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RESEARCH ARTICLE

STUDY OF COAGULATION PROFILE IN TYPE 2 DIABETES MELLITUS

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Abstract

Introduction: Diabetes mellitus is a chronic condition which has high risk for microvascular and macrovascular comorbidities by the process of binding of glucose molecules to various proteins involved in the coagulation mechanism. The current study was carried out to determine the coagulation profiles of type 2 diabetes mellitus patients in comparison with apparently healthy controls.

Methods: This was a comparative cross-sectional study carried out at Tertiary care teaching institute Ahmedabad. Platelet parameters were determined by using Horiba Pentra XLR automated Hematology analyzer, whereas coagulation analysis was done using ACL TOP 300 CTS Fully Automated Coagulometer. The descriptive and analytical analysis was performed using Microsoft Excel and SPSS software. We used student t-test to analyze the difference between the means. AP-value less than 0.05 was set for the statistical significance determination.

Result: The mean PT, INR and APTT in the Diabetic case group were 11.46 ± 1.63 , 0.98 ± 1.14 and 29.83 ± 4.09 respectively. There were significant differences (p value < 0.05) in the PT, INR and APTT between case and healthy control groups. The mean platelet count was 257.92 ± 75.48 and the mean MPV was 8.00 ± 1.03 .

Conclusion: The present study revealed reduced values of PT, INR, APTT and no significant differences in platelet counts and MPV between diabetic patients and healthy controls. Thus, the finding is suggestive of hyper-coagulable tendencies of diabetic patients compared to controls.

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Introduction:-

Diabetes mellitus is a complex metabolic disorder sharing the common feature of hyperglycemia caused by defects in insulin secretion, insulin action or most commonly both.⁽¹⁾ Type 2 diabetes is recognized as a serious public health concern with a considerable impact on human life and health expenditures.⁽²⁾ Chronic hyperglycaemia is a well-known phenomenon of diabetes mellitus which affects many organs due to microvascular and macrovascular complications like neuropathy, retinopathy, nephropathy etc.⁽³⁾ Increased risk of thrombotic complications is noted in diabetics and it

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is due to hyperglycemia contributing to platelet hyperreactivity, hyperfibrinogenemia, increased thrombin formation and reduced fibrinolysis.⁽⁴⁾ Therefore coagulation profile must be a part of investigations in diabetes mellitus.

Hence aim of the study is to compare coagulation profile of Type 2 diabetic individuals (cases) with healthy individuals (controls) by doing coagulation tests below mentioned:

- 1) Prothrombin time (PT), INR
- 2) Activated partial thromboplastin time (APTT)
- 3) Plasma fibrinogen
- 4) Platelets count

PT is used to identify disease involving activity of the factors I, II, III, IV, V, VII, & X of the extrinsic & common pathways. APTT is used to screen for abnormalities of intrinsic and common pathways involving activity of factors I, II, V, VIII, IX, XI, & XII. Shortened PT and APTT could therefore be the expression of a hypercoagulable state.⁽⁵⁾

Materials and Methods:-

The present study was done on 200 subjects among which 100 were type 2 diabetes mellitus cases and 100 were non diabetic healthy control of age group 31-90 yrs in the Department of Pathology, Tertiary care teaching institute Ahmedabad. The diagnostic criteria for diabetes mellitus patients (cases) were set by the American diabetes association (ADA) and World Health Organization (WHO). These criteria included of the presence of random blood sugar level ≥ 200 mg/dl, a fasting blood sugar level ≥ 126 mg/dl, a glycated hemoglobin level $\geq 6.5\%$, or the postprandial blood sugar level ≥ 200 mg%. Controls were healthy non diabetic male or female individuals above the age of 18 years. The subjects with a history of venous thromboembolism, known inherited coagulation disorder, septicemia, liver disease, renal disease, cancer, hyperthyroidism, pregnancy, recent surgery and patients on anticoagulant treatment were excluded.

Peripheral blood samples from all study subjects were collected under aseptic precautions. The blood was collected in 3.2% sodium citrate vacuette (blood to anti coagulant ratio of 9:1) for coagulation profile and EDTA vacuette for platelet count and HbA1c. Platelet parameters were determined by using Horiba Pentra XLR automated Hematology analyzer, whereas coagulation analysis was done using ACL TOP 300 CTS Fully Automated Coagulometer. Each citrated sample was then centrifuged for 15 minutes at 4000 rpm and then following tests were performed Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT) and Fibrinogen. We used student t-test for independent samples to analyze the difference between the means. A P-value less than 0.05 was set for the statistical significance determination.

Results:-

Out of the 200 subjects enrolled in the study, all the subjects were between the age group of 31-90 years. Mean age of the subjects in the case and control group were found to be 55.19 and 53.07 respectively. There was no significant difference in mean age between the case and control group. (p value > 0.05). Out of 100 cases 59% were males and 41% were females and out of 100 controls 67% were males and 33% were females. Males were predominant among case and control group. Out of 100 cases, 27 cases had < 5 years duration and 73 cases had > 5 years duration of type 2 Diabetes Mellitus. In coagulation profile, we studied there was no significant difference between platelet and MPV in cases and controls. (p value > 0.05) (Table I)

Table I:- Platelet in cases and controls.

	Cases		Controls		Mean difference	P Value
	Mean	SD	Mean	SD		
Platelet ($\times 10^9/L$)	257.92	75.48	255.44	84.42	2.48	0.41
MPV (fl)	8.00	1.03	7.91	0.83	0.08	0.25

There was significantly decrease in prothrombin time (PT), INR, activated partial thromboplastin time (APTT) and increased mean value of fibrinogen in the case group compared to the control group with p value < 0.0001 . (Table II)

Table II:- PT, INR, APTT and Fibrinogen in cases and controls.

	Cases		Controls		Mean difference	P Value
	Mean	SD	Mean	SD		
PT (Sec)	11.46	1.63	12.92	1.79	1.46	< 0.0001
INR	0.98	0.14	1.104	0.15	0.12	< 0.0001
APTT (Sec)	29.83	4.09	32.7	3.40	2.86	< 0.0001

Fibrinogen (mg/dl)	325.08	73.31	183.06	57.52	142.02	<0.0001
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Table III;- Coagulation parameters of cases according to HbA1C values.

HBA1C(%)		<7 % (Group 1)	7-7.9 % (Group 2)	>8 % (Group 3)
FBS(mg/dl)	Mean	122.31	149.79	167.12
PP2BS(mg/dl)	Mean	208.37	258.13	289.36
PT(Sec)	Mean	11.21	11.14	11.70
	SD	0.70	1.33	1.91
	P value	0.26		
APTT(Sec)	Mean	30.5	29.8069	29.64909
	SD	2.89	3.69	4.55
	P value	0.77		
INR	Mean	0.96	0.95	1.00
	SD	0.05	0.11	0.16
	P value	0.28		
Fibrinogen(mg/dl)	Mean	289.81	322.31	336.8
	SD	80.29	71.22	68.69
	P value	0.07		
Platelet(x 10 ⁹ /L)	Mean	209.25	244.55	279.12
	SD	40.00	71.03	77.45
	P value	0.0021		
MPV(fl)	Mean	7.91	7.88	8.08
	SD	0.72	1.02	1.09
	P value	0.66		
Total cases		16	29	55

As shown in table III After analysis, no significant difference was found in mean values of PT, INR, APTT and MPV with increasing HbA1c value. However, nonsignificant increasing trend was noted in mean values of plasma fibrinogen and significant increasing trend was noted in mean values of platelets with increasing HbA1c values.

Table IV;- Coagulation parameters of cases with duration of DM.

Duration		<5 Years	>5 Years
FBS (mg/dl)	Mean	145	158.60
PP2BS (mg/dl)	Mean	252.74	272.75
PT (Sec)	Mean	11.44	11.46
	SD	1.64	1.63
	P value	0.93	
APTT (Sec)	Mean	32.07	29.0
	SD	3.54	3.97
	P value	0.0007	
INR	Mean	0.98	0.98
	SD	0.14	0.14
	P value	0.47	
Fibrinogen (mg/dl)	Mean	277.77	342.57
	SD	8.82	62.69
	P value	0.00002	
Platelets (x 10 ⁹ /L)	Mean	257.33	258.13
	SD	85.67	71.34
	P value	0.48	
MPV	Mean	7.98	8.01
	SD	0.82	1.09
	P value	0.44	
Total cases		27	73

As seen in table IV, cases were divided into two groups according to the duration since diabetes is diagnosed. No significant difference was noted in mean values of PT, INR, Platelets and MPV, between two groups. But, significant difference was noted in mean values of APTT and Plasma fibrinogen with longer duration of disease

Discussion:-

In the present study there is male predominance. Present study reported mean age of case group was 56.8 years. This result is similar with other studies done by Gupta et al.⁽⁷⁾, Bembde AS et al.⁽⁸⁾, Jabeen et al.⁽⁹⁾ (TableV)

Table V:- Comparison of case demographic with other studies.

	Present study	Ephraim et al. ⁽⁶⁾	Gupta P et al. ⁽⁷⁾	Bembde AS et al. ⁽⁸⁾	Jabeen et al. ⁽⁹⁾
Age	55.19±12.0years	55.9±14.1years	53.61±11.99 years	56.4years	51.08±07 years
Male	59 (59%)	24(40%)	58(63.74%)	57(57%)	93(54.70%)
Female	41(41%)	36(60%)	33(36.26%)	43(43%)	77(45.29%)
M:F	1.43:1	0.6:1	1.75:1	1.3:1	1.2:1

In Present study, we analysed that with increased HbA1c value there was significant increased platelets count in diabetic cases. There was no significant difference in platelet levels in the Diabetic patients in comparison to the control group. (TableVI)

Table VI:- Comparison of platelet and MPV with other studies.

	Platelet(x 10 ⁹ /L)			MPV(fl)		
	Case	Control	Pvalue	Case	Control	P value
Presentstudy	257.92±75.48	255.44±84.42	0.41	8.00±1.03	7.91±0.83	0.25
EphraimRK et al. ⁽⁶⁾	179.85 ± 66.15	168.55 ± 35.77	0.32	-	-	-
Ikechukwu EA et al. ⁽¹⁰⁾	238.0±77.0	235.0±53.0	>0.05	-	-	-
Akinsegum A et al. ⁽¹¹⁾	235.29±76.81	211.32±66.44	0.038	8.69±0.67	8.91±0.80	0.59
Jindal Set al. ⁽¹²⁾	-	-	-	12.08±1.54	11.42±1.40	0.015
Madan Ret al. ⁽¹³⁾	2.02±0.61	2.44±0.63	0.002			
Mohammed OI et al. ⁽¹⁴⁾	194.54±79.31	262.95±70.72	0.001	-	-	-

In the present study there was significant decrease in PT and APTT in diabetic case group as compared to healthy control group. There was significantly decreased APTT in diabetic patients along with increased duration of diabetes. (Table VII)

Table VII:- Comparison of PT and APTT with other studies.

	PT (Seconds)			APTT (Seconds)		
	Case	Control	Pvalue	Case	Control	Pvalue
Presentstudy	11.46±1.63	12.92±1.79	<0.0001	29.83±4.09	32.7±3.40	<0.0001
Karim Fet al. ⁽¹⁵⁾	9.54±0.58	11.18±0.41	<0.001	19.94±0.62	31.88±2.20	<0.001
Ephraim RK et al. ⁽⁶⁾	11.03±2.06	14.46±1.86	<0.0001	20.88 ± 5.19	21.23 ± 5.41	<0.0001
Ankalayya B et al. ⁽¹⁶⁾	10.35±0.32	12.58±0.38	<0.001	27.81±1.49	30.36±1.29	<0.001
Zhao Yet al. ⁽¹⁷⁾	11.5±1.4	11.7±1.3	0.016	27.6±6.5	28.8±7.0	<0.001
Acang Net al. ⁽¹⁸⁾	10.1±1.31	11.04±0.93	<0.05	29.2±3.69	32.16±3.77	<0.05
SaulsDL et al. ⁽¹⁹⁾	11.3±0.5	11.9±0.6	0.005	25.6±3.7	29.3±3.4	0.006

Elhassade AS et al. ⁽²⁰⁾	14.04±2.96	13.5±1.54	>0.05	29.85±7.54	34.12±2.82	0.006
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In the present study, we observed that there was marked increase in fibrinogen in diabetics when compared to healthy controls. There was also significant increase in Fibrinogen in diabetic patients along with increased duration of diabetes. A positive correlation between plasma glucose and fibrinogen levels has been reported in large epidemiological studies.⁽²¹⁾

Table VIII:- Comparison of Fibrinogen with other studies.

	Fibrinogen (mg/dl)		
	Case	Control	P value
Present study	325.08±	183.06±	<0.0001
Gupta P etal. ⁽⁷⁾	386.04±13.92	314.37±9.94	<0.001
Bembde AS etal. ⁽⁸⁾	656 ± 130	324 ± 139	<0.01
Coban E etal. ⁽²²⁾	449	216	<0.05
Sapkota etal. ⁽²³⁾	388.57 ± 60.90	320.89 ± 10.20	0.000
Acang N etal. ⁽¹⁸⁾	442.92±92	349.2±35.26	<0.05
Madan R etal. ⁽¹³⁾	252.75±40.23	227.5±22.8	0.002

Conclusion:-

We concluded that PT and APTT were decreased and plasma fibrinogen was increased significantly in type 2 diabetic patients in comparison with that of nondiabetics which could be expression of hypercoagulable state in T2DM individuals.

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