

# Determination of Carbohydrate Antigen 19-9 Level in Sera of Iraqi Patients with Type 2 Diabetes Mellitus

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## Abstract

**Background:** Diabetes mellitus is a major medical problem worldwide that can be qualified as the last stage of chronic pancreatitis; on the other hand, chronic pancreatitis is considered as a risk factor for pancreatic cancer. Therefore, the evaluation of carbohydrate antigen 19-9 (CA 19-9) level in patients with diabetes mellitus makes it imperative to find normal range for CA 19-9 level for this patient to eliminate the additional interventional approaches. **Objectives:** The objectives of this study were to define the normal range (cutoff value) of CA 19-9 in type 2 diabetic patients using enzyme-linked immunosorbent assays. **Materials and Methods:** This study included 80 patients diagnosed as type 2 diabetes mellitus (T2DM) with mean age ( $46.5625 \pm 1.1054$  years) who were divided into two groups. In Group I, 40 patients with T2DM have a mean duration of ( $6.6 \pm 0.9421$  years) and take medication. Group II consisted of 40 patients who were newly diagnosed with type 2 diabetic and do not take medication. Totally, 40 healthy individuals with mean age ( $44.7 \pm 1.4539$ ) were classified as the control group. **Results:** The mean  $\pm$  standard error (SE) serum level of CA 19-9 in patients with T2DM in Groups I and II was  $30.22933 \pm 3.2434$  U/ml and  $32.58443 \pm 2.7997$  U/ml, respectively, which was significantly higher than the mean  $\pm$  SE serum level in control group ( $6.4328 \pm 1.3087$  U/ml). When using a serum CA 19-9 concentration of 49.5 U/ml as a cutoff value to differentiate between T2DM and pancreatic cancer, sensitivity was 88.8% and specificity 77.5%. **Conclusion:** Define the normal range (cutoff value) of CA 19-9 in type 2 diabetic patients is useful in discriminating pancreatic cancer patients from type 2 diabetic patients.

**Keywords:** Level of CA19-9, T2DM, pancreatic cancer

## INTRODUCTION

Type 2 diabetes mellitus (T2DM), which represent 90%–95% of all diabetics, is a major medical problem worldwide with a big economic impact. The prevalence of the disease has tripled in the last 30 years.<sup>[1-6]</sup> Persons in middle age or older and who are also overweight or obese are the common victims of type 2 or noninsulin-dependent diabetes mellitus; they also can develop in obese adolescents. It occurs more frequently in women with previous history of gestational diabetes. The risk of development of this type increases with age, lack of physical activity, and obesity.<sup>[7-9]</sup>

In fact, 75%–85% of patients with type 2 diabetes have obesity, dyslipidemia, insulin resistance, and hyperinsulinemia before developing to T2DM.<sup>[10]</sup>

In this type, the production of insulin is still constant, but the real problem comes from dual defect: impaired  $\beta$ -cell function (insulin secretion) and impaired insulin action. Impaired insulin

action, that is, insulin resistance, is reduced sensitivity of body tissues to the insulin action and that occurs when target tissue is incapable to respond to normal concentration of insulin; as a result,  $\beta$ -cells in pancreas need to increase the amount of insulin secretion to keep euglycemia.<sup>[11,12]</sup>

Over time, the functional defect in insulin secretion works to prevent the  $\beta$ -cell from keeping the high rate of insulin secretion. Subsequently, glucose tolerance is impaired and eventually type 2 diabetes develops.<sup>[13,14]</sup>

Carbohydrate antigen 19-9 (CA 19-9) has been widely utilized for diagnosis of different kinds of cancer, for example, pancreatic cancer, cancer of upper gastrointestinal

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tract, hepatocellular cancer, liver cancer, colorectal cancer, and ovarian cancer and can also be used as an indicator of pancreatic tissue damage that may be caused by diabetes.<sup>[15,16]</sup>

In healthy adults, serum level of CA 19-9 is lower than 37 U/ml. If the serum level of CA19 is <100 U/ml, it is considered as value in benign pancreatic diseases. In malignant tumors, the value of CA 19-9 may be higher than 100,000 U/ml. CA 19-9 is neither organ specific nor tumor specific.<sup>[17-19]</sup>

Hence, the elevation level of CA 19-9 in patients with diabetes mellitus makes it imperative to find a normal range for CA 19-9 level for this patient to eliminate the additional interventional approaches.<sup>[20-22]</sup>

## MATERIALS AND METHODS

This study included 80 patients diagnosed as T2DM with standard error of mean (SEM) age ((mean ± SE) 46.5625 ± 1.1054 years) who were divided into two groups: Group I consisted of 40 patients with T2DM with an SEM duration ([mean ± SE] 6.6 ± 0.9421 years) and take medication. Group II consisted of 40 patients who were newly diagnosed with type 2 diabetic and do not take medication. Totally 40 healthy individuals with SEM age (44.7 ± 1.4539 years) were classified as control group. Blood sample was collected from all 120 participants from Al-Imamain Al-Kadhmain Medical City, Baghdad, Iraq, from February 2015 to May 2015. The research is approved by the Research Ethics Committee in Al-Nahrain University/College of Medicine.

Patients with any malignancies or who suffered from pancreatic, thyroid, liver, and renal diseases in their medical history; pregnant women; and smokers were excluded from the study.

Blood samples (5 ml) were centrifuged at 3000 rpm and serum was stored at -20°C. Serum CA 19-9 levels were measured by monoclonal antibody enzyme-linked immuno sorbent assay technique.

The values of laboratory test were presented as SEM. The comparison of means between the different groups was performed using the Student's (*t*-test).

Receiver operator characteristic (ROC) curve was constructed to plot sensitivity against specificity of high serum CA 19-9 level as diagnostic tests for DM. The area under the ROC curve (AUC) was calculated and compared with the AUC (0.5) of the nondiagnostic test (the line with the slope).

All the other analyses were done using IBM SPSS statistics version 20.0 computer software (Statistical Package for

Social), U.S. Government Users Restricted Rights. *P* < 0.05 level of significance was considered statistically significant.

## RESULTS

The concentrations of serum CA 19-9 of the studied individuals were summarized in Table 1. Serum CA 19-9 levels were significantly higher in the T2DM patients' groups compared with the controls (*P* < 0.05).

No significant differences were observed between the two diabetic groups because *P* value between the two diabetic groups in this study is equal 0.308.

The ROC curve shows a significant discriminatory ability of increase serum CA 19-9 levels in type 2 diabetic patients. The AUC for serum CA 19-9 was 0.914. A significant difference was found in the type 2 diabetic patients group (*P* < 0.001) as seen in Figure 1 and Table 2.

When the serum CA 19-9 concentration of 49.5 U/ml was used as the cutoff value for differentiating between T2DM and pancreatic cancer, the sensitivity was 88.8% and specificity was 77.5% as shown in Table 2.

## DISCUSSION

Diabetes mellitus is a chronic inflammatory disease of the pancreas and the mechanism of glucose intolerance comprises insulin resistance and devastation of beta cells.<sup>[23]</sup>

The United Kingdom Prospective Diabetes Study found that the beta cell functions were already reduced by 50% at diagnosis in addition to a subsequent deterioration that

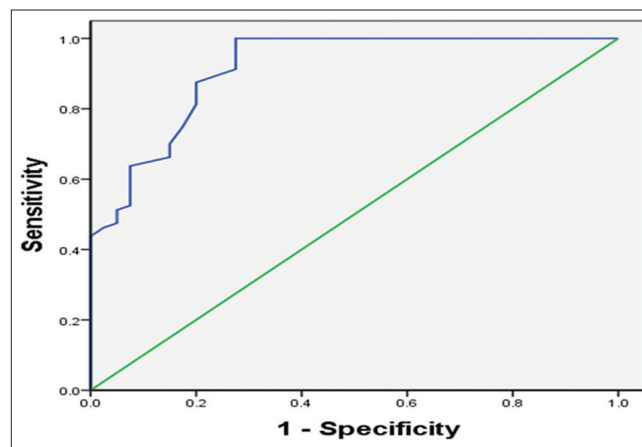


Figure 1: Receiver operator characteristic for carbohydrate antigen 19-9 in control and patients groups

Table 1: Summary carbohydrate antigen 19-9 levels

CA 19-9U/ml	With treatment (n=40)	Control (n=40)	Newly diagnosis (n=40)	Control (n=40)
Mean±SE	30.229±3.243	6.433±1.309	32.584±2.764	6.433±1.309
Median (range)	22.03 (10.142-99.568)	1.68 (0.001-28.965)	30.19 (10-63.667)	1.68 (0.001-28.965)
<i>P</i>	<0.001		<0.001	

SE: Standard error, CA 19-9: Carbohydrate antigen 19-9

**Table 2: Sensitivity and specificity carbohydrate antigen 19-9 in controls and patient groups**

Cutoff value	Specificity (%)	Sensitivity (%)	AUC	P
49.50 U/ml	77.5	88.8	0.914	<0.001

AUC: Area under the curve

appears regardless of therapy.<sup>[24]</sup> Hence, diabetes mellitus can be qualified as the last stage of chronic pancreatitis;<sup>[25]</sup> on the other hand, chronic pancreatitis was considered as a risk factor for pancreatic cancer.<sup>[26]</sup>

Carbohydrate antigen CA 19-9 was used mainly in the pancreatic cancer diagnosis but was also utilized as a marker of pancreatic tissue damage that might be caused by diabetes.<sup>[27]</sup> Hence, the elevation degree in CA 19-9 levels may be helpful in differentiating the pancreatic inflammatory conditions from pancreatic adenocarcinoma.<sup>[28]</sup> Therefore, the evaluation CA 19-9 levels in patients with diabetes mellitus makes it imperative to find normal range for CA 19-9 level for these patients to eliminate the additional interventional approaches.

The results of the present study found that patients suffering from T2DM have a serum CA 19-9 levels significantly higher than that in the control group. Regression analysis showed a positive correlation between CA 19-9 and diabetes independent of gender, age, HbA1c level, and glucose level; there is no obvious difference between the patients who are undergoing treatment (with a standard error of mean duration (mean  $\pm$  SE) 6.6  $\pm$  0.9421 years) and those who did not take the treatment (newly diagnosis patients) which is similar to Benhamou *et al.* study which concluded that CA 19-9 levels in diabetic patients were elevated in acute metabolic situations that correlated very well with the concentration of blood glucose.<sup>[28]</sup>

In contrast, Banfi *et al.* proved no correlation between biochemical markers of metabolic compensations in diabetes and CA 19-9 level;<sup>[29]</sup> Their study had only 28 samples with noninsulin dependent diabetes, which makes their result vulnerable to bias.

The present study also agrees with Uygur-Bayramicli *et al.* study which found that CA 19-9 level was higher in diabetic patients when compared with control individuals and a positive correlation was found between CA 19-9 and diabetes independent of gender, age, HbA1c level, and glucose level.<sup>[30]</sup> While Bedi *et al.* concluded that CA 19-9 levels in excess of 300 U/mL in mass lesions in chronic pancreatitis were always indicative of malignancy,<sup>[31]</sup> also chronic pancreatitis related with diabetes and pancreatic cancer is reported to be attendant by elevated CA 19-9 levels.<sup>[32]</sup>

Esteghamati *et al.* suggest that CA 19-9 levels more than 10.83 U/mL in the absence of other pathologies are in favor of glycemic impairments. CA 19-9 values above 34.30 U/mL may accompany an 84% frequency of diabetic participants, while CA 19-9 values of <6.46 U/mL are likely to rule out the presence of diabetes.<sup>[33]</sup>

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## Conflicts of interest

There are no conflicts of interest.

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