b) DMT2 patients (c)	30.40 $\pm$ 4.45 31.62 $\pm$ 4.54 31.56 $\pm$ 4.90	$p > 0.05$ N.S	a vs. b $p > 0.05$ N.S a vs. c $p > 0.05$ N.S b vs. c $p > 0.05$ N.S
Serum glucose (mg/dl)	Healthy subject (a) Prediabetes subject (b) DMT2 patients (c)	92.31 $\pm$ 7.80 108.17 $\pm$ 20.73 171.72 $\pm$ 54.44	$p \leq 0.05$ S	a vs. b $p \leq 0.05$ S a vs. c $p \leq 0.05$ S b vs. c $p \leq 0.05$ S
HBA1C %	Healthy subject (a) Prediabetes subject (b) DMT2 patients (c)	5.15 $\pm$ 0.32 5.95 $\pm$ 0.19 8.66 $\pm$ 1.40	$p \leq 0.05$ S	a vs. b $p \leq 0.05$ S a vs. c $p \leq 0.05$ S b vs. c $p \leq 0.05$ S

Sig. level consider at  $p \leq 0.05$



**Fig. 1 :** Mean  $\pm$  SD for serum Glucose of all subjects

### 1. Serum Dermcidin

Serum Dermcidin showed non- significant difference among groups ( $p > 0.05$ ), when healthy subject compared with Prediabetes subject showed non-significant ( $p > 0.05$ ) difference with mean  $\pm$  SD (1.10  $\pm$  0.23, 1.31  $\pm$  0.20). While, healthy subject showed significant difference ( $p \leq 0.05$ )

compared with diabetes mellitus type2 patients with mean  $\pm$  SD (1.10  $\pm$  0.23, 2.23  $\pm$  3.91) Respectively, Prediabetes subject when compared with diabetes mellitus type 2 patients also showed significant ( $p \leq 0.05$ ) difference with mean  $\pm$  SD (1.31  $\pm$  0.20, 2.23  $\pm$  3.91) Respectively.

**Table 2 :** Mean  $\pm$  SD for serum dermcidin in the healthy subject , Prediabetes subject and DMT2 patients.

Studied parameters	Studied groups	Mean $\pm$ SD	F-Test sig	LSD sig
S.Dermcidin ng/mL	Healthy subject (a) Prediabetes subject (b) DMT2 patients (c)	1.10 $\pm$ 0.23 1.31 $\pm$ 0.20 2.23 $\pm$ 1.90	$p > 0.05$ N.S	a vs. b $p > 0.05$ N.S a vs. c $p \leq 0.05$ S b vs. c $p \leq 0.05$ S

Sig. level consider at  $p \leq 0.05$

**2. Parameters studied under stress state**

Serum Glucose, HbA1c and serum Dermcidin and show significant ( $p \leq 0.05$ ) difference (Table 3) (Fig. 2 A, B, C).

**Table 3 :** Mean  $\pm$  SD parameters in the healthy subject, Prediabetes subject and DMT2 patients under stress state .

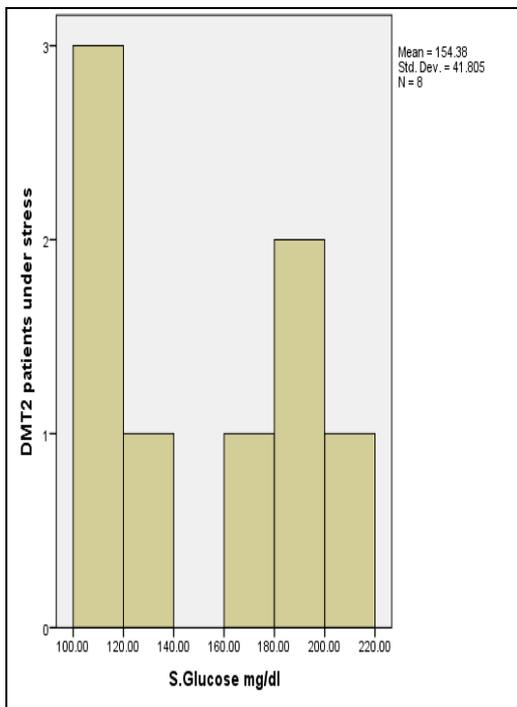
Parameters	Prediabetes under stress mean $\pm$ SD (7)	DMT2 under stress mean $\pm$ SD (8)	Sig
age	47.9 $\pm$ 10.2	51.5 $\pm$ 10.00	$p > 0.05$
BMI	29.70 $\pm$ 5.17	33.61 $\pm$ 3.99	$p > 0.05$
s.Glucose	118.90 $\pm$ 37.3	154.40 $\pm$ 41.80	$p \leq 0.05$
HbA1c	6.10 $\pm$ 0.14	9.03 $\pm$ 1.54	$p \leq 0.05$
s.DCN	1.03 $\pm$ 0.24	1.30 $\pm$ 0.13	$p \leq 0.05$

Sig. level consider at  $p \leq 0.05$

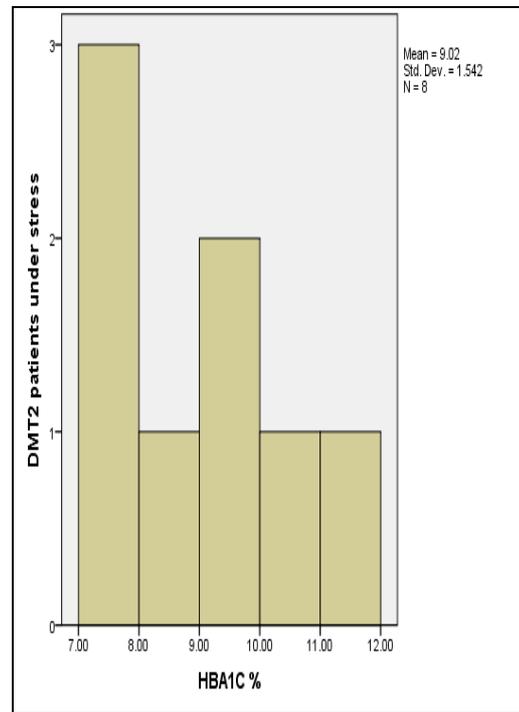
The sensitivity and specificity, area under curve and cut-off point for serum dermcidin (Fig. 2D) Illustrated by Table (4)

**Table 4 :** Sensitivity and specificity, area under curve and cut-off point for stress serum dermcidin.

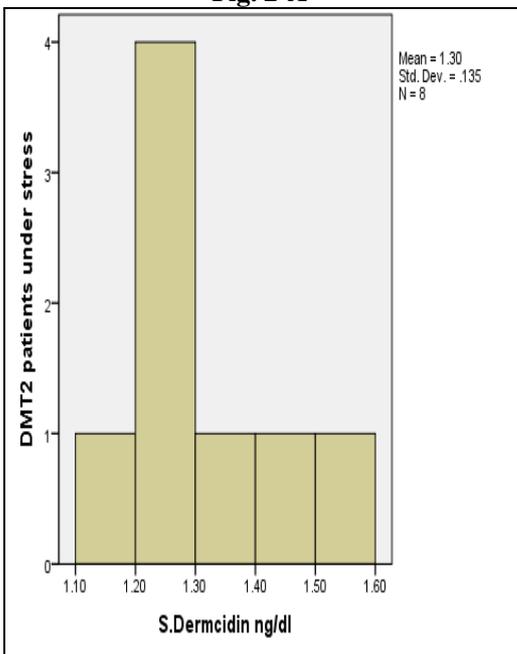
Parameter	Sensitivity	Specificity	AUC	Cut off value
s. dermcidin	93%	79%	0.57	1.22



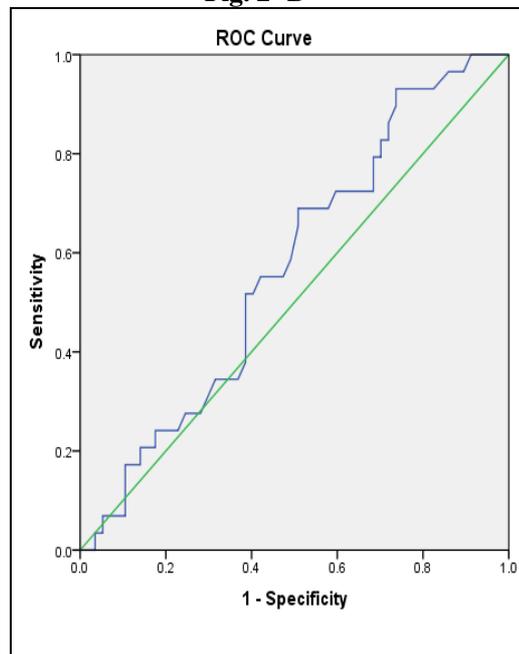
**Fig. 2-A**



**Fig. 2- B**



**Fig. 2-C**



**Fig. 2-D**

**Fig. 2 :** Mean  $\pm$  SD parameters in the healthy subject , Prediabetes subject and DMT2 patients under stress state and ROC analysis.

## Discussion

High significant difference ( $p \leq 0.05$ ) among and between groups for fasting serum glucose and glycated haemoglobin (HbA1c) with mean  $\pm$  SD ( $171.72 \pm 54.44$ ) ( $8.66 \pm 1.40$ ) Respectively for T2DM patients there is no clear definition of the corresponding fasting serum glucose goal to achieve control glucose, while glycated haemoglobin (HbA1c) levels below 7% to achieve long-term glucose control (Kerner and Brückel, 2014; Forouhi and Wareham, 2019; Prevention, 2014; Thomas *et al.*, 2018) to lower the risk of diabetic complications (i.e. kidney disease, heart disease and nerve disease). Dermcidin isoform-2 (DCN-2), a small, environmentally stress-induced protein 11 kDa, plays a major role in IR and induces atherosclerosis in the heart's pericardial arteries, leading to cardiac cell death and acute MI (AMI) develop (Harrison and Wentworth, 2020; Faradji, Barriga-Menchaca and de la Maza, 2019), DCN-2 has also been reported to be involved in different types of cancer progression and metastasis; dermcidin gene expression has been involved in the development Especial of prostate cancer microenvironment in hypoxia (Stewart *et al.*, 2007) And accordingly, the protein was also shown to be responsible for platelet aggregation and inhibition of the effect of aspirin in AMI patients, DCN-2 protein acts as an inhibitor of all types of nitric oxide synthase and inhibits insulin action in acute ischemic heart disease (AIHD) It was found from our previous study that DCN was a protein caused by stress found in the circulation of acute myocardial infarction (AMI) (Harrison and Wentworth, 2020) And also in case of sickness at high altitude (Bank *et al.*, 2014) Systemic impairment of insulin function caused by DCN-2 inhibition of NO may lead to essential hypertension (Ghosh *et al.*, 2014). study parameters (S. glucose, HbA1c, and S. dermcidin) under stress state that show all parameters significant ( $p \leq 0.05$ ) difference, Stress is a major concern for diabetes patients. Different studies have shown that stress and psychological distress play an important role in diabetes development, intensification and chronicity (Alonso-Morán *et al.*, 2014). study of the sensitivity, specificity, area under curve and cut-off value for serum dermcidin The ROC curve reflects a mapping of the sensitivity versus 1 – specificity for all possible cut-point values between cases and controls. The ROC study provides two key results: the test's predictive accuracy and the optimum cut-point value for the test. Cut-points dichotomize the test values, so diagnosis (diseased or not) is given. Identifying the cut point value involves an evaluation of sensitivity and specificity at the same time (Pepe, 2003), sensitivity and specificity represent Two common measures of the inherent statistical validity of a medical test are the probabilities among the true diseased subjects and true non-diseased subjects of detecting correct diagnosis via study, Area under the curve is considered an important indicator of a diagnostic test's inherent validity, through this curve finding an optimal cut-off point to at least misclassify subjects with or without disease, AUC closer to 1 indicates good test results (Kumar and Indrayan, 2011). Sensitivity or true positive rate (TPR) is conditional probability that the diseased will be correctly diagnosed. the result of sensitivity is 93%, while Specificity or true negative rate (TNR) is a conditional probability that a non-illness is correctly established. The result of specificity is 62%, 79% for S.dermcidin which indicate that the effect of dermcidin by other pathogenesis.

## Conclusion

This study demonstrated that a small, environmentally stress-induced protein 11 kDa called dermcidin isoform-2 (DCN-2) significant with patients of type2 diabetes under stress state, while non-significant with patients under normal condition. but to early considered the dermcidin peptide responsible for the occurrence and severity of diabetes type2 before take the large sample of patients under stress state and make sure that they are free of some disease that causes this hormone to rise such as [atherosclerosis, acute ischemic heart disease (AIHD), acute myocardial infarction (AMI) and some of skin diseases.

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