

THE 14th INTERNATIONAL CONGRESS OF
ENDOCRINE DISORDERS
22nd - 24th November 2023

Diabetes Mellitus and Cancer Incidence: A retrospective cohort study

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INTRODUCTION



- The global prevalence :9.3% equal to 463 million people by 2019 and 10.2% of the population (578 million people) in 2030
- evidence supporting a link between diabetes and cancer
- Hyperglycemia and hyperinsulinemia are among the most reliable explained mechanisms



INTRODUCTION



- Hyperglycemic states :
 - foster a pro-inflammatory environment ►►
 - stimulating signals involved in cell proliferation promotion, and anti-apoptotic pathways, which can also impose chemotherapy resistance .
 - support nutrition for the rapid-proliferating and glucose-consuming tumor cells
 - upregulate the expression of genes involved in cancer cell proliferation and invasion



INTRODUCTION

- Hyperinsulinemia:
- promotes cancer development through various mechanisms ►►
 - increased cell growth due to growth factor stimulation, promotion of inflammation, insulin resistance, and angiogenetic pathways



INTRODUCTION

- increase the mortality rates within cancer patients up to 2.5-fold in several cancers
- chemotherapeutic complications such as peripheral neuropathy more prominent in diabetic patients compared to non-diabetic



INTRODUCTION

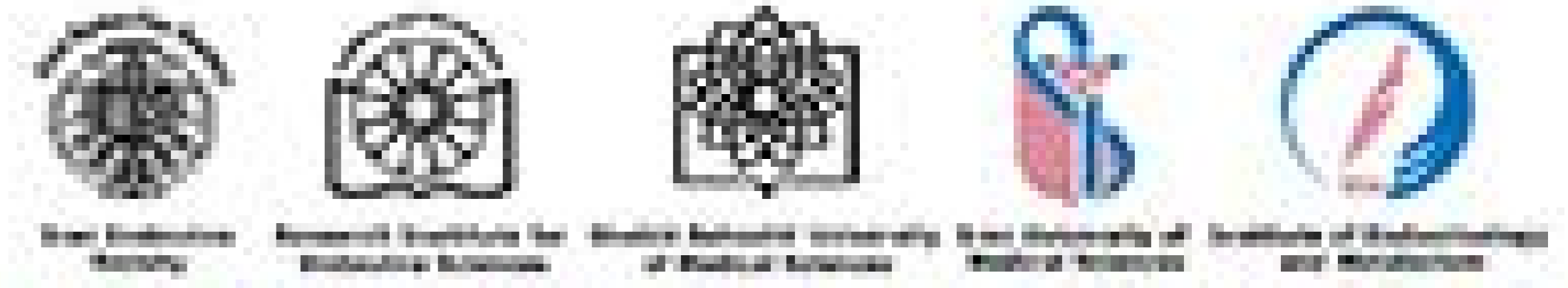


- high morbidity and mortality of cancer
 - the present cohort study aimed to investigate the relationship between diabetes mellitus and cancer incidence.



Methods

- Study design and participants :
 - retrospective cohort study in POCM
 - checklist of patient demographic information, Anteropometric parameter, body components, BMR ,DH, PMH
 - Kind of treatment for diabetic patients
- Among those who developed cancer:
 - cancer type
 - benignity or malignancy
 - diagnosis time
 - patient outcome



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- patient's biochemistry lab values:
 - CBC , FBS, lipid profile, ALT, AST ,TSH,BUN and creatinine
- Inclusion and exclusion criteria:
 - Diabetic (type2)patients of the cohort samples were included, non-diabetic individuals classified as the control group.
 - Gestational diabetic patients, patients receiving Metformin for Polycystic ovary syndrome were excluded



Results

- A total of 3143 patients included :
 - 503 diabetic patients as diabetic group
 - 2460 non-diabetic as control group
- 1889 were males and 1254 were female, (P=0.87).
- The average age was significantly higher among diabetic group (57.7 ± 10.1 vs 46.1 ± 10.3 years, $P < 0.001$)



Results

- comparison of anthropometric characteristics:
 - average height and weight in the non-diabetic group and BMI, waist to hip ratio as well as neck, chest, abdomen, back and wrists are more in the diabetic group(p-value<0/05)
- The evaluation of body composition:
 - total body water, intercellular water, protein, minerals, soft tissue massbody, body fat-free mass, skeletal muscle mass, bone mineral content and BMR in non-diabetic people was significantly higher than diabetic people (p value<0.05)
 - but fat mass of the body in diabetic people was significantly higher than non-diabetic people(p value<0.05)



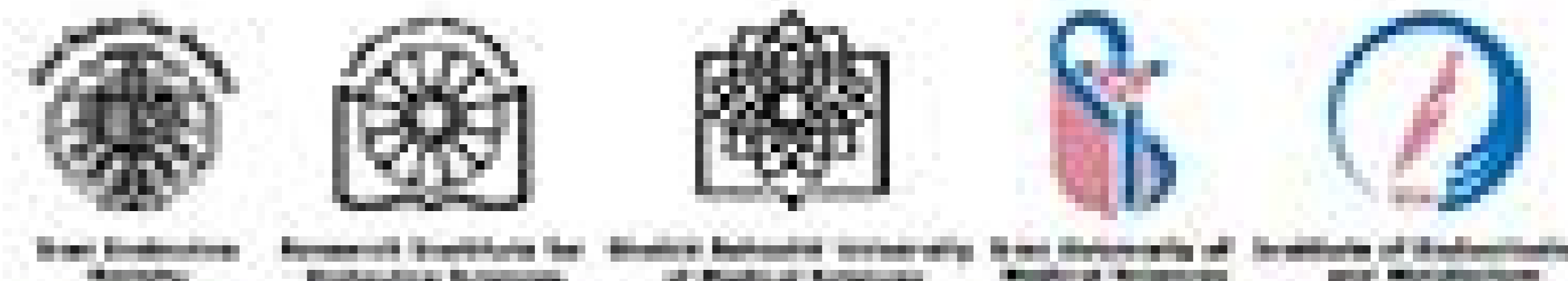
Clinical laboratory findings

Variable		Case N(%)	Control	Total	P-value
Blood Group	A	145 (32.8%)	652 (30.6%)	797 (31%)	0.2
	B	102 (23.1%)	569 (26.7%)	671 (26.1%)	
	AB	50 (11.3%)	191 (9%)	241 (9.4%)	
	O	145 (32.8%)	718 (33.7%)	863 (33.6%)	
FBS		140 (116-179)	93(86-102)	95.5 (87-107)	<0.0001
Lipid panel	LDL	84.7±35.1	101.2±28.5	97.6±31.3	<0.0001
	HDLC	51±10.6	53.8±11.9	55.7±12.6	<0.0001
	TG	130 (98-180)	108(76.5-154)	112 (79-160)	<0.0001
	CHOL	166.6±41	181±33.2	179.2±37.3	<0.0001
CBC	WBC	6.4±1.6	6±1.4	6.1±1.5	<0.0001
	RBC	4.9 (4.6-5.3)	5±0.5	5±0.5	0.02
	HGB	14.2±1.7	14.7±1.6	14.7±1.6	<0.0001
	HCT	41.9 (38.5-44.9)	42.5±4.4	42.6±4.6	<0.0001
	MCV	85 (81.9-87.9)	85.7(82.8-88.7)	85.6 (82.7-88.6)	0.01
	MCH	29.3 (27.8-30.6)	29.7(28.3-30.9)	29.7 (28.2-30.9)	0.02
	MCHC	34.5±1.7	34.5±1.4	34.5±1.6	0.37
	PLT	214.8±53.7	212(183.75-245)	212 (183-246)	0.81
	LY	38.7±9.1	40.1±8.4	40.5±8.7	<0.0001



Results

Variable		Case N(%)	Control	Total	P-value
CBC	MO	4.4±1.5	4(2.9-5.2)	4 (2.9-5.2)	0.09
	GR	56.9±9.8	55.3±9.2	55.2±9.5	0.01
	RDWCV	10.9 (10.5-11.5)	11(10.6-11.5)	11 (10.6-11.5)	0.24
	PCT	0.17 (0.15-0.21)	0.17(0.15-0.2)	0.17 (0.15-0.2)	0.65
	MPV	8.1±0.6	8.2±0.6	8.3 (7.9-8.825)	0.01
	PDW	17.3±0.7	17.1(16.6-17.6)	17.1 (16.7-17.6)	0.01
Renal function tests	BUN	32 (27-37)	31.6±7.7	30 (26-36)	<0.0001
	Creatinine	1.17 (1-1.34)	1.2±0.2	1.14 (0.98-1.31)	0.01
Liver function test	AST	20 (16-25)	21(18-26)	21 (17-25)	0.52
	ALT	24 (19-33)	23(17-33)	23 (17-33)	0.39
	ALP	190.2±57.4	171(143-207)	173 (144-209)	<0.0001
	GGT	27 (21-38)	23(18-32)	24 (18-33)	<0.0001
Thyroid function test	TSH	1.4 (1-2.3)	1.44(0.96-2.22)	1.44 (0.97-2.24)	0.13



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**comparison
 of medication
 among
 diabetics and
 non-diabetics**

Variable		Case N(%)	Control	Total	P-value
Statin	No	328 (65.2%)	2491 (94.4%)	2819 (89.7%)	<0.0001
	Yes	175 (34.8%)	149 (5.6%)	324 (10.3%)	
Fenofibrate	No	496 (98.6%)	2633 (99.7%)	3129 (99.6%)	0.001
	Yes	7 (1.4%)	7 (0.3%)	14 (0.4%)	
Gemfibrozil	No	497 (98.8%)	2635 (99.8%)	3132 (99.7%)	<0.0001
	Yes	6 (1.2%)	5 (0.2%)	11 (0.3%)	
Metformin	No	131 (26%)	2615 (99.1%)	2746 (87.4%)	<0.0001
	Yes	372 (74%)	25 (0.9%)	397 (12.6%)	
Insulin	No	443 (88.1%)	2640 (100%)	3083 (98.1%)	<0.0001
	Yes	60 (11.9%)	0 (0%)	60 (1.9%)	



Results

- 11 diabetic patients (2.2%) developed cancer
- 18 non-diabetic patients (0.7%) had developed cancer, statistically significant relation between cancer and diabetes. ($p=0.001$)
- **skin, colorectal** and **bladder** cancer were reported to be significantly higher in diabetic patients than control group.



Comparison of family and cancer history

Variable		Case N(%)	Control	Total	P-value
First degree family history of Cancer	No	416 (82.7%)	2222 (84.2%)	2638 (83.9%)	0.41
	Yes	87 (17.3%)	418 (15.8%)	505 (16.1%)	
Second degree family history of Cancer	No	419 (83.3%)	1994 (75.5%)	2413 (76.8%)	<0.0001
	Yes	84 (16.7%)	646 (24.5%)	730 (23.2%)	
Overall family history of cancer	No	353 (70.2%)	1680 (63.6%)	2033 (64.7%)	0.01
	Yes	150 (29.8%)	960 (36.4%)	1110 (35.3%)	
Overall family history of Diabetes	No	120 (25.9%)	1257 (51.9%)	1377 (47.7%)	<0.0001
	Yes	344 (74.1%)	1163 (48.1%)	1507 (52.3%)	
History of Skin Cancer	No	500 (99.4%)	2639 (100%)	3139 (99.9%)	0.001
	Yes	3 (0.6%)	1 (0%)	4 (0.1%)	
History of Breast Cancer	No	501 (99.6%)	2630 (99.6%)	3131 (99.6%)	0.95
	Yes	2 (0.4%)	10 (0.4%)	12 (0.4%)	
History of Colorectal Cancer	No	502 (99.8%)	2640 (100%)	3142 (100%)	0.02
	Yes	1 (0.2%)	0 (0%)	1 (0%)	
History of Bladder Cancer	No	501 (99.6%)	2639 (100%)	3140 (99.9%)	0.02
	Yes	2 (0.4%)	1 (0%)	3 (0.1%)	
History of hepatocellular carcinoma	No	503 (100%)	2639 (100%)	3142 (100%)	0.66
	Yes	0 (0%)	1 (0%)	1 (0%)	
History of Prostate Cancer	No	502 (99.8%)	2637 (99.9%)	3139 (99.9%)	0.62
	Yes	1 (0.2%)	3 (0.1%)	4 (0.1%)	
History of Brain And CNS Cancer	No	502 (99.8%)	2638 (99.9%)	3140 (99.9%)	0.41
	Yes	1 (0.2%)	2 (0.1%)	3 (0.1%)	
History of Ovarian Cancer	No	502 (99.8%)	2639 (100%)	3141 (99.9%)	0.19
	Yes	1 (0.2%)	1 (0%)	2 (0.1%)	
History of Chronic Lung Disease	No	476 (94.6%)	2561 (97%)	3037 (96.6%)	0.007
	Yes	27 (5.4%)	79 (3%)	106 (3.4%)	
History of cardiovascular disease	No	421 (83.7%)	2508 (95%)	2929 (93.2%)	<0.0001
	Yes	82 (16.3%)	132 (5%)	214 (6.8%)	



Results

- Logistic regression was used to predict cancer incidence according to the studied variables:
- the relationship between these parameters and cancer was significant :
 - BMR, SMM, FFM, SLM, Minerals, Protein, TBW, Weight, Height, BMC, measured neck circumference, measured chest circumference
 - BUN, HCT, HGB, RBC
 - Age, blood pressure, history of cardiovascular disease



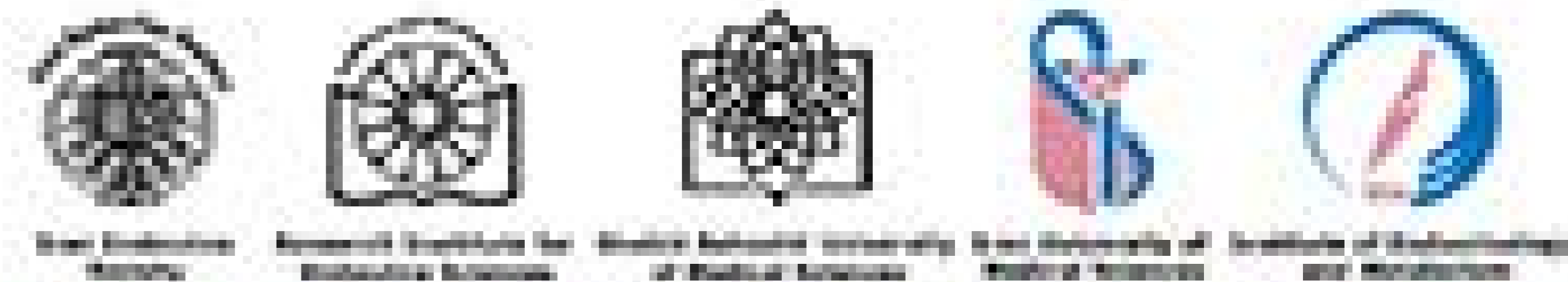
Results

- In the analysis of body composition, the probability of getting cancer decreases with the increase of TBW, Protein, Minerals, SLM, FFM, SMM, BMC according to $OR < 1$.
- For BMR, the probability of getting cancer decreases by 0.996% with an increase in basal metabolism.
- Increase of neck and chest circumference, the probability of getting cancer decreases by 0.877 and 0.931.



Relation between laboratory data and cancer

Variables	Univariate			
	B	S.E	OR (95% CI)	P-Value
Age	0.082	0.017	1.086 (1.051 - 1.122)	0.000
FBS	0.003	0.005	1.003 (0.993 - 1.012)	0.576
LDL	-0.0002	0.006	1 (0.988 - 1.012)	0.978
HDLC	-0.02	0.016	0.98 (0.949 - 1.012)	0.222
TG	0.0005	0.002	1 (0.997 - 1.004)	0.805
CHOL	-0.001	0.005	0.999 (0.989 - 1.008)	0.768
WBC	-0.109	0.137	0.897 (0.686 - 1.173)	0.427
RBC	-1.18	0.35	0.307 (0.155 - 0.61)	0.001
HGB	-0.312	0.106	0.732 (0.594 - 0.901)	0.003
HCT	-0.119	0.04	0.888 (0.822 - 0.96)	0.003
MCV	0.02	0.036	1.02 (0.951 - 1.094)	0.583
MCH	0.037	0.081	1.038 (0.885 - 1.217)	0.651
LY	0.017	0.022	1.017 (0.975 - 1.061)	0.440
GR	-0.015	0.02	0.985 (0.948 - 1.024)	0.453
MPV	-0.474	0.28	0.622 (0.36 - 1.077)	0.090
PDW	0.083	0.107	1.086 (0.88 - 1.34)	0.442
BUN	0.037	0.014	1.038 (1.009 - 1.066)	0.008
Creatinine	0.841	0.523	2.319 (0.832 - 6.464)	0.108
ALP	-0.002	0.004	0.998 (0.991 - 1.005)	0.662
GGT	-0.006	0.012	0.994 (0.971 - 1.017)	0.605
TSH	-0.056	0.134	0.946 (0.727 - 1.229)	0.676



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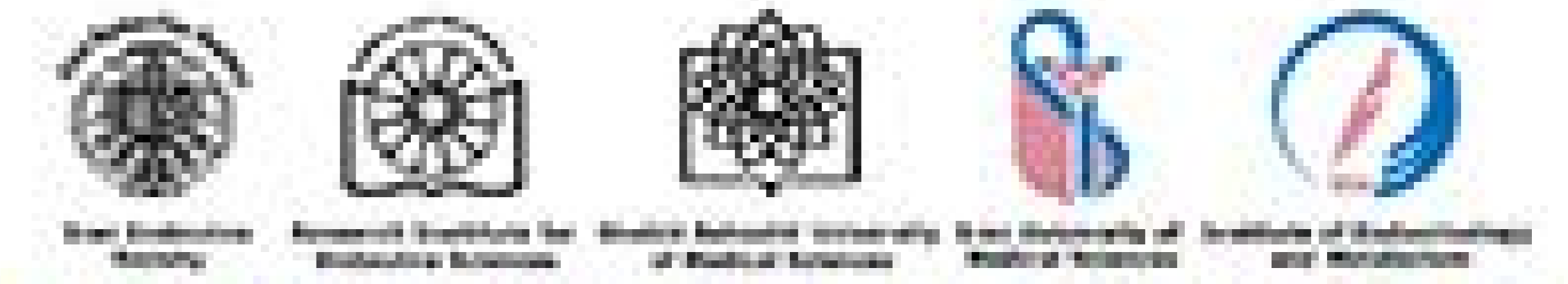
results of univariate analysis of several factors such as history and medication within cancer development

Variables	Univariate			
	B	S.E	OR (95% CI)	p-value
First-degree family history of Diabetes	-0.817	0.44	0.442 (0.187 - 1.047)	0.063
Taking Statin	0.301	0.511	1.351 (0.497 - 3.676)	0.555
Taking Fenofibrate	-16.939	10545.44	0 (0 - 0)	0.999
Taking Gemfibrozil	-16.982	11926.06	0 (0 - 0)	0.999
Taking Metformin	-0.556	0.621	0.573 (0.17 - 1.936)	0.370
History of Hypertension	0.916	0.428	2.498 (1.08 - 5.78)	0.032
History of Cardiac Disease	1.392	0.461	4.025 (1.632 - 9.928)	0.003
History of Myocardial Infarction	1.265	0.765	3.543 (0.79 - 15.884)	0.098
History of Stroke	1.178	1.059	3.247 (0.408 - 25.856)	0.266
History of Renal Failure	2.168	1.106	8.74 (1 - 76.355)	0.050
History of Fatty Liver	0.755	0.401	2.128 (0.97 - 4.668)	0.060
History of Thyroid Disease	-0.094	0.618	0.911 (0.271 - 3.057)	0.880
History of cardiovascular disease	1.426	0.443	4.162 (1.746 - 9.919)	0.001



Discussion

- A cohort study of total of 407157 subjects in Italy: significant increased cancer occurrence among diabetics (IRR: 1.22, 95%CI:1.15-1.29). hepatic, pancreatic, colorectal and bladder cancer
- A 2018 cohort study in UK ,333438 diabetic patients and 333438 non-diabetics revealed significant increased risk of hepatic cancer (IR 26 vs 8.9, 95% CI 24–28 vs 7.7–10), pancreatic cancer (IR 65 vs 31, 95% CI 62–69 vs 28–34) and colorectal cancer (IR 119 vs 109, 95% CI 114–124 vs 104–114) among diabetic patients



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Discussion

- A finish cohort study revealed an increased cancer incidence of 16% in diabetic patients compared to general population.
- significant increase in rates of lip , hepatic, pancreatic, gastric, colonic, cholecyste, skin, renal , bladder and thyroid cancers (SIR ranging from 1.15 to 2.44) .
- reduced risk of prostate cancer in this study , which is in line with findings of several other studies which is probably due to lower levels of androgens and prostate specific antigen in diabetic men



limitations



- Even though our study was a prospective cohort in nature which provides valuable and strong cancer risk assessment within diabetic patients, it was not free of limitations
- We were not able to investigate other carcinogenic factors such as environmental toxins or alcohol consumption.
- We encourage future researchers to investigate and compare morbidity and mortality of cancer within diabetic patients



**THANKS FOR YOUR
ATTENTION**

