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DYSLIPIDEMIA PATTERN AND IMPACT OF DURATION OF TYPE 2 DIABETES MELLITUS AND INCREASING AGE ON INSULIN RESISTANCE, INSULIN LEVELS AND DYSLIPIDEMIA

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Abstract:

Aim: *To investigate dyslipidemia pattern in patients with type 2 diabetes and to determine the correlation of increasing age and duration of the disease with dyslipidemia, insulin level and insulin resistance in diabetic patients.*

Methods: *A cross-sectional study was held in the Medicine department of Mayo Hospital Lahore for six months duration from October 2019 to March 2020 among 112 selected patients Triglycerides, Serum total cholesterol, high density lipoproteins, low density lipoproteins, and insulin levels in both cases and control. Insulin resistance was calculated using a homeostatic model to assess insulin resistance. The correlation between the increase in age and duration of disease was determined using biochemical parameters. SPSS 17 was used for statistical analysis.*

Results: *Of the 112 participants in the study, 72 (64%) were patients and 40 (36%) were healthy controls. Of these cases, 44 (61%) patients had hypertriglyceridemia followed by low density hypertriglyceridemia 36 (50%). Among the controls, 20 (50%) patients had low density hypertriglyceridemia followed by 17 (42.5%) hypertriglyceridemia. The duration of the disease was not correlated with dyslipidemia or insulin resistance ($p > 0.05$). The duration of the disease had a strong negative correlation with serum insulin levels ($p = 0.03$). Regression analysis showed no significant correlation with age dyslipidemia, serum insulin levels, or insulin resistance (each $p > 0.05$).*

Conclusion: *Hypertriglyceridemia is the most common dyslipidemia in type diabetes, whereas hypertriglyceridemia is a risk factor in healthy people. In addition, disease duration was in reverse correlated with serum insulin levels and positively correlated with dyslipidemia.*

Key words: *diabetes, dyslipidemia, insulin resistance.*

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INTRODUCTION:

The universal pervasiveness of diabetes is projected at 171 million in 2000, and is projected to rise to 366 million by 2030. In Pakistan, the national incidence of diabetes is 6.76% and the comparative incidence of diabetes is 7.90%. Obesity is strongly associated with type 2 diabetes (DM2). Dyslipidemia, insulin levels and insulin resistance usually get worse as the disease progresses and as they get older[1-2]. Dyslipidemia occurs in metabolic syndrome, and international and national studies have shown different models of dyslipidemia in T2DM and obesity. In the Pakistani population, most studies have shown high-levels of triglycerides (TG), total cholesterol (TC) and low-density lipoproteins (LDL), while few studies have only reported high density lipoproteins (HDL). DM2. Very few studies have shown normal HDL levels in DM[3-4]. Dyslipidemia worsens with the duration of the disease and is the cause of diabetic complications. International studies report that increasing age and disease progression is a risk factor for dyslipidemia, decreased insulin levels, and increased insulin resistance in T2DM[5]. While some studies have so far reported on the effect of age on biochemical parameters in DM2, no study in Pakistan highlighted the impact of disease duration on biochemical parameters in Pakistani individuals.

No study in Pakistan has associated the increased age and duration of illness with dyslipidemia, insulin levels and insulin resistance, but dyslipidemia patterns have been reported in many studies[6]. This study shows not only the dyslipidemia pattern in DM2 patients and healthy people, but also dyslipidemia a, insulin levels and insulin.

PATIENTS AND METHODS:

This cross-sectional study was held in the Medicine department of Mayo Hospital Lahore for six months duration from October 2019 to March 2020. Using an incredible fitness sampling technique, DM2 patients were selected according to World Health Organization (WHO) criteria with history of T2DM for at least one year with fasting blood glucose >7mmol/L and >11.1mmol/L 2 hours after breakfast. Patients with type 1 DM (T1DM), co-existent endocrine disease, chronic renal failure, already on insulin or lipid-lowering drugs, smokers and those suffering from acute or chronic inflammatory disease were excluded. Exclusion criteria was ensured on the basis of history, physical examination and laboratory investigations, including blood complete picture (CP), erythrocyte sedimentation rate (ESR) after one hour by Westergren's method, 16 and renal function tests. All subjects were advised not to use or change their eating habits for at least two weeks prior to blood sampling. Informed written consent was obtained from each participant.

Then, 10 ml of venous blood sample was taken from the vein of the elbow with a clean vein under aseptic conditions in a disposable syringe from each person. Blood was allowed to clot for 30 minutes at room temperature. After removing the clot, the serum was separated by centrifugation at 3000 rpm for 15 minutes. The serum was then transferred to small sterile tubes and stored at -20 ° C before biochemical analysis. Blood CP was performed on an automatic Sysmex analyzer, ESR was determined by Westergren method, glucose oxidase serum 16 method, CT serum immunohydridization method, triglycerides (TG), serum by calorimetric method, serum LDL by immunological inhibition, HDL serum by Freidewald's formula and insulin serum by enzyme-dependent immunosorbent analysis (ELISA). Insulin resistance was calculated using the Homeostatic Insulin Resistance Assessment Model. Statistical analysis was performed using SPSS17.

The mean ± standard deviation (SD) of patient age, disease duration, serum CT, TG, HDL, LDL, insulin and insulin resistance was determined using HOMA-IR. A Spearman correlation analysis was performed to assess the relationship among dyslipidemia, insulin levels and insulin resistance with age and duration of disease. P <0.05 was considered statistically significant. Of these cases, 44 (61%) patients had hypertriglyceridemia followed by low density lipoprotein hypercholesterolemia in 36 patients (50%). Of the control patients, 20 (50%) had low density hypercholesterolemia, followed by 17 with hypertriglyceridemia (42.5%).

RESULTS:

Of the 112 study participants, 72 (64%) were patients and 40 (36%) were healthy controls. Forty (55.5%) cases are men and 32 (45.5%) women. 27 (67.5%) controls were male and 13 (32.5%) female. Average values of age, disease duration, BMI, serum CT, TG, LDL, HDL, insulin and insulin resistance were recorded for both the test and control groups (Table 1).

Table-1: Demographic & biochemical parameters in Type 2 diabetes mellitus patients and healthy controls.

S. No.	Parameter	Study group Mean ± SD (Range) n = 72	Control group Mean± SD (Range) n = 40	P value
1	Mean age (years)	42.92 ± 3.09	36.65 ± 4.54	0.6
	Range	(30-50)	(30-50)	
2	Male n (%)	40 (55.5%)	27 (67.5%)	-
	Female n (%)	32 (45.5%)	13 (32.5%)	
3	Mean duration (years)	4.3 ± 4.27	-	-
	Range	(1-18)		
4	BMI	27.29 ± 4.12	24.78 ± 5.16	0.006
	Kg/m^2	(19.23 – 38.4)	(15.69 – 35.6)	
5	Mean S.TC (mg/dl)	182.13 ± 37.12	167.82 ± 35.96	0.04
	Range	(113.68-261.79)	(85.84-242.45)	
6	Mean S.TG (mg/dl)	200±102.65	148.67±90.27	0.008
	Range	(69.03-525.66)	(43.36-472.57)	
7	Mean S.LDL-C (mg/dl)	100.54±28.61	104.4±27.6	0.47
	Range	(23.2-178.65)	(42.54-163.95)	
8	Mean S.HDL-C (mg/dl)	42.53±9.66	39.44±8.12	0.04
	Range	(18.94-90.48)	(29-63.8)	
9	Mean S. insulin (mIU/ml)	13.2 ±6.93	13.47 ± 5.12	0.83
	Range	(4.9-43.1)	(7.1-26.98)	
10	HOMA-IR	4.78 ± 2.61	3.14 ± 1.2	0.001
		(1.45-18.8)	(1.58-6.28)	

The average duration of the disease was 4.3 ± 4.27 years. The patients BMI was 27.29 ± 4.12 kg / m2), and the control BMI was 24.78 ± 5.16 kg / m2 (p = 0.006). CT, serum TG, insulin resistance (IR) were significantly higher in DM2 (p <0.05) than healthy controls, and HDL was lower, while serum LDL and insulin levels were similar in both groups (p> 0.05). In both groups of patients were divided into obese and non-obese individuals with hypercholesterolemia, hypertriglyceridemia, LDL hypercholesterolemia and low HDL. The cut-off value for BMI was> 25 kg / m2 for obesity,> 200 mg / dl for CT,> 150 mg / dl for TG,> 100 mg / dl for LDL and <40 mg / dl for HDL. The cut-off value for normal insulin was 10 µIU / L and 2.5 for HOMA-IR and insulin resistance.

46 (63.8%) cases were not obese and 26 (36.2%) were not obese. Among the controls, 20 (50%) were obese and 20 (50%) were not obese. Hypercholesterolemia in 22 (30.5%) cases, 7 (17.5%) controls, 44 (61%) cases of hypertriglyceridemia and 17 (42.5%) controls, 36 (50%) cases of LDL hypercholesterolemia (24 (50%) controls and 10 (13.8%) low HDL values and 12 (30%) controls were compared (Table 2).

Table-2: Comparison of dyslipidemia, insulin levels and insulin resistance between study and control group.

Parameters	T2DM	Healthy
Obesity n (%)	46 (63.8%)	20 (50%)
Hypercholesterolemia-total n (%)	22 (30.5%)	7 (17.5%)
Hypertriglyceridemia n (%)	44 (61%)	17 (42.5%)
Hypercholesterolemia-LDL n (%)	36 (50%)	24 (60%)
Low HDL n (%)	10 (13.8%)	12 (30%)
Hyperinsulinism n (%)	50 (70%)	08 (20%)
Insulin resistance n (%)	74 (88.8%)	*23 (59%)

*In obese persons only T2DM: Type 2 diabetes mellitus HDL: High-density lipoprotein.

Two years after the disease there was a clear increase in the percentage of patients with serum TG above 150 mg / dL from 23.6% to 5 years after 37.5%. Similarly, in patients with hypercholesterolemia, LDL increased from 18% after 2 years to 32% after 5 years. There was no clear increase in TC and HDL in serum with DM duration. In Spearman's correlation analysis, disease duration was not associated with dyslipidemia or insulin resistance, but disease duration had a weak negative correlation with serum insulin levels ($p < 0.03$; $R = -0.247$) (Table-3; Figure- 1).

Table-3: Correlation between serum insulin with duration of disease and insulin resistance.

Spearman's Correlation	p value	R coefficient	R^2coefficient
Duration vs. serum insulin	0.03	-0.247	0.057
Serum insulin vs. HOMA-IR	0.0001	0.864	0.775

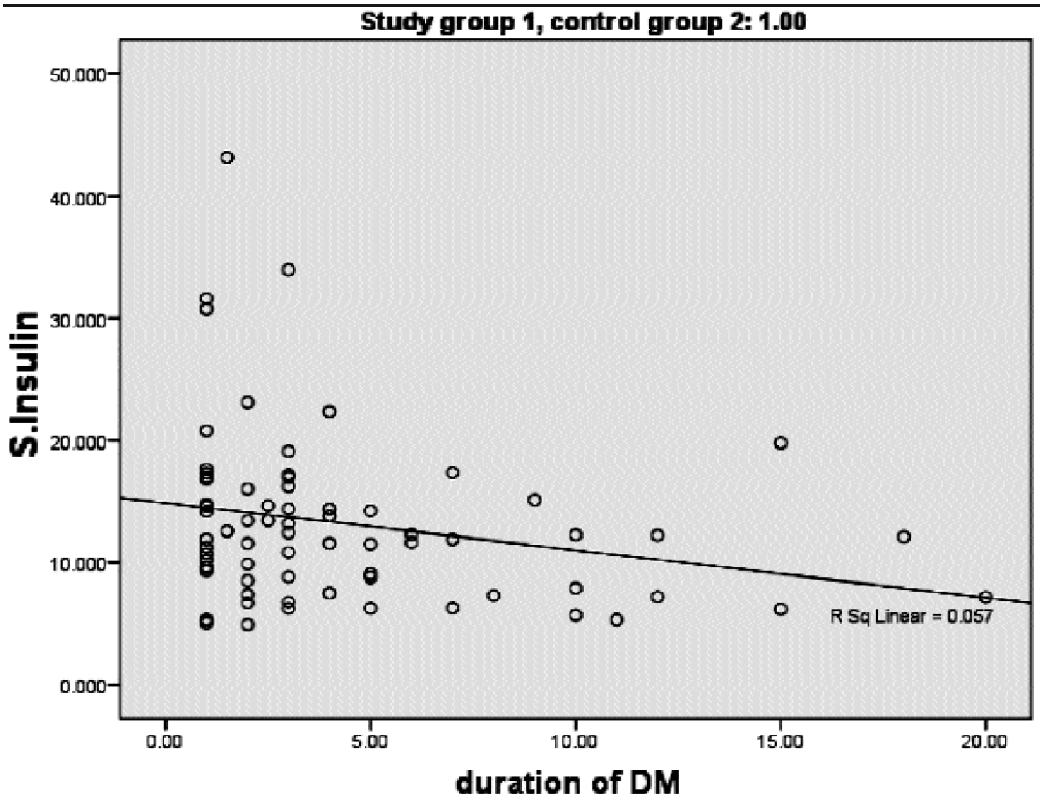

Figure-1: Correlation of serum insulin levels with duration of the disease in type 2 diabetes mellitus.

In statistical analysis, age dyslipidemia did not show a significant correlation with serum insulin levels or insulin resistance.

Hyperinsulinemia was detected in 50 patients (70%) and insulin resistance in 64 patients (88.8%). In the study group, 42 (58%) had severe resistance and 30 (42%) had mild insulin resistance. In obese but otherwise healthy people, 11 (59%) had mild insulin resistance compared to the HOMA-IR index, indicating the risk of T2DM in obese people. In the Spearman correlation analysis, serum insulin in DM2 patients showed a strong positive correlation with insulin resistance ($p < 0.0001$; coefficient $R = 0.864$) (Fig. 2).

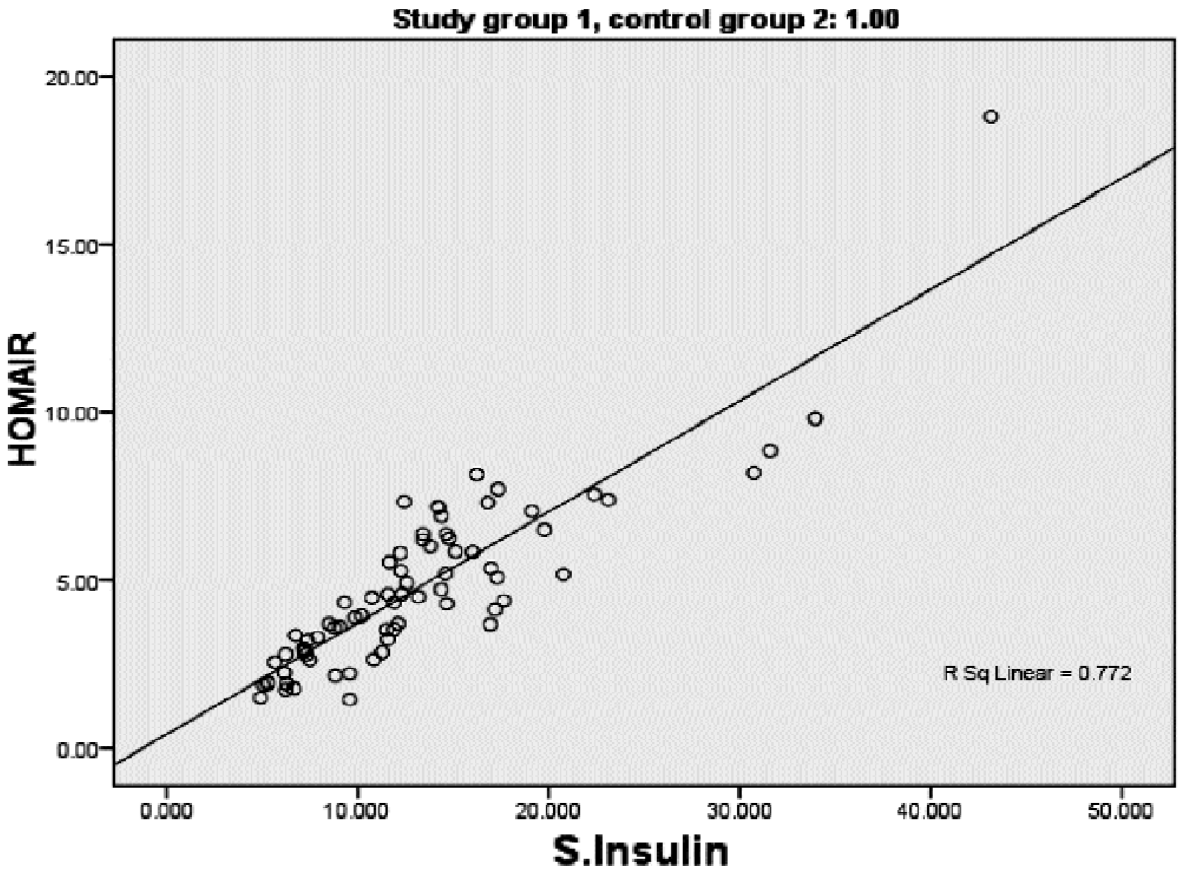

Figure-2: Correlation of serum insulin levels with insulin resistance in type 2 diabetes mellitus.

DISCUSSION:

This study is the first to report dyslipidemia, insulin levels, and increased age and duration of disease in Pakistani T2DM patients. The types and frequencies of dyslipidemia are described in the literature on T2DM and in many international and national studies on healthy obese and non-obese individuals. No study in patients in Pakistan has shown that disease duration correlates with dyslipidemia, insulin levels, and insulin resistance.

In our study, hypertriglyceridemia (61%) was accompanied by LDL hypercholesterolemia (50%), hypercholesterolemia (30.5%) and low HDL (13.8%) in patients with diabetes. This finding is consistent with many other national studies in which Pakistani patients with DM2 have shown that hypertriglyceridemia is the most common dyslipidemia. One study found hypertriglyceridemia followed by LDL hypercholesterolemia, male hypercholesterolemia followed by LDL hypercholesterolemia. The most common dyslipidemia in patients with Pakistan DM2. In another study, S.TG was higher in patients with DM, and as in our case after LDL, the percentage of patients with dyslipidemia was higher in another study[7]. Contrary to our results, some studies reported low HDL levels as the most common dyslipidemia in patients with DM, while others reported hypercholesterolemia as the most common finding in patients with Pakistani DM2[8]. In one study, unlike our results, none of the DM patients had low HDL levels. A study in Karachi has shown that the most common finding is a combination of high LDL and low HDL. Another study showed that high DML was more common in patients with Pakistani DM2 than in high CT[9]. Different dyslipidemia patterns in patients with T2DM diabetes may depend on the variable sample size, variable disease duration, and BMI of the samples tested[10]. After analyzing the misleading factors, a large-scale mass cohort should be investigated to draw a final conclusion on the most common dyslipidemia pattern in the Pakistani population. International studies also show different results regarding the dyslipidemia pattern in DM2[11]. Chinese patients with DM2 had the most common hypertriglyceridemia followed by high CT followed by LDL as in our study. Dyslipidemia was more pronounced in women. The most common dyslipidemia in healthy obese and non-obese people in our study is LDL hypercholesterolemia (60%) followed by hypertriglyceridemia (42.5%), low HDL (30%) and total hypercholesterolemia (17.5%). In some studies, high serum TG and low HDL serum were the most common dyslipidemia in healthy controls[12].

Our study found a clear worsening of dyslipidemia as the disease progressed, but the correlation was not significant in the statistical analysis. We found a weak negative correlation between disease duration and serum insulin levels (p> 0.003; R-factor: -0.247) (Fig. 1). Other studies have shown a positive relationship between dyslipidemia and the duration of the disease[13]. One study found that TC, HDL and LDL in the serum were absent, but serum TG and very low-density lipoprotein (VLDL) showed a positive correlation with DM time. Although serum TC, TG, HDL and VLDL correlated with age increase in the same study, this was not the case in our study[14]. Another study showed that dyslipidemia worsens with increasing age in the Iranian population. In our study, the duration of the disease was not correlated with insulin resistance. International data show that with age and longer duration of DM2 insulin resistance decreases and insulin resistance increases[15].

In our study, the hyperinsulinism and insulin resistance found in most patients with DM2 are consistent with other studies. In our study there was a strong positive correlation among insulin resistance and serum insulin levels (p <0.0001; R ratio: 0.864) in DM2 (Fig. 2). Among healthy controls, insulin resistance was found in obese people, but not in weak people. Future large-scale studies may highlight the occurrence of dyslipidemia and insulin resistance in the healthy population of Pakistan. Our study showed that serum insulin levels decreased in DM2 and dyslipidemia worsened with the duration of the disease. Dyslipidemia and hyperglycemia instead of hyperglycemia alone are the cause of diabetic complications. Dyslipidemia tends to increase and should be managed with blood sugar control in patients with T2DM. The limitation of our study was the small sample size. In addition, BMI-based subgroups were not studied. External validity can be verified by repeating the test in a larger sample. Generalization of the target population in relation to the study population cannot be performed due to the small sample size, and the study can be obtained by multiplying with a larger sample size.

CONCLUSION:

While hypertriglyceridemia is the most common dyslipidemia in DM2, hypercholesterolemia is a risk factor in healthy people. The duration of the disease is inversely correlated with serum insulin levels and positively correlated with dyslipidemia in DM2.

REFERENCES:

1. Koren, Dorit, and Elsie M. Taveras. "Association of sleep disturbances with obesity, insulin resistance and the metabolic syndrome." *Metabolism* 84 (2018): 67-75.
2. Seko, Yuya, Yoshio Sumida, Saiyu Tanaka, Kojiroh Mori, Hiroyoshi Taketani, Hiroshi Ishiba, Tasuku Hara et al. "Insulin resistance increases the risk of incident type 2 diabetes mellitus in patients with non-alcoholic fatty liver disease." *Hepatology research* 48, no. 3 (2018): E42-E51.
3. Artha, I. Made Junior Rina, Agha Bhargah, Nyoman Khrisna Dharmawan, Utami Wijayaswari Pande, Komang Agus Triyana, Pande Agung Mahariski, Jessica Yuwono et al. "High level of individual lipid profile and lipid ratio as a predictive marker of poor glycemic control in type-2 diabetes mellitus." *Vascular health and risk management* 15 (2019): 149.
4. Imga, Narin Nasiroglu, Alper Cagri Karci, Dilek Oztas, Dilek Berker, and Serdar Guler. "Effects of vitamin D supplementation on insulin resistance and dyslipidemia in overweight and obese premenopausal women." *Archives of medical science: AMS* 15, no. 3 (2019): 598.
5. Zabeen, Bedowra, Ana Margarida Balsa, Nasreen Islam, Mukta Parveen, Jebun Nahar, and Kishwar Azad. "Lipid profile in relation to glycemic control in type 1 diabetes children and adolescents in Bangladesh." *Indian journal of endocrinology and metabolism* 22, no. 1 (2018): 89.
6. Patel, Roma, Sayantani Pramanik Palit, Nirali Rathwa, A. V. Ramachandran, and Rasheedunnisa Begum. "Genetic variants of tumor necrosis factor-α and its levels: A correlation with dyslipidemia and type 2 diabetes susceptibility." *Clinical nutrition* 38, no. 3 (2019): 1414-1422.
7. Kajingulu, Francois M., Francois B. Lepira, Fiston I. Mbutiwi, Jean-Robert Makulo, Ernest K. Sumaili, Justine B. Bukabau, Vieux M. Mokoli, Augustin L. Longo, and Nazaire M. Nseka. "Albuminuria status and patterns of dyslipidemia among type 2 diabetes black patients managed at a tertiary health-care hospital: A Post hoc analysis." *Saudi Journal of Kidney Diseases and Transplantation* 29, no. 3 (2018): 649.
8. Haghighatpanah, Mohammad, Amir Sasan Mozaffari Nejad, Maryam Haghighatpanah, Girish Thunga, and Surulivelrajan Mallayasamy. "Factors that correlate with poor glycemic control in type 2 diabetes mellitus patients with complications." *Osong public health and research perspectives* 9, no. 4 (2018): 167.
9. Waldman, Meryl, Joan C. Han, Daniela P. Reyes-Capo, Joy Bryant, Kathryn A. Carson, Baris Turkbey, Peter Choyke et al. "Alström syndrome: Renal findings in correlation with obesity, insulin resistance, dyslipidemia and cardiomyopathy in 38 patients prospectively

evaluated at the NIH clinical center." *Molecular genetics and metabolism* 125, no. 1-2 (2018): 181-191.

10. Zhao, Ren Ru, Anthony J. O'Sullivan, and Maria A. Fiatarone Singh. "Exercise or physical activity and cognitive function in adults with type 2 diabetes, insulin resistance or impaired glucose tolerance: a systematic review." *European Review of Aging and Physical Activity* 15, no. 1 (2018): 1.
11. Barchetta, I., V. Ceccarelli, F. A. Cimini, L. Bertoccini, A. Fraioli, C. Alessandri, A. Lenzi, M. G. Baroni, and M. G. Cavallo. "Impaired bone matrix glycoprotein pattern is associated with increased cardio-metabolic risk profile in patients with type 2 diabetes mellitus." *Journal of endocrinological investigation* 42, no. 5 (2019): 513-520.
12. Athyros, Vasilios G., Michael Doumas, Konstantinos P. Imprialos, Konstantinos Stavropoulos, Eleni Georgianou, Alexandra Katsimardou, and Asterios Karagiannis. "Diabetes and lipid metabolism." *Hormones* 17, no. 1 (2018): 61-67.
13. Bello-Ovosi, Beatrice Ohunene, Joseph Ogirima Ovosi, Modupe Arinola Ogunsina, Sunday Asuke, and Muhammed Sani Ibrahim. "Prevalence and pattern of dyslipidemia in patients with type 2 diabetes mellitus in Zaria, Northwestern Nigeria." *Pan African Medical Journal* 34, no. 123 (2019).
14. Bene, Judit, Kinga Hadzsiev, and Bela Melegh. "Role of carnitine and its derivatives in the development and management of type 2 diabetes." *Nutrition & diabetes* 8, no. 1 (2018): 1-10. Bene, Judit, Kinga Hadzsiev, and Bela Melegh. "Role of carnitine and its derivatives in the development and management of type 2 diabetes." *Nutrition & diabetes* 8, no. 1 (2018): 1-10.
15. Ebrahimpour-Koujan, Soraiya, Bahram Pourghassem Gargari, Majid Mobasseri, Hadi Valizadeh, and Mohammad Asghari-Jafarabadi. "Lower glycemic indices and lipid profile among type 2 diabetes mellitus patients who received novel dose of Silybum marianum (L.) Gaertn.(silymarin) extract supplement: A Triple-blinded randomized controlled clinical trial." *Phytomedicine* 44 (2018): 39-44.