Association of Preeclampsia with Obesity

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ABSTRACT

Objective: The objective of this study was to determine the association of obesity with preeclampsia in the Khyber Pakhtunkhwa (KP) Province of Pakistan.

Methodology: This is a case-control study conducted in Lady Reading Hospital (LRH), Khyber Teaching Hospital (KTH) and Hayatabad Medical Complex (HMC) Peshawar. Forty pregnant females (aged 15-35 years), with a diagnosis of preeclampsia during their third trimester of pregnancy were taken as cases. The basic diagnosis was made on the basis of pregnancy-induced hypertension (systolic 140 mmHg and above, diastolic 90 mmHg and above). For controls, forty pregnant females (aged 15-35 years) who remained normotensive throughout pregnancy and were in their third trimester were taken. BMI was determined using Asian BMI criteria. Tests of normality were performed and the association between obesity and preeclampsia was determined using the Mann Whitney-U test.

Results: The results showed that the distribution of BMI varied among cases and controls, $p<0.001$. Moreover, stats showed, 33 obese among the 40 cases (preeclamptic), that is about 82.5%. And among the 40 controls (normotensives) there were 25 obese, that is, 62.5%.

Conclusions: Hence, it is concluded that preeclampsia is more common among obese women.

To cite this article
[Salman, H., Hamid, N., Zafar, U., Marwat, S. & Khan, M. (2019). Association of Preeclampsia with Obesity. *The Journal of Middle East and North Africa Sciences*, 5(5), 34-37]. (P-ISSN 2412- 9763) - (e-ISSN 2412-8937). www.jomenas.org**. 5**

Keywords: Preeclampsia; Obesity; Pregnancy; Hypertension.

1. Introduction:

Preeclampsia is defined as the new onset of hypertension (>140/90mmHg) and proteinuria (> 0.3 gm per 24 hours) after 20 weeks of gestation (ACOG Committee on Practice Bulletins-Obstetrics, 2001). Preeclampsia is a serious disease which leads to maternal and fetal morbidity and even mortality worldwide (Steegers et al., 2010). It is responsible for approximately 15 million preterm deliveries annually around the world (Vogel et al., 2014). The exact cause for preeclampsia is still not known. One theory is that a number of a different underlying condition like immunological and/or genetic factors alone or in combination with environmental conditions, or some underlying disease leads to defective trophoblastic invasion of spiral arteries within the placenta during the first trimester of pregnancy (Redman & Sargent, 2005).

This causes ischemia in the fetoplacental unit which in turn will send a signal to the mother to increase the placental blood flow by increasing maternal blood pressure. Obesity is believed to be one of the major risks factors for preeclampsia (ACOG Committee on Practice Bulletins-Obstetrics, 2001).

Obesity is becoming a global epidemic (Roberts et al., 2011). The incidence of obesity is increasing at an alarming rate throughout the world (Misra & Khurana, 2008). Various studies suggest that maternal obesity increases the risk of adverse pregnancy outcomes like preeclampsia, hypertensive disorders, gestational diabetes, abortion, preterm babies, fetal malformation, cesarean section, large for dates babies and stillbirths (Yogev & Catalano, 2009). Obesity increases the risk of preeclampsia 2-3 times (Bodnar et al., 2005a). In contrast to other factors for preeclampsia, the importance of obesity is due to its modifiable nature (Sorensen et al., 2003). Weight loss prior to pregnancy in obese and overweight subjects decreases the risk of adverse complications like preeclampsia (Yogev & Catalano, 2009). Preeclampsia increases the risk of

future cardiovascular diseases (Osol & Moore, 2014). In addition, obesity is also an important risk factor for cardiovascular diseases (Roberts et al., 2011). Both these conditions share the same pathophysiological changes like insulin resistance, oxidative stress, endothelial dysfunction, inflammation, adipokines and angiogenic factors (Steegers et al., 2010; Roberts et al., 2011).

According to previous studies, preeclampsia serves as a marker for future risk of cardiovascular, cerebrovascular and other chronic diseases (Hermes et al., 2012). Maternal obesity also increases the risk of obese offspring and hence, increases the risk of future preeclampsia in female offspring (Freeman, 2010).

Adipose tissue is hormonally active tissue producing cytokines and adipokines (Briana & Malamitsi-Puchner, 2009). These, in turn, cause insulin resistance and increases inflammatory response (Greenberg, & Obin, 2006). The inflammatory mediators produced by adipose lead to endothelial dysfunction (Briana & Malamitsi-Puchner, 2009). The increase in free fatty acids and inflammation leads to oxidative stress in obese subjects (Dandona et al., 2005).

Adipose tissue also produces metabolically active agents like leptin and adiponectin which are related to cardiovascular diseases (Matsuzawa, 2006). During preeclampsia maternal leptin levels are high (Teppa et al., 2000). Leptin correlates with maternal BMI and it is responsible for hypertension in obesity (Chappell et al., 2002). This study was conducted to determine the association of preeclampsia with obesity.

2. Methodology:

This was a case-control study, conducted in the Gynaecology/Obstetric departments of three tertiary health care centers of Khyber Pakhtunkhwa (KP) province of Pakistan, Lady Reading Hospital (LRH), Khyber Teaching Hospital (KTH) and Hayatabad Medical Complex (HMC) Peshawar.

Forty pregnant females (aged 15-35 years), with a diagnosis of preeclampsia during their third trimester of pregnancy were taken as cases. Preeclampsia was diagnosed on the basis of pregnancy-induced hypertension (systolic 140 mmHg and above, diastolic 90 mmHg and above) and the presence of proteins in the urine sample. For controls, forty pregnant females (aged 15-35 years) who remained normotensive throughout pregnancy and were in their third trimester were taken.

Ethical approval was obtained from the institutional ethical committee of Khyber Medical University, Peshawar. Written informed consents were taken from the head of departments of concerned Gynaecology/Obstetric departments of all the three hospitals. Written informed consents were also taken from the subjects included in the study.

Clinical methods included measurement of height, weight, body mass index (BMI), pulse, blood pressure, the presence of edema. Anthropometric measurements were conducted with the individuals wearing light clothes and being without shoes. Using the portable health scale ZT-120, the height was measured to the nearest 0.1 cm. In the upright position, weight was measured to the nearest 0.1 kg using health scale ZT-120.

BMI was calculated by Quelet's Formula i.e. dividing weight (kg) by height squared (m^2). Asian criteria of BMI, was considered: underweight (<18 kg/m^2) normal weight (18-23 kg/m^2), overweight (23-25kg/m^2) and obesity (>25kg/m^2). Pulse was recorded from the radial artery. Blood pressure was recorded using a mercury sphygmomanometer (Certeza EN1060, Germany).

Data were managed and analyzed using SPSS version 20.0. Tests of normality were performed and the association between obesity and preeclampsia was determined using the Mann Whitney-U test.

4. Results:

The results show that out of forty preeclamptic subjects, 33 had preeclampsia, which is a whopping 82.5%. When Mann Whitney U test was applied, it came out to be highly significant, $p<0.001$. Hence, the null hypothesis that the distribution of BMI is the same across cases and controls; was rejected.

Table 1. *Stratification of patients, on the basis of Body Mass Index (BMI).*

Subjects	BMI categories				Total
	Under weight	Normal	Over weight	Obese	
Preeclampsia	0	3	4	33	40
Normal	2	9	4	25	40
Total	2	12	8	58	80

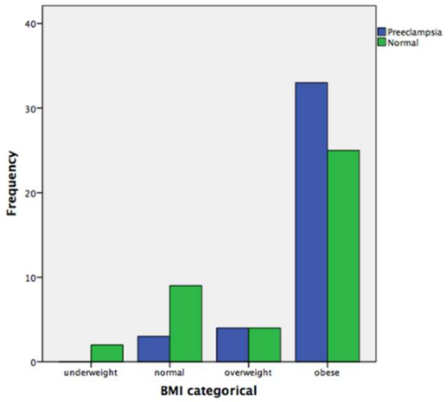

Figure 1. Comparison of the frequency of underweight, normal, overweight and obese subjects among the two groups.

5. Discussion:

Preeclampsia and eclampsia, also known as hypertensive disorders of pregnancy, are responsible for both maternal and fetal morbidity and mortality. About 14% of maternal deaths occur due to preeclampsia and eclampsia throughout the world (Bethesda & WHO, 2005). Preeclampsia also increases the risk of future cardiovascular/cerebrovascular diseases in the patient (Hermes et al., 2012). The exact cause and pathophysiology of preeclampsia still remain unclear. The basic pathophysiology seems to be a decrease in the fetoplacental circulation secondary to vasospasm and activation of the coagulation system (Ness & Sibai, 2006). The ischemia in the fetoplacental unit is compensated by an increase in the maternal blood pressure which increases placental blood flow. Obesity is a well-known risk factor for both preeclampsia and cardiovascular diseases (Roberts et al., 2011). Metabolic and physiological changes occur in the body with obesity because adipose tissue is hormonally active producing cytokines and adipokines (Briana & Malamitsi-Puchner, 2009). These substances are responsible for insulin resistance, metabolic syndrome, inflammation and oxidative stress (Greenberg, & Obin, 2006).

Insulin resistance is found in two third of obese people. It is a risk factor for both type-2 diabetes and heart diseases. Insulin resistance is commonly found in preeclampsia and can persist for many years after the preeclamptic pregnancy thereby increasing the risk for future cardiovascular diseases (Laivuori et al., 2000).

Inflammation commonly occurs in preeclampsia, obesity and cardiovascular diseases. It is due to the release of inflammatory mediators by adipocytes. C-reactive protein (CRP) is found to be higher in obese persons because apart from the liver, it is also produced by the adipocytes thereby, predisposing the obese individuals to cardiovascular diseases. Elevated levels of CRP in early pregnancy, lead to preeclampsia especially in obese women (Bodnar et al., 2005b). Other inflammatory mediators like interleukin-6 and tumor necrosis factor alpha (TNF-α) are found in higher concentrations in obese and preeclamptic women. These factors lead to vascular damage, insulin resistance and oxidative stress (Kupferminc et al., 1994).

The oxidative stress occurs in obesity as well as preeclampsia secondary to inflammation, free fatty acids and decreased level of anti-oxidants (Wallström et al., 2001).

Adipose tissue, produce leptin and adiponectin. In obese people, the leptin level is high while adiponectin level is low. These substances have a strong association with cardiovascular diseases (de Gusmao Correia, & Haynes, 2004). Leptin levels are significantly higher during preeclampsia (Teppa et al., 2000) Adiponectin is inversely related to cardiovascular diseases. It has insulin-sensitizing effects and is decreased in obesity (Roberts et al., 2011).

Table 1 shows the distribution of the subjects in both the groups into 4 categories on the basis of BMI i.e. underweight, normal, overweight and obese. We can see that out of 40 preeclamptic women, 33 were obese i.e. 82.5% whereas in the control group 25 were obese i.e. 62.5%. The findings of our study are in close agreement with the statement of the American College of Obstetricians and Gynecologists Technical Bulletin 219, (ACOG Committee on Practice Bulletins-Obstetrics, 2001). which states that high BMI increases the risk for preeclampsia by 3:1. Also, a study done in Pittsburgh showed a three-fold increase in the risk of preeclampsia in obese women (Bodnar et al., 2005b).

6. Conclusion

It is concluded that preeclampsia is more common in obese women. Therefore, weight reduction prior to pregnancy and also avoiding excessive weight gain during pregnancy will help to reduce the risk of preeclampsia.

If regular physical activity is performed in the year before pregnancy and also during early pregnancy, there will be a reduced risk of preeclampsia (Sorensen et al., 2003).

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References:

1. ACOG Committee on Practice Bulletins-Obstetrics. (2001). Diagnosis and management of preeclampsia and eclampsia. *Obstet Gynecol*, *98*, 159-167.
2. Bethesda, M. D., & WHO 2004. (2005). Global Burden of Disease for the Year 2001 by World Bank Region, for Use in Disease Control Priorities in Developing Countries. National Institutes of Health. WHO? Make every mother and child count. World Health Report.
3. Bodnar, L. M., Ness, R. B., Markovic, N., & Roberts, J. M. (2005a). The risk of preeclampsia rises with increasing prepregnancy body mass index. *Annals of epidemiology*, *15*(7), 475-482. [PubMed]
4. Bodnar, L. M., Ness, R. B., Harger, G. F., & Roberts, J. M. (2005b). Inflammation and triglycerides partially mediate the effect of prepregnancy body mass index on the risk of preeclampsia. *American journal of epidemiology*, *162*(12), 1198-1206. [PubMed]
5. Briana, D. D., & Malamitsi-Puchner, A. (2009). Reviews: adipocytokines in normal and complicated pregnancies. *Reproductive Sciences*, *16*(10), 921-937. [PubMed]

6. Chappell, L. C., Seed, P. T., Briley, A., Kelly, F. J., Hunt, B. J., Charnock-Jones, D. S., ... & Poston, L. (2002). A longitudinal study of biochemical variables in women at risk of preeclampsia. *American journal of obstetrics and gynecology*, *187*(1), 127-136. [PubMed]
7. Dandona, P., Aljada, A., Chaudhuri, A., Mohanty, P., & Garg, R. (2005). Metabolic syndrome: a comprehensive perspective based on interactions between obesity, diabetes, and inflammation. *Circulation*, *111*(11), 1448-1454. [PubMed]
8. de Gusmao Correia, M. L., & Haynes, W. G. (2004). Leptin, obesity and cardiovascular disease. Current opinion in nephrology and hypertension, 13(2), 215-223. [PubMed]
9. Freeman, D. J. (2010, April). Effects of maternal obesity on fetal growth and body composition: implications for programming and future health. In *Seminars in Fetal and Neonatal Medicine* (Vol. 15, No. 2, pp. 113-118). WB Saunders.
10. Greenberg, A. S., & Obin, M. S. (2006). Obesity and the role of adipose tissue in inflammation and metabolism. *The American journal of clinical nutrition*, *83*(2), 461S-465S. [PubMed]
11. Hermes, W., Van, F. K., & De, C. G. (2012). Preeclampsia and cardiovascular risk. *Minerva ginecologica*, *64*(4), 281-292.
12. Kupferminc, M. J., Peaceman, A. M., Wigton, T. R., Rehnberg, K. A., & Socol, M. L. (1994). Tumor necrosis factor-α is elevated in plasma and amniotic fluid of patients with severe preeclampsia. *American journal of obstetrics and gynecology*, *170*(6), 1752-1759. [PubMed]
13. Laivuori, H., Kaaja, R., Koistinen, H., Karonen, S. L., Andersson, S., Koivisto, V., & Ylikorkala, O. (2000). Leptin during and after preeclamptic or normal pregnancy: its relation to serum insulin and insulin sensitivity. *Metabolism*, *49*(2), 259-263.
14. Matsuzawa, Y. (2006). The metabolic syndrome and adipocytokines. *FEBS letters*, *580*(12), 2917-292. [PubMed]
15. Misra, A., & Khurana, L. (2008). Obesity and the metabolic syndrome in developing countries. *The Journal of Clinical Endocrinology & Metabolism*, *93*(11_supplement_1), s9-s30. [PubMed])
16. Ness, R. B., & Sibai, B. M. (2006). Shared and disparate components of the pathophysiologies of fetal growth restriction and preeclampsia. *American journal of obstetrics and gynecology*, *195*(1), 40-49.
17. Osol, G., & Moore, L. G. (2014). Maternal uterine vascular remodeling during pregnancy. *Microcirculation*, *21*(1), 38-47. [Google Scholar] [CrossRef] [PubMed]).
18. Redman, C. W., & Sargent, I. L. (2005). Latest advances in understanding preeclampsia. *Science*, *308*(5728), 1592-1594.
19. Roberts, J. M., Bodnar, L. M., Patrick, T. E., & Powers, R. W. (2011). The role of obesity in preeclampsia. *Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health*, *1*(1), 6-16. [PMC free article] [PubMed]
20. Sorensen, T. K., Williams, M. A., Lee, I. M., Dashow, E. E., Thompson, M. L., & Luthy, D. A. (2003). Recreational physical activity during pregnancy and risk of preeclampsia. *Hypertension*, *41*(6), 1273-1280. [PubMed]
21. Steegers, E. A., Von Dadelszen, P., Duvekot, J. J., & Pijnenborg, R. (2010). Pre-eclampsia. *The Lancet*, *376*(9741), 631-644. [Google Scholar] [CrossRef]
22. Teppa, R. J., Ness, R. B., Crombleholme, W. R., & Roberts, J. M. (2000). Free leptin is increased in normal pregnancy and further increased in preeclampsia. *Metabolism-Clinical and Experimental*, *49*(8), 1043-1048. [PubMed]
23. Vogel, J. P., Lee, A. C., & Souza, J. P. (2014). Maternal morbidity and preterm birth in 22 low-and-middle-income countries: a secondary analysis of the WHO Global Survey dataset. *BMC pregnancy and childbirth*, *14*(1), 56. [Google Scholar] [CrossRef] [PubMed]
24. Wallström, P., Wirfält, E., Lahmann, P. H., Gullberg, B., Janzon, L., & Berglund, G. (2001). Serum concentrations of β-carotene and α-tocopherol are associated with diet, smoking, and general and central adiposity. *The American journal of clinical nutrition*, *73*(4), 777-785. [PubMed]
25. Yogev, Y., & Catalano, P. M. (2009). Pregnancy and obesity. Obstetrics and Gynecology Clinics, 36(2), 285-300. [PubMed]

Received April 04, 2019; reviewed April 07, 2019; accepted April 13, 2019; published online May 01, 2019