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A STUDY TO COMPARE THE CHANGES ON HAEMATOLOGICAL PARAMETERS IN OBESE MALE AND FEMALE SUBJECTS WITH AND WITHOUT INSULIN RESISTANCE

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Abstract

Background: Insulin resistance is an important component of metabolic syndrome. Insulin resistance is a prominent feature of noninsulin- dependent diabetes mellitus (type 2 diabetes mellitus) and is also associated with other conditions such as obesity, polycystic ovarian syndrome. Aim: The present study was planned to study the relationship between insulin resistance and haematological parameters in obese population. Materials and Methods: 50 obese subjects with age group of 30 to 50 years of both the sex and they are grouped into 33 obese subjects with insulin resistance and 17 obese subjects without insulin resistance. In all the subjects we have measured height and weight, and calculated body mass index. We have also collected fasting blood samples and measured fasting plasma glucose and fasting plasma insulin. Insulin resistance in the subjects was calculated by homeostasis model assessment index (HOMA-IR) and haematological parameters such as red blood cell counts, haemoglobin concentration, haematocrit value, total leucocyte count, platelet count and fibrinogen level estimated in all the subjects. Result & Conclusion: The means are compared using student's 't' test and proportion compared using chi-sqare test. We found that the incidence of insulin resistance in obese subjects was 66%. In obese subjects, the occurrence of insulin resistance was more in females compared to males, though not significant. The red blood cell count (p=0.001), haemoglobin concentration (p=0.004) and haematocrit values (p=0.002) were significantly increased in obese subjects with insulin resistance, when compared to obese subjects without insulin resistance. The changes in total leucocyte count (p=0.673), platelet count (p=0.541) and fibrinogen level (p=0.759) were not statistically significant and we also observed that in obese subjects with insulin resistance group, increase in platelet count was statistically significant in females, and increase in total leucocyte count was statistically significant in males.

INTRODUCTION

Insulin resistance is a decreased biological response to normal levels of circulating insulin.^[1] Insulin resistance is related with genetic susceptibility and obesity. Both obesity and insulin resistance may lead to non-insulin dependent diabetes mellitus.^[2] Insulin resistance is a prominent feature of noninsulin- dependent diabetes mellitus (type 2 diabetes mellitus) and is also associated with other conditions such as obesity,^[3] polycystic ovarian syndrome.^[4] Some researchers also believe that there may be link between insulin resistance and some forms of cancer.^[5] A substantial fraction of hypertensive population also have insulin resistance.^[6] Patients suffering from acanthosis nigricans and persons with insulin receptor antibodies also develop insulin resistance.^[7] It is seen that increase in red blood cell count haemoglobin content and haematocrit values are important predictors of acute cardiovascular events like myocardial infarction/unstable angina.^[8] Increased white blood cell and platelet counts and increased fibrinogen levels are associated with increased risk of atherosclerosis and cardiovascular diseases.^[9,10] Insulin resistance is also associated with development of number of alterations in biochemical parameters associated with metabolic syndrome like increase in plasma triglycerides, hyperuricemia, decreased high density lipoprotein and higher circulating level of plasminogen activator inhibitor1. Hypertension is also a component of metabolic syndrome.[11,12] In some studies it is seen insulin that resistance/hyperinsulinemia alone is an important predictor of ischemic heart disease.^[13]

MATERIALS AND METHODS

After the institutional ethics committee approved our study protocol, We have conducted a crosssectional study on 50 Subjects with age group 30 to 50 years of both the sex and they are grouped into 33 obese subjects with insulin resistance and 17 obese subjects without insulin resistance were chosen for the study. Informed consent was taken from all the subjects. In all the subjects body mass index (BMI) was calculated by measuring weight and height of subjects (Quetelet's index) and fasting plasma insulin and fasting plasma glucose levels were estimated and HOMA-IR was calculated by using the formula.

 $(Glucose \ concentration \ in \ mmol/l=glucose \ concentration \ (mg/dl) \ x0.055)$

Inclusion and Exclusion Criteria: The case group: Subjects with body mass index \geq 30 are categorized as obese and Presence of insulin Resistance as assessed by HOMA-IR were considered as the case group for the present study. Those with a History of hypertension, pulmonary, hepatic, immunological, haematological and malignant diseases were excluded from the present study.

Control group: Subjects with body mass index >30 were considered as the control group for the present study. Those with a History of hypertension, Diabetes Mellitus, Presence of insulin Resistance as assessed by HOMA-IR were excluded from the present study.

In all the subjects (Test group+ Control group) following haematological parameters were assessed.

- 1. Estimation of haemoglobin, Red Blood Cell count, Haematocrit value, Total Leucocyte count and platelet count Blood sample was collected from ante cubital vein under aseptic condition in E.D.T.A. vial for above mentioned parameters were estimated by Beckman Coulter's automatic analyzer.
- Plasma Fibrinogen Blood sample was collected under aseptic precautions. 9 parts of freshly collected blood was mixed with 1 part of trisodium citrate, (3.2%). Sample was centrifuged immediately for 15 minutes at 1500-3000 rpm. Plasma was transferred into a clean test tube and measured by Quantia – Fibrinogen is a turbidimetric immunoassay.

RESULTS

Out of 33 obese subjects with insulin resistance 15 subjects (45.5%) were males and 18 subjects were females (54.5%).

Females had higher incidence of insulin resistance than males but the difference was statistically insignificant (p>0.05).

Table 1: Occurrence of insulin resistance in obese males and females							
	Sex	Total					
	Male	Female					
Cases without IR*	10 (58.8%)	07 (41.2%)	17				
Cases with IR	15 (45.5%)	18 (54.5%)	33				

Table 2: Hb, RBC, PCV, TLC, Platelets and Fibrinogen levels in obese subjects with IR (IR) and obese subjects without -IR (IS)

Name of the	Hb	RBC	PCV	TLC	Platelets	Fibrinogen
Group						Level
IS(n=17)	13.28 <u>+</u> 1.23	4.82±0.41	39.03 <u>+</u> 3.57	8788 <u>+</u> 870.9	2894 <u>+</u> 5889	2.77 <u>±</u> 0.59
IR(n=33)	14.08±0.66	5.17±0.28	41.55±1.87	8897 <u>+</u> 849.8	2782±6197	2.84±0.70
P - Value	.004	.001	.002	.673	.541	.759

Table 3: Hb, RBC, PCV, TLC, Platelts and Fibrinogen level in Male and Female obese subjects with IR (Insulin resistance)

Sex	Hb	RBC	PCV	TLC	Platelets	Fibrinogen
Males	14.24±0.77	5.14 <u>+</u> 0.32	41.67 <u>+</u> 2.12	9266 <u>+</u> 942.3	2515±7323	2.75±0.62
Females	13.94 <u>+</u> 0.53	5.19 <u>±</u> 0.26	41.46 <u>±</u> 1.70	8588 <u>+</u> 637.9	3004±4074	2.91±0.77
P -Value	0.195	0.620	0.753	0.020	0.021	0.54

Red blood cell count (p=0.001), haemoglobin concentration (p=0.004) and haematocrit values (p=0.002) were significantly increased in obese subjects with insulin resistance, when compared to obese subjects without insulin resistance. The changes in total leucocyte count (p=0.673), platelet count (p=0.541) and fibrinogen level (p=0.759) were not statistically significant. [Table 2]

There was no significant difference in haematological parameters such as red blood cell (p=0.620), haemoglobin concentration count (p=0.195), haematocrit value (p=0.753) and fibrinogen levels (0.548), between males and females in obese insulin resistant subjects. The total leucocyte counts was significantly increased (p=0.020) in males and platelet count was significantly increased in females (p=0.021). [Table 3]

DISCUSSION

Obesity is a worldwide problem which is closely associated with insulin resistance. Adipose tissue release adipocytokines which seem to produce insulin resistance.^[2,3] This study to investigate the association of insulin resistance and haematological parameters in obese people, as obesity is closely associated with insulin resistance. Insulin resistance is a part of metabolic syndrome and it also has a role in the pathogenesis of type 2 diabetes mellitus.

In our study It has been observed that, in the 50 cases (obese), 33 subjects (66%) were having insulin resistance and rest 17(34%) were not having insulin resistance. Out of 33 obese subjects with insulin resistance, 18 subjects (54.5%) were females and 15 were males (45.5%). So, we have observed that the, occurrence of insulin resistance was more in females, but it was not statistically significant.

We compared the haematological parameters between obese subjects with insulin resistance and without insulin resistance. We found that red blood cell count (p=0.001), haemoglobin concentration (p=0.004) and haematocrit values (p=0.002) were significantly increased in obese subjects with insulin resistance, when compared to obese subjects without insulin resistance. These values were statistically significant (p<0.05). The changes in total leucocyte count (p=0.673), platelet count (p=0.541) and fibrinogen level (p=0.759) were not statistically significant.

Various cytokines and growth factors play a role in regulation of erythropoiesis. Among these factors erythropoietin is required for differentiation and development of erythrocyte progenitors.^[18] Insulin has a synergistic effect together with erythropoietin in stimulating the proliferation of erythroid colony.^[19,20] In previous studies it was found that, physiological concentration of insulin, directly stimulates the proliferation of late erythroid progenitor in a culture of murine fetal liver.^[15] In other studies it was found that insulin promotes growth in both human bone marrow and circulating erythroid progenitor cells in vitro.^[14,15,16,17] The stimulatory effect of human insulin on human bone marrow CFU-E and BFU-E and the relation between insulin and erythropoietin has been proven.^[16,17,21] In these reports, it was postulated that insulin receptor itself might play a role in erythrocyte proliferation. Insulin receptor has been detected in various stages of human erythrocyte development.^[16] Therefore, it was also assumed that insulin affects all stages of erythropoiesis.

In our study, there was no significant change in total leucocyte count between obese subjects with insulin resistance and obese subjects without insulin resistance. Any change seen in total leucocyte count might be because of obesity. There are many studies, which show that, some cytokines are generated in obesity, which seem to have a role in insulin resistance. There are also some studies, which show that cytokines released from adipose tissue have a proliferatory action on white blood cell.^[22]

In our study, there was no significant change in platelet count and fibrinogen between obese subjects with insulin resistance and obese subjects without insulin resistance.

We also compared changes in haematological parameters between obese male and female subjects with insulin resistance. It was observed that total leucocyte counts was significantly increased (p=0.020) in males and platelet count was significantly increased in females (p=0.021). There was no significant difference in other haematological parameters such as red blood cell count (p=0.620), haemoglobin concentration (p=0.195), haematocrit value (p=0.753) and fibrinogen levels (0.548), between males and females in obese insulin resistant subjects.

CONCLUSION

In the present study it can be concluded that the incidence of insulin resistance in obese subjects was 66%. In obese subjects, the occurrence of insulin resistance was more in females compared to males, though not significant. There was statistically significant increase in red blood cell count, haemoglobin concentration and haematocrit values in obese subjects with insulin resistance than obese subjects without insulin resistance. In obese subjects with insulin resistance in platelet count was statistically significant in females, and increase in total leucocyte count was statistically significant in males.

REFERENCES

 Wondmkun YT. Obesity, Insulin Resistance, and Type 2 Diabetes: Associations and Therapeutic Implications. Diabetes Metab Syndr Obes. 2020;13:3611-3616. doi: 10.2147/DMSO.S275898.

- Al-Goblan AS, Al-Alfi MA, Khan MZ. Mechanism linking diabetes mellitus and obesity. Diabetes Metab Syndr Obes. 2014;7:587-91. doi: 10.2147/DMSO.S67400.
- Esteve E, Ricart W, Fernández-Real JM. Adipocytokines and insulin resistance: the possible role of lipocalin-2, retinol binding protein-4, and adiponectin. Diabetes Care. 2009;32 Suppl 2(Suppl 2):S362-7. doi: 10.2337/dc09-S340.
- Park JS, Kim CS, Nam JY, Kim DM, Jo MH, Park J, et al. Characteristics of type 2 diabetes in terms of insulin resistance in Korea. Yonsei Med J. 2005;46(4):484-90. doi: 10.3349/ymj.2005.46.4.484.
- Orgel E, Mittelman SD. The links between insulin resistance, diabetes, and cancer. Curr Diab Rep. 2013;13(2):213-22. doi: 10.1007/s11892-012-0356-6.
- Zhou MS, Wang A, Yu H. Link between insulin resistance and hypertension: What is the evidence from evolutionary biology? Diabetol Metab Syndr. 2014 Jan 31;6(1):12. doi: 10.1186/1758-5996-6-12. PMID: 24485020; PMCID: PMC3996172.
- Phiske MM. An approach to acanthosis nigricans. Indian Dermatol Online J. 2014 Jul;5(3):239-49. doi: 10.4103/2229-5178.137765. PMID: 25165638; PMCID: PMC4144206.
- Kobayashi T, Miyoshi Y, Yamaoka K, Yano E. Relationship between Hematological Parameters and Incidence of Ischemic Heart Diseases among Japanese White-Collar Male Workers. J Occup Health. 2001; 43: 85–89.
- Zakai NA, Katz R, Jenny NS, Psaty BM, Reiner AP, Schwartz SM, Cushman M. Inflammation and hemostasis biomarkers and cardiovascular risk in the elderly: the Cardiovascular Health Study. J Thromb Haemost. 2007;5(6):1128-35. doi: 10.1111/j.1538-7836.2007.02528.x.
- Lowe GD. Blood viscosity, lipoproteins, and cardiovascular risk. Circulation. 1992;85(6):2329-31. doi: 10.1161/01.cir.85.6.2329.
- Reaven GM. Insulin resistance/compensatory hyperinsulinemia, essential hypertension, and cardiovascular disease. J Clin Endocrinol Metab. 2003;88(6):2399-403. doi: 10.1210/jc.2003-030087.
- Petrie JR, Guzik TJ, Touyz RM. Diabetes, Hypertension, and Cardiovascular Disease: Clinical Insights and Vascular Mechanisms. Can J Cardiol. 2018;34(5):575-584. doi: 10.1016/j.cjca.2017.12.005.
- Després JP, Lamarche B, Mauriège P, Cantin B, Dagenais GR, Moorjani S, Lupien PJ. Hyperinsulinemia as an independent risk factor for ischemic heart disease. N Engl J

Med. 1996;334(15):952-7. 10.1056/NEJM199604113341504.

- 14. Bersch N, Groopman JE, Golde DW. Natural and biosynthetic insulin stimulates the growth of human erythroid progenitors in vitro. J Clin Endocrinol Metab. 1982;55(6):1209-11. doi: 10.1210/jcem-55-6-1209.
- Kurtz A, Jelkmann W, Bauer C. Insulin stimulates erythroid colony formation independently of erythropoietin. Br J Haematol. 1983;53(2):311-6. doi: 10.1111/j.1365-2141.1983.tb02025.x.
- Aoki I, Taniyama M, Toyama K, Homori M, Ishikawa K. Stimulatory effect of human insulin on erythroid progenitors (CFU-E and BFU-E) in human CD34+ separated bone marrow cells and the relationship between insulin and erythropoietin. Stem Cells. 1994;12(3):329-38. doi: 10.1002/stem.5530120309.
- Ratajczak J, Zhang Q, Pertusini E, Wojczyk BS, Wasik MA, Ratajczak MZ. The role of insulin (INS) and insulin-like growth factor-I (IGF-I) in regulating human erythropoiesis. Studies in vitro under serum-free conditions--comparison to other cytokines and growth factors. Leukemia. 1998;12(3):371-81. doi: 10.1038/sj.leu.2400927.
- Wu H, Klingmüller U, Acurio A, Hsiao JG, Lodish HF. Functional interaction of erythropoietin and stem cell factor receptors is essential for erythroid colony formation. Proc Natl Acad Sci U S A. 1997;94(5):1806-10. doi: 10.1073/pnas.94.5.1806.
- Akahane K, Tojo A, Urabe A, Takaku F. Pure erythropoietic colony and burst formations in serum-free culture and their enhancement by insulin-like growth factor I. Exp Hematol. 1987;15(7):797-802.
- Muta K, Krantz SB, Bondurant MC, Wickrema A. Distinct roles of erythropoietin, insulin-like growth factor I, and stem cell factor in the development of erythroid progenitor cells. J Clin Invest. 1994;94(1):34-43. doi: 10.1172/JCI117327.
- Sawada K, Krantz SB, Dessypris EN, Koury ST, Sawyer ST. Human colony-forming units-erythroid do not require accessory cells, but do require direct interaction with insulinlike growth factor I and/or insulin for erythroid development. J Clin Invest. 1989;83(5):1701-9. doi: 10.1172/JCI114070.
- Patchen ML, MacVittie TJ, Williams JL, Schwartz GN, Souza LM. Administration of interleukin-6 stimulates multilineage hematopoiesis and accelerates recovery from radiation-induced hematopoietic depression. Blood. 1991;77(3):472-80.

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