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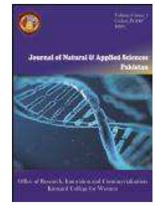

DYSLIPIDEMIA AS A RISK FACTOR FOR DEVELOPING HYPERTENSION AND CARDIOVASCULAR DISEASE IN FEMALES OF REPRODUCTIVE AGE

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Abstract

Obesity is the foremost contributor to the global load of chronic disability and disease acting as risk factor for diabetes, cardiovascular disease, certain types of cancer, stroke and hypertension which ultimately lead to premature death. The current research was conducted to estimate the correlation of lipid profile in all BMI categories (underweight, normal, overweight & obese) with development of hypertension and cardiovascular disease (CVD) in females of reproductive age. Hormonal changes during reproductive age of the females affect their metabolism in ways that increase their risk of developing cardiovascular diseases (e.g. arthrosclerosis). It has been found that women are 4-8 times prone to develop CVD than any other disease thus making it the leading cause of death in females of this age group. A total number of 80 females aged between 25-45 years categorized according to BMI categories (underweight, normal, overweight and obese) were recruited for the current study. Their anthropometric and demographic information was collected using a carefully designed questionnaire while their lipid profile was estimated using corresponding kits by Human® Germany. Lipid profile estimation revealed that obese individuals had very high levels of cholesterol and triglycerides, as much as 300mg/dL and 281mg/dL, respectively, significantly higher than the described normal range. Obese individuals were also found to have very low concentration of HDL, i.e. below 39mg/dL. The statistical analysis using SPSS analysis indicates a significant correlation (p=0.000) between BMI and all the parameters of lipid profile i.e. cholesterol, triglycerides, HDL and LDL. A direct relationship between dyslipidemia and hypertension has also been a significant finding of the current study, corresponding to past reports. The overall results indicated an increasing trend towards hypertension and cardiovascular disease with the increasing BMI and more importantly due to impaired lipid profile i.e. dyslipidemia. The present study point towards a strong need to create awareness among masses to not only monitor but maintain their lipid profiles and optimum BMI to avoid being at risk of hypertension and eventually various fatal cardiovascular diseases.

1. Introduction

Obesity is technically defined as the abnormal accumulation of $\geq$ 20% of body fat above the individual's ideal weight of body. Main cause of excessive overweight and obesity is the imbalance between energy intake and expenditure. Excess gain in weight, especially when it is associated with increased visceral adiposity is the major cause of high blood pressure or hypertension (Hall, do Carmo, da Silva, Wang, & Hall, 2015; Jiang, Lu, Zong, Ruan, & Liu, 2016). Obesity is related to arterial hypertension characterized by sympathetic nervous system activation and eventual activation of renin-angiotensin system (Segura & Ruilope, 2007). The body mass index (BMI) is a way of characterizing the amount of tissue mass i.e. muscle, fat and bone, in an individual. The BMI can be calculated by dividing the mass of body (kg) by square of height (m^2) of an individual. BMI is categorized into four categories, underweight, normal weight, overweight and obese. According to the World Health Organization, BMI of $\leq$18.5 kg/m^2 is categorized as underweight, normal BMI falls in between the range of 18.5 kg/m^2 to 24.9 kg/m^2, overweight BMI between 25 kg/m^2 to 29.9 kg/m^2 and obese BMI has a value above 30 kg/m^2 (Nuttall, 2015).

Blood pressure is the force by which the heart pumps blood through arteries to all parts of the body. Throughout each heartbeat cycle, the pressure of blood falls and rises. In each cycle the highest pressure held when the heart contracts to pump the blood is called systolic blood pressure (SBP) which can also be felt as a pulse. However, the diastolic pressure (DBP) is the lowest pressure when heart relaxes between beats and refills (Kumalasari, Hilmi, & Priyandoko, 2017).

Obese individuals with high blood pressure also suffer from serious insulin resistance owing to high level of free fatty acid influx as compared to those with normal blood pressure. This insulin resistance in turn leads eventually to changes in the lipid profile (Juliaty, Sari, Daud, & Lisal, 2015). There is thus an obvious relationship between BMI, hypertension and total cholesterol levels (Brown *et al.*, 2000).

Hypertension (HT) is not just a major cause but the most significant factor causing cardiovascular diseases (CVD) worldwide (Leon & Maddox, 2015). Even in the presence of effectual intensive research data and antihypertensive drugs, a lot of patients in clinical practice still suffer from uncontrolled HT (Petrák *et al.,* 2016). In 2010, the National Health Survey of Pakistan (NHSP) measured that HT affects as much as 18% adults with almost 33% adults aged above 45 years. It was also reported that every third person over the age of 40 is becoming increasingly susceptible to a wide range of diseases. It has been noted that 50% of HT patients seek treatment after diagnosis, suggesting only 12.5% of cases being controlled (Saleem, Dua, Hassali, & Shafie, 2010). Lipid profile is the measure of the lipid components of blood, i.e. cholesterol, triglycerides and high and low density lipoproteins. In addition to indigenous production by our body, the diet is also another source of cholesterol. However, if cholesterol exceeds beyond a certain limit, it will consequently get attached with the arterial walls as plaque. This condition is called as atherosclerosis which narrows the arteries or can even cause blockage leading to serious consequences like hypertension and heart diseases (Ozner, 2010, Santos *et al.,* 2016).

The lipoproteins facilitate the transport of cholesterol and triglycerides in the blood. The high density lipoproteins (HDL) also called as good or healthy cholesterol are mostly composed of the proteins with less cholesterol. HDL is also called good cholesterol and should be present in the blood in appropriate amounts for many other bodily mechanisms to functions properly (Eren, Yilmaz, & Aydin, 2012, Daniels, Killinger, Michal, Wright Jr, & Jiang, 2009). Whereas, LDL (low-density lipoproteins) are a type of bad cholesterol who's higher than normal levels can cause cardiovascular diseases. Thus, LDL deposits in blood vessels as opposed to HDL which have a role in clearing (Pencina *et al.*, 2015).

Cardiovascular diseases (CVDs) include heart failure, coronary artery disease, myocardial infarction, atherosclerosis, cardio-myopathy, peripheral artery disease, cardiac arrest and angina pectoris (Wang, Hess, Hiatt, & Goldfine, 2016). It has been found that if proper lifestyle is not adapted and preventive measures are not taken, high lipid profile levels can lead to serious consequences ultimately developing stroke and heart diseases (Heiland, 2018). Hypertension can have familial presentation as well and the chances of having high blood pressure can increase based on race, ethnicity and age (Mannino, Thorn, Swensen, & Holguin, 2008).

2. Methodology

The study group comprised of 80 females in reproductive age (25-45 years) with n=20 for each of the BMI categories i.e. underweight, normal, overweight and obese. The purpose and nature of the study were clearly described to all study participants and a written formulated consent was also obtained from them. The height and weight of all the subjects was measured to estimate the BMI value along with measuring of blood pressure using manual sphygmomanometer. The BMI was calculated using the formula: weight (kg)/height (m^2). A carefully structured questionnaire was used for collection of all their clinical history/information, physical information, work routine, lifestyle and eating habits. The subjects were requested to provide samples after 12 hours of fasting for collection of their blood samples. Venous blood was drawn from them and collected in red cap BD® vacutainers. Blood was then allowed to clot at room temperature for almost 15-30 minutes, followed by centrifugation at 1000-4000rmp. The clot was removed and the supernatant was collected as serum in the sterilized eppendorfs. The serum levels of cholesterol, triglycerides, HDL and were measured by following standard protocol of corresponding kits by Human®, Germany. The lipid profile estimation was done on UV visible spectrophotometer SPECORD® 200 plus (Analytik Jena, Germany). The LDL was calculated using formula: LDL cholesterol (mg/dL) = Total cholesterol-HDL cholesterol-triglycerides/5. The data collected from the serum analysis and anthropometric measurements was evaluated using IBM-SPSS version 25 (2017). Descriptive statistics from SPSS were used for estimating the significance of correlations while the percentage and graphs were plotted using Microsoft Office Excel 2007.

3. Results and Discussions

Upon informed consent of the participants, their anthropometric measurements were taken based on a carefully design questionnaire. Table 1, shows a summary of the measurements taken, the ranges of data obtained as well as their mean values.

Table 1: Anthropometric measurements of study participants.

Serial No:	Parameters		Units	Mean	Range*
1.	Age		years	31.16	18-60
2.	Weight		kg	63.8	37-112
3.	Height		meters	1.57	1.49-1.701
4.	BMI	Underweight	kg/m^2	17.15	14.1-18.5
5.		Normal		21.46	18.15-24.8
		Overweight		27.39	25.6-29.77
		Obese		32.66	29.95-40.28

*ranges observed in data obtained.

While analysing the lipid profile of study participants, a direct relationship was found between increasing BMI and dyslipidemia. The estimation of cholesterol revealed that maximum number of individuals in the obese category had cholesterol above the normal upper limit i.e. 200mg/dL as shown in Figure 1 (a). The results of the second parameter of lipid profile i.e. the triglycerides (TG) showed results contrary to previous findings. A strong association between hyper-triglycerides, abdominal obesity and increased risk of hypertension and cardiovascular disease has been found in many previous studies (Pimenta, Kac, Gazzinelli, Corrêa-Oliveira, & Velásquez-Meléndez, 2008). It was surprising to note that that only very few participant females had serum triglycerides within the normal range in our study, with highest triglyceride levels in overweight women on average [Figure 1 (b)].

HDL (high density lipoproteins) were also analysed in current study and their relationship with increasing obesity was also evaluated in the participants. It was found that majority of individuals who were overweight and obese had lower levels of HDL (<50mg/dL) indicating clear dyslipidemia with higher risk of developing cardiovascular disease as evident in Figure 1 (c). The last lipid profile parameter to be analysed was LDL (low density lipoprotein) and it was found that a significantly higher percentage of individuals (almost 80%) of obese had extremely high levels of LDL. When the results were analysed with respect to BMI categories, it was found that overweight and obese individuals have more concentrations of LDL as compared to normal and underweight [Figure 1 (d)].

The SPSS analysis of the data revealed a direct association of BMI with dyslipidemia. p value=0.000 indicating a strong correlation between dyslipidemia and increasing obesity was found using statistical paired sample T-test. It is valid when the level of significance is 0.05 with confidence level set at 95%. This clearly reflects that not only does dyslipidemia have a direct relationship with obesity (BMI i.e. overweight & obese categories) but it also correlates with higher risk of developing hypertension and cardiovascular disease eventually.

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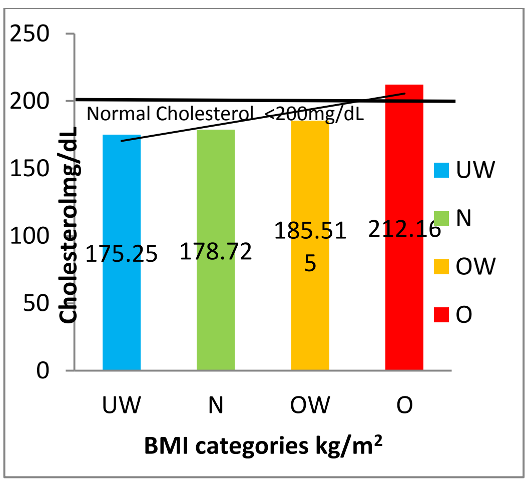

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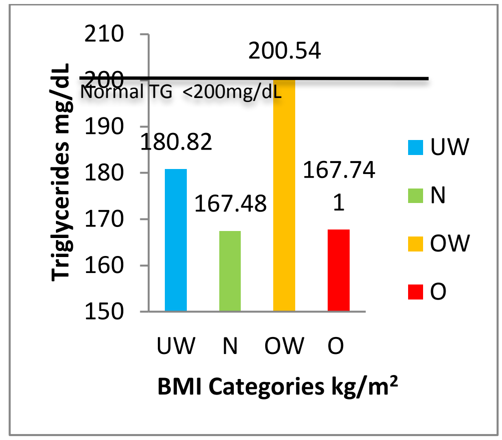

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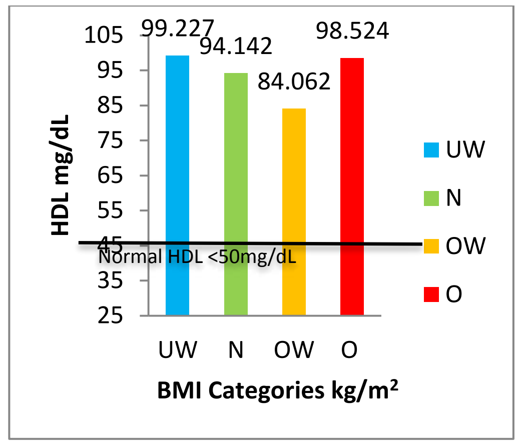

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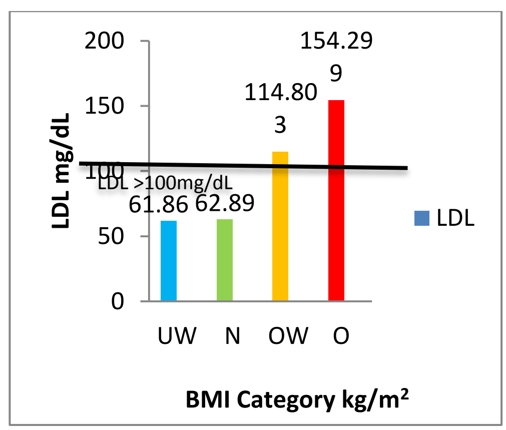


Figure 1: Graphical representation of relationship of BMI with a) cholesterol; b) triglycerides; c) HDL and d) LDL. The coloured bars along the X-axis indicate the average values based on their respective BMI categories [blue for underweight (UW), green for normal (N), orange for overweight (OW) and red for obese (OB)]. The black line across the horizontal axis depicts the normal range.

The 3 categories of blood pressures that were evaluated in this research were *normotensive* (NT) with BP being <120/80 mmHg, *pre-hypertensive* (PH) having systolic BP between 130-139mmHg and diastolic BP within the range of 80-89mmHg respectively. The last category is *hypertensive* (HT) having BP above 140/100mmHg (Stabouli *et al.*, 2009). Whereas it was also found that obese individuals had a very high percentage of hypertensive participants with very little representation of normo- or pre-hypertensive individuals in the obese category. Thus it can be concluded that obesity and hypertension share a direct relationship (Figure 2).

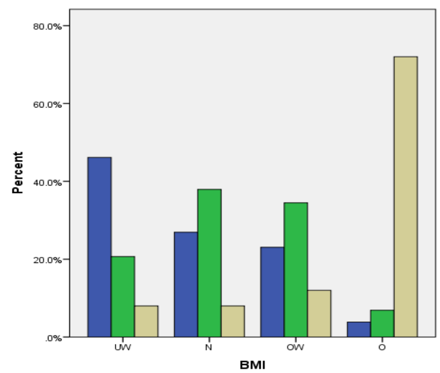
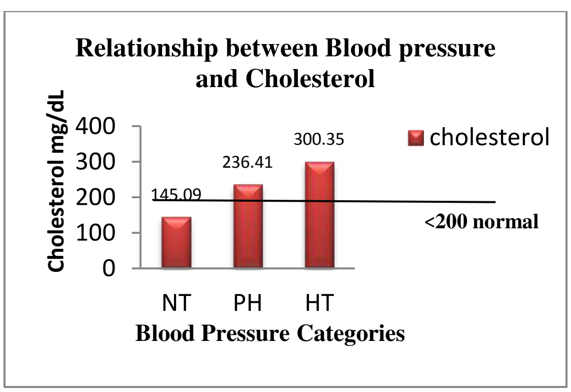


Figure 2: Graphical representation of relationship between BMI and blood pressure categories (Normotensive (NT) represented as blue bars, Pre-hypertensive (PH) as green bars and Hypertensive (HT) as cream bars).



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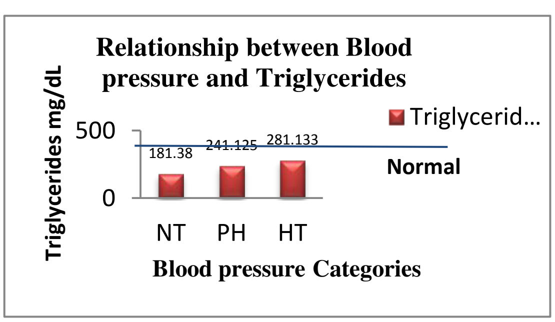

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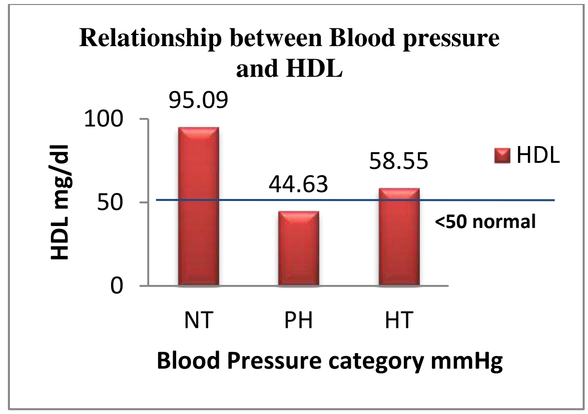

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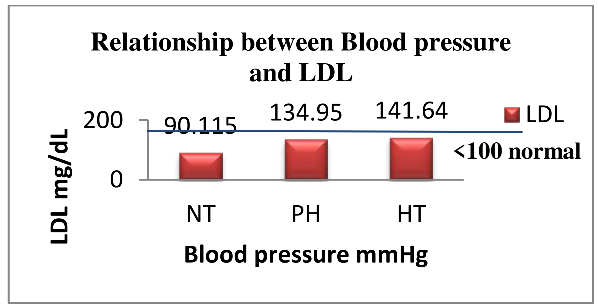
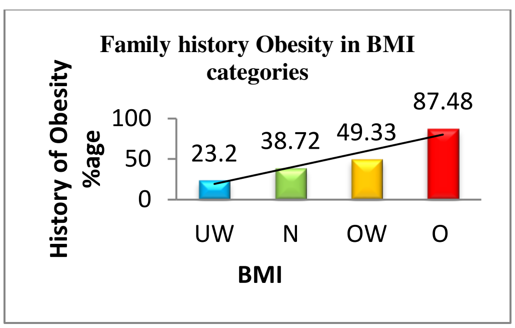


d)

Figure 3: Bar charts representing the relationship between blood pressure categories [normotensive (NT), pre-hypertensive (PH) and hypertensive (HT)] and **a)** cholesterol, **b)** triglycerides, **c)** HDL and **d)** LDL.

The study participant's categorized based on blood pressure were also analysed for their relationship with cholesterol, triglycerides, HDL and LDL. As expected, with the severity of dyslipidemia, an increasing trend towards hypertension was observed. Among normotensive, pre-hypertensive and hypertensive individuals, it was the hypertensive participants that had very high levels of serum cholesterol Figure 3(a). Similar trend was observed with triglycerides and LDL too, Figure 3(b) and (d). However, the relationship between HDL and blood pressure was a little alarming, as the pre-hypertensive individuals rather than hypertensive showed the lowest levels of HDL (Figure 3(c)). The highest HDL levels were observed in the normotensive individuals further strengthening the hypothesis that increased quantity of good cholesterol co-relates with normal blood pressure.

To evaluate the genetic predisposition of obesity, hypertension and risk for cardiovascular disease in females of reproductive age, all participants were inquired about their family history for each of the above disorders. A clear cut positive relationship between family history of obesity, hypertension and cardiovascular diseases was observed with increasing obesity (Figure 4).This an important finding as it corresponds with previous studies showing heritability of these traits between 30 to 70% (Anjum & Khairnar; Bucher *et al.*, 1988; Dupuis *et al.*, 2005; Kraja *et al.*, 2005; Lima-Oliveira, Valentim, & Guidi, 2017; Lin *et al.*, 2005; Luo *et al.*, 2010; Nigam, 2011; Pankow *et al.*, 2001; Rankinen, Sarzynski, Ghosh, & Bouchard, 2015; Retterstol, Eikvar, & Berg, 2003; Santos-Gallego, Ibanez, & Badimon, 2008). A pair-wise co-variation as well as familial clustering between obesity and hypertension was found; these two being CVD risk factors because owing to genetic pleiotropy (Bener *et al.*, 2004; Kannel, D'Agostino, & Cobb, 1996; Thayer, Yamamoto, & Brosschot, 2010; Zalesin, Franklin, Miller, Peterson, & McCullough, 2008).



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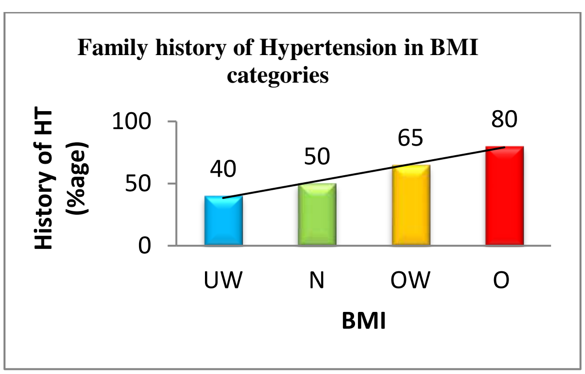

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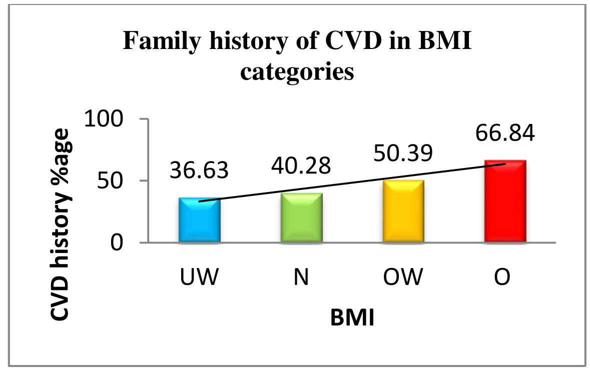

c)

Figure 4: Graphical representation of Family history of **a)** obesity, **b)** hypertension and **c)** cardiovascular diseases (CVD) in various BMI categories [blue for underweight (UW), green for normal (N), orange for overweight (OW) and red for obese (OB)].

4. Conclusion

The present study was designed to evaluate the extent of dyslipidemia in females as their metabolism is at the disposal of changing hormonal levels during reproductive ages. Dyslipidemia has not only been found as the leading factor for causing CVD as it is the leading cause of death in women belonging to this age group. In the current study, we estimated the serum lipid profile in females and its correlation with the development of hypertension and cardiovascular disease during their reproductive years. A significant relationship between lipid profile and obesity has been established via all the lipid profile parameters, i.e. cholesterol, triglycerides, HDL and LDL. From the results discussed here, it is resolved that individuals with dyslipidemia are clearly more susceptible to hypertension and cardiovascular diseases. A very stark co-relation between BMI and hypertension has also been observed here indicating a positive trend towards hypertension with increasing obesity. Lastly, the familial aspect of these traits, i.e. obesity, hypertension and prevalence of cardiovascular diseases has also been found, which is a very significant finding and suggests the need of genetic studies of these traits in Pakistan. Since more than 70% of Pakistani population practices consanguinity (Jafar et al., 2004), a study to understand how these traits are inherited in relation to consanguinity is an important aspect that needs to be looked into.

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