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Research Article
Relationship between a Pro-thrombotic State and Anthropometric Parameters in Young Saudi Females: A Preliminary Study

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Abstract

Background and Objective: A global epidemic increase in obesity prevalence has been observed in most of the countries. This phenomenon is an emerging health problem that is associated with increasing prevalence of obesity-related co-morbidities. This study sought to investigate whether a pro-thrombotic state is related to anthropometric parameters in a student population. **Materials and Methods:** Forty young adult females aged 20-30 years (mean age: 21.0±3.04 years) were included in the study. Participants were sub-divided into three groups: The lean (n = 12) group, which included individuals with a body mass index (BMI) between 18 and 24.9 kg m^{-2}, the overweight/obese (n = 16) group, which included individuals with a BMI $\geq$25 kg m^{-2} and the obese diabetic group (n = 16), which included individuals with a BMI $\geq$30 kg m^{-2} and diabetes mellitus (DM). Anthropometric measurements, including BMI, waist circumference (WC), hip circumference (HC) and the waist/hip (W/H) ratio were determined and calculated in this study and hemostatic metrics were assessed. **Results:** The mean prothrombin times (PTs) were 11.9±0.9, 11.2±0.4 and 11.7±0.9 sec in the lean, overweight/obese and obese diabetic groups, respectively. The examined groups exhibited a negative correlation between PT and BMI (r = -0.4, p = 0.06) and a positive correlation between PT and W/H ratio (r = 0.5, p = 0.04). No other significant correlations between BMI or W/H ratio and other hematological indices were observed. **Conclusion:** Obesity could be associated with hemostatic changes that favor the development of thrombosis, this possibility highlights the need for the implementation of preventative measures.

Key words: Obesity, body mass index, waist/hip ratio, prothrombin time, partial thromboplastin time

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

According to the World Health Organization (WHO), approximately seven hundred million adults were obese in 2015[1]. Several studies have indicated that individuals from younger generations are at greater risk of being overweight and obese than their parents[2].

In Saudi Arabia, obesity is regarded as a major health problem. Its prevalence has increased to epidemic levels among male adults and to a greater extent among female adults. Many studies have indicated that for Saudis between 14 and 70 years of age, approximately 13% of males and 20% of females are obese[3]. The later authors found that these values are higher than those reported for American, British, Australian and Italian populations.

Obesity can be defined as a body mass index (BMI) "of 30 kg divided by height in meters squared (kg m^{-2}) or above"[4]. Obese individuals have elevated risks of developing diabetes, osteoarthritis and many types of cancers, including breast cancer. Dyslipidemia and hypertension are additional complications associated with obesity[5].

Central obesity is part of a phenotypic picture that involves excess intra-abdominal adipose tissue and decreased subcutaneous adipose tissue expansion and ectopic triglyceride storage in various organs (mainly the liver, pancreas and muscles)[6]. The combination of metabolic alterations that are closely linked to this phenotype is known as metabolic syndrome. It has been reported that obesity and insulin resistance may be associated with alterations in hemostasis that cause a pro-thrombotic state[7]. This state could favor the development of atherothrombosis and deep vein thrombosis. Therefore, this study sought to discover relationships between a pro-thrombotic state and various anthropometric parameters, including BMI, in a population of female Saudi students to identify subjects who are likely to develop obesity-related co-morbidities and to thereby promote the use of additional preventative measures.

MATERIALS AND METHODS

Subjects: The starting sample for this descriptive study was 69 randomly selected female undergraduate students in the Faculty of Medicine and Nursing of Northern Border University, although the group of individuals who consented to complete this study by providing a blood sample were consisted of 40 students. The enrolled participants were 21.0±3.04 years of age and included 32 (80%) nursing students (who were participating in either a regular or bridging program) and 8 (20%) medical students recruited from the Research Faculty from December, 14-25, 2016.

All subjects completed a questionnaire that included assessments of dietary history and physical activity and were subjected to an assessment of anthropometric variables by the same researcher. Body weight in light clothing and height without shoes were measured to the nearest 0.1 kg and 0.1 cm, respectively. A digital electronic scale was used for weight determination and a standard steel strip stadiometer was used for height measurement. BMI values were calculated, overweight was defined as "a BMI$\geq$25 kg m^{-2} and obesity was defined as a BMI$\geq$30 kg m^{-2}" [8]. Flexible anthropometric tape was used to measure waist circumference (WC), which was assessed "at the midway point between the lower rib margin and the superior iliac crest in a horizontal plane" in accordance with the standard approach in the literature and hip circumference (HC), which was measured "at the maximal gluteal protrusion or at the most prominent area of the buttocks at the level of the symphysis pubis in a horizontal plane"[9]. Waist/hip ratio (WHR) was calculated by dividing WC by HC and abdominal obesity was diagnosed if WHR>0.8. WHtR was calculated as "the ratio of waist (cm) and height (cm)". Abdominal obesity was defined using a WHtR cut-off of 0.5[10]. Participants were subdivided into three groups: The lean group, which included subjects with a BMI between 18 and 24.9 kg m^{-2}, the overweight/obese group, which included subjects with a BMI$\geq$25 kg m^{-2} and the obese diabetic group, which included subjects with a BMI$\geq$30 kg m^{-2} and diabetes mellitus (DM). Subjects in the control and overweight/obese groups were not participating in a diet program, taking medications or performing any physical activity that would affect the study results. A history of pregnancy for married subjects and a history of any hypercoagulable disorders or related drug use would influence the study results and subjects with either of these characteristics were, therefore, excluded. This study was conducted in accordance with guidelines in the Declaration of Helsinki and was approved by the relevant local research ethics committee. Informed consent was obtained from all participants.

Laboratory analysis

Sample collection and preparation: For all subjects, a 4 mL blood sample was drawn under sterile conditions and divided into 2 portions, 2 mL of this sample was placed in a clean tube containing sodium citrate (200 µL of 3.8%) anticoagulant and the remaining 2 mL was mixed with one drop of EDTA and used as whole blood. The citrated blood tubes were centrifuged at 2500 rpm for 20 min (Jouan CR422 centrifuge, France) and the plasma was separated into clean Eppendorf tubes marked with the date and each subject's specific ID number. Part of the plasma was used to immediately

measure prothrombin time (PT), international normalized ratio (INR) and partial thromboplastin time (PTT).

Complete blood count (CBC) test: Hemoglobin (Hb), White Blood Cell (WBC) count, Platelets (PLT), Red Blood Cell count (RBC), Hematocrit (Hct), Mean Corpuscular Volume (MCV), Mean Corpuscular Hb (MCH) and RBC distribution width were estimated using a fully automated hematological analyzer (Sysmex XT 2000i, Germany) in accordance with standard methods[11].

PT and PTT tests: PT and PTT were measured as described by Poller *et al.*[12] using an automated chemistry analyzer (Sysmex CA-1500, Germany).

Statistical analysis: General statistical analyses were performed using TexaSoft WINKS 4.651 (Texas, USA). Data were expressed as means±standard deviation (SD). Frequencies of categorical variables were expressed as percentages. Pearson correlation coefficients (r) were used to determine relationships between various anthropometric parameters, including BMI and hematological and prothrombotic status for the studied groups. Measurements of the strength of the linear relationship between two variables were defined. The p-values, which refer to "the probability of getting the observed difference in the sample purely by chance from a population", were also calculated. A calculated p-value greater than 0.05 was indicating that the results in question could have occurred by chance.

RESULTS

Clinical, anthropometric and laboratory data for the study population: A total of 40 female participants were enrolled in this study, including 12 students in the lean group, 16 students in the overweight/obese group and 16 students in the overweight/obese with DM group. Descriptive data for the study sub-groups are presented in Table 1. Hematological parameters and certain hemostatic parameters for the study subjects are summarized in Table 2 and 3, respectively.

Table 1: Clinical and anthropometric characteristics of the study subjects

Parameters	Control (n = 16)	Overweight/obese (n = 12)	Overweight/obese diabetic (n = 12)
Age (years)	19.9±0.4	22.5±6.1	20.0±0.0
FH of obesity (+/-)*	2/16	6/12	8/12
Weight (kg)	55.6±9.4	70.7±13.0	67.7±9.9
Height (m)	1.6±5.3	1.6±2.9	1.6±4.8
Body mass index, BMI (kg m^{-2})	22.0±2.8	28.6±5.6	27.7±3.9
Waist circumference (cm)	68.1±20.6	86.5±13.8	78.2±10.4
Hip circumference (cm)	101.4±40.8	113.8±10.3	111.5±7.5
Waist/hip ratio (WHR)	0.7±0.1	0.8±0.1	0.7±0.1
Waist/height ratio (WHtR)	0.4±0.1	0.6±0.1	0.5±0.1

FH: Family history, values are expressed as Mean±SD or as numbers, *frequencies (percentage)

Table 2: Hematological parameters of the study subjects

Items	Normal range	Control (n = 16)	Overweight/obese (n = 12)	Overweight/obese Diabetic (n = 12)
Hb (g dL^{-1})	11.5-15.5*	12.1±0.9	11.9±1.1	13.3±0.9
Hematocrit (%)	36-48*	38.8±1.9	37.7±1.5	41.1±2.0
Red cell count (×10^{12} L^{-1})	3.9-5.6*	4.7±0.3	4.8±0.5	4.7±0.3
Mean cell volume (MCV) (fl)	80-95	82.9±4.8	80.4±9.6	86.9±3.7
Mean cell hemoglobin (MCH) (pg)	27-34	26.0±2.4	25.3±4.8	28.1±1.7
Mean cell hemoglobin concentration (g dL^{-1})	30-35	31.3±1.4	31.3±2.2	32.3±1.1
WBCs (×10^{3} μL^{-1})	8.4-1.9	8.3±1.9	7.2±2.4	8.2±1.2

Hb: Haemoglobin, WBCs: White blood cells. *Normal range for female only. Other parameters for males and females

Table 3: Some of the hemostatic parameters of the study subjects

Items	Normal range	Control (n = 16)	Overweight/obese (n = 12)	Overweight/obese diabetic (n = 12)
Platelets (×10^{3} μL^{-1})	150-400	297.5±107.5	313.3±74.6	290.0±63.3
PT (sec)	10-14	11.9±0.9	11.2±0.4	11.7±0.9
INR (%)	0.8-1.2	1.0±0.9	1.0±0.3	1.1±0.2
PTT (sec)	30-40	30.9±4.4	29.1±3.0	31.4±2.5

PT: Prothrombin time, INR: International normalized ratio, PTT: Partial thromboplastin time

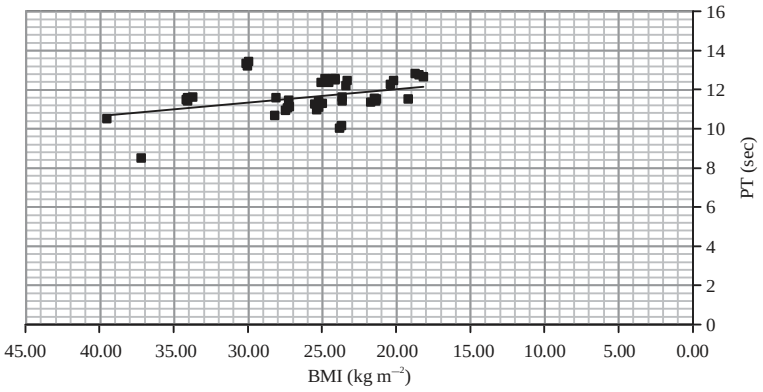

Fig. 1: Correlation between prothrombin time (in sec) and body mass index (BMI) for the study subjects
Correlation coefficient (r) = -0.4, p = 0.05

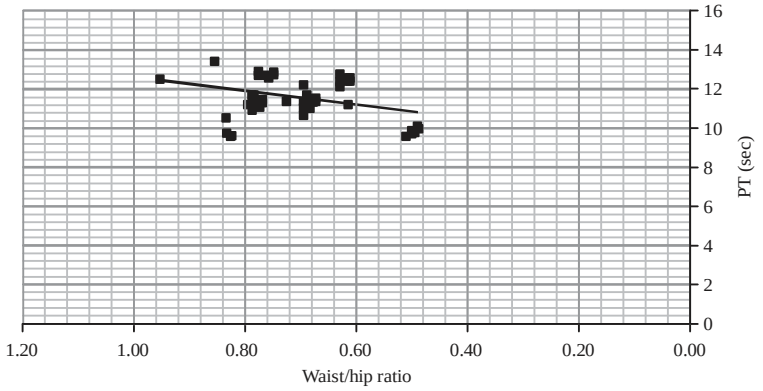

Fig. 2: Correlation between prothrombin time (in sec) and waist/hip ratio for the study subjects
Correlation coefficient (r) = 0.5, p = 0.04

Hematological, hemostatic and anthropometric parameters: There was a clear, significant correlation between BMI and WHtR ($r = 0.77$, $p<0.001$) (data not shown). The examined groups exhibited a negative correlation between PT and BMI ($r = -0.4$, $p = 0.06$ (borderline significance), Fig. 1) and a positive correlation between PT and waist/hip (W/H) ratio ($r = 0.5$, $p = 0.04$, Fig. 2). There were no other significant correlations observed between either BMI or W/H ratio and other hematological indices.

DISCUSSION

The present study is the first investigation to assess the relationship of BMI and anthropometric parameters with a pro-thrombotic state in a female Saudi population in the researchers' geographic region. This cohort study has shown that BMI and waist/hip ratio could have an impact on one of the the pro-thrombotic indices in term of PT.

Increasing adipose tissue is a hallmark of obesity that involves "increased fat-cell number (hyperplasia) and increased fat-cell size"[13]. At present, obesity is extremely common in the global population and may be replacing infectious diseases and under-nutrition as a contributor to illness. It currently affects 30 and 35.5% of the adult population in the United States and Saudi Arabia, respectively[14]. This high prevalence of obesity among Saudi females may be partially attributable to limit physical activity as a consequence of the popularity of housemaids, exercise facility constraints for girls and women in Saudi Arabia due to local social and cultural restrictions and limited general population awareness regarding obesity-associated health risks has been documented both locally and in other areas of Saudi Arabia[8,15].

The present study showed that female obesity is linked to shorter PT (with a moderate negative correlation), this finding is consistent with the results obtained by

Stoppa-Vaucher *et al.*[16], who found that "obesity is linked to an increased endogenous thrombin potential, a shortening of PT and an increase of fibrinogen and D-dimer levels compared with lean subjects".

In addition, Kornblith *et al.*[17] recently found that during longitudinal follow-up, obese trauma patients exhibited a hypercoagulable state compared with the state of similarly injured normal-weight counterparts. These researchers reported that BMI could be an independent predictor for the development of thromboembolic complications, with the probability of such complications after injury increased by almost 85% for every increase of 5 kg m^{-2} in BMI.

As reviewed previously, the pro-thrombotic tendency associated with obesity is the result of "a group of alterations involving intrinsic and extrinsic coagulation pathways, platelet function and fibrinolysis", each of which cooperates to favor thrombotic processes. Furthermore, in obese individuals, an increased level of circulating monocyte chemoattractant protein 1 (MPS 1), which acts as a pro-thrombotic factor that increases the delivery of pro-thrombotic factors and other proteins that participate in hemostatic mechanisms, is clearly involved in coagulation dysfunction and enhanced atherothrombotic risk[16]. In addition, obesity-related hypercoagulability can be partially attributed to various other factors, including enhanced thrombin generation due to excess tissue factor release from adipose tissue[18,19], leptin- and adiponectin-induced thrombogenic modulation of platelet aggregation[18,20,21], the excessive release of plasminogen activator inhibitor-1 (PAI-1) from adipose tissues, which decreases fibrinolysis[22] and the possible increased synthesis of coagulation factors (including fibrinogen) due to obesity-induced alterations in liver metabolism[17].

Although certain study data were statistically significant, the researchers acknowledge that the findings presented here are preliminary because of the small number of subjects and that this study requires confirmation in a separate, larger cohort that includes subjects of both genders. However, as stated by Montilla *et al.*[23], "since PT and PTT are relatively inexpensive tests, it might allow the identification of a subset of patients at major risk of thromboembolic complications who deserve more aggressive antithrombotic preventive measures". Moreover, a broad epidemiological study is needed to examine the possible associations suggested by the current findings, with the objective of increasing the number of parameters that can be used to assess pro-thrombotic states. The implementation of health education programs, including programs focused on dietary issues and/or lifestyle changes, is highly recommended. Follow-up for the high-risk group identified in this study is also recommended.

CONCLUSION

It is concluded that obesity could be associated with hemostatic changes that favor the development of thrombosis, this possibility highlights the need for the implementation of preventative measures.

SIGNIFICANCE STATEMENT

This study discovers the possible association of obesity with hemostatic changes that favor the development of thrombosis. This study will help the researchers to uncover the critical area of pro-thrombotic state associated with obesity that many researchers were not able to explore. Thus, a new strategy of preventive measures, especially at the local area, may be arrived at.

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