FREQUENCY OF PRE-ECLAMPSIA IN PATIENTS WITH ABNORMAL UTERINE ARTERY DOPPLER AT TWENTY TWO TO TWENTY FOUR WEEKS OF GESTATION.

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ABSTRACT... Objectives: To determine the frequency of pre-eclampsia among pregnant ladies with abnormal uterine artery Doppler at 22-24 weeks of gestation at a tertiary care hospital. Study Design: Cross sectional study. Setting: Department of Obstetrics and Gynecology, Nishtar Medical University / Hospital Multan. Period: All the women (n=160) with abnormal uterine artery Doppler from 01-07-2018 to 30-06-2019 were included. Material & Methods: The pulsatility index (PI) of uterine artery Doppler was taken by taking average of 3 consecutive waveforms to determine the abnormal uterine artery Doppler. These study cases were followed till delivery to document pre-eclampsia. Results: Of these 160 study cases, 89 (55.6 %) had gestational age up to 23 weeks while 71 (44.4 %) had gestational age more than 23 weeks having mean age of 25.44 ± 4.77 years. Of these 160 pregnant ladies with abnormal uterine artery Doppler, 72 (45.0 %) were resident of rural areas and 88 (55.0 %) were resident of urban areas and family history of pre-eclampsia was 42 (26.3%). Previous history of pre-eclampsia was noted in 41 (25.6%). Mean parity was 2.24 ± 1.06 and 113 (70.6%) had parity up to 3. Mean gravidity of our study cases was 3.87 ± 1.16 and 89 (55.6%) had gravidity up to 4. Obesity was present in 30 (18.8 %) having mean body mass index 25.23 ± 1.92 kg/m². Mean interpregnancy interval was 14.19 ± 6.82 months and 83 (51.9 %) had interpregnancy interval more than 1 year and pre-eclampsia was noted in 125 (78.1%). Conclusion: Very high frequency of pre-eclampsia was noted in our study in pregnant women presenting with abnormal uterine artery Doppler at 22 – 24 weeks of gestation. Pre-eclampsia was significantly associated with age, family history of pre-eclampsia, previous history of pre-eclampsia and interpregnancy interval.

Key words: Abnormal Uterine Artery Doppler, Frequency, Pre-eclampsia.

INTRODUCTION
Pre-eclampsia complicates around 5–7 % of total pregnancies all over the world and is specified with placental and maternal vascular dysfunction which leads to adverse perinatal outcomes e.g. hypertension, placental abruption, intrauterine growth restriction, eclampsia and even feto-maternal mortalities.¹² It is regarded as one of the leading causes of maternal and neonatal morbidities and mortalities.³⁴ Additionally pre-eclamptic patients are always at increased risk of development of cardiovascular diseases in later ages of their life. Various risk factors implicated in the development of pre-eclampsia may include; obesity, extreme maternal age (less than 15 years and more than 35 years), diabetes, twin pregnancies, chronic renal diseases and African American race.⁵⁻⁷

Recent estimates of World Health Organization (WHO) have reported worldwide mortalities associated with pre-eclampsia as over 100 000 every year, particularly in developing countries.⁸ These estimates point towards precise prediction of pre-eclampsia to improve services delivery of antenatal surveillance and therapy, with an objective to improve pregnancy outcomes. Under these circumstances, potential target is believed to be associated with assessment of uteroplacental circulation in high risk population such as obese, diabetic, positive family history, extreme maternal ages and previous history. Assessment of uteroplacental circulation is usually achieved by Doppler Ultrasonography.
Traditionally, pre-eclampsia is believed to be caused by certain underlying conditions such as; abnormalities in placental formation, by abnormal trophoblast patterns of spiral arteries and enhanced resistance observed in the uteroplacental circulation.\textsuperscript{9} Pregnancies associated with higher diastolic blood flow velocity and early diastolic notch up to 22 weeks of pregnancy have been found to result in normal term deliveries whereas those pregnancies which exhibit increased resistance waveforms having early diastolic notch have been reported to be destined to result in increased rates of preterm deliveries, placental abruption and IUGR due to pre-eclampsia.\textsuperscript{10} Barati et al\textsuperscript{11} reported as high as 88.2 \% pre-eclampsia in patients with abnormal uterine artery Doppler.

This study was planned to document frequency of pre-eclampsia in patients with abnormal uterine artery Doppler in our local population, owing to genetic diversity and life style modifications as it was noted that there is no published study available in our local database of Pakistan, though we treat such patients with abnormal uterine artery Doppler frequently in our routine duties.

**MATERIAL & METHODS**

This cross-sectional study was done at Department of Obstetrics and Gynecology, Nishtar Hospital Multan. The study extended from 01-07-2018 to 30-06-2019. All the women, whether primigravida or multigravida, having age ranging from 20-40 years, with abnormal uterine artery Doppler at 22-24 weeks of gestation (assessed on LMP) were recruited. Sample size was (n=160), calculated by formula: 
\[ n = \frac{z^2 \times p \times q}{d^2} \]
Where \( z = 1.96 \), \( p = 88.2 \% \), \( d = 5 \% \). The mean pulsatility index (PI) from the left and right uterine arteries was calculated at 22-24 weeks of gestation using Doppler ultrasonography and mean PI more than 1.45, the flow velocity waveform and presence of bilateral early diastolic notches was considered abnormal.

Twin pregnancy, patients of renal disease (having raised serum creatinine level > 2 mg/dl), cardiovascular disease (known patients with valvular heart disease, congenital heart diseases, IHD which was confirmed from patient record file), liver disease (known cases of CLD diagnosed on ultrasonography and laboratory report), diabetes (known diabetic patients who are taking hypoglycemic drugs), diagnosed cases of thyroid dysfunction (showing derangement in any of T3, T4 and TSH) and patients having malignancies (on histopathology report) were excluded from our study. Detailed history (like age, parity, gestational age, residential status and obesity) and physical examination was conducted. These study cases were followed till delivery to document pre-eclampsia. Data entry and analysis was done by SPSS Version 20. Frequencies and percentages were tabulated for categorical variables like resident status, family history of pre-eclampsia, parity, gravidity, obesity, previous history of preeclampsia and age groups. Effect modifiers like age, residential status, family history of pre-eclampsia, parity, gravidity, Obesity (BMI > 27.5 kg/m\textsuperscript{2}), interpregnancy interval and gestational age were controlled by stratification of data along with chi-square test at 95\% CI.

**RESULTS**

A total of 160 patients with abnormal uterine artery Doppler were taken, 89 (55.6 \%) had gestational age up to 23 weeks while 71 (44.4 \%) had gestational age more than 23 weeks. Mean age was 25.44 ± 4.77 years with 20–38 years range and 137 (85.6 \%) were aged up to 30 years. Of these 160 pregnant ladies with abnormal uterine artery Doppler, 72 (45.0 \%) were resident of rural areas and 88 (55.0 \%) were resident of urban areas. Family history of pre-eclampsia was 42 (26.3\%). Previous history of pre-eclampsia was noted in 41 (25.6\%). Mean parity of our study cases was 2.24 ± 1.06 and 113 (70.6 \%) had parity up to 3. Mean gravidity of our study cases 3.87 ± 1.16 and 89 (55.6 \%) had gravidity up to 4. Obesity was present in 30 (18.8 \%) having mean body mass index 25.23 ± 1.92 kg/m\textsuperscript{2}. Mean interpregnancy interval was 14.19 ± 6.82 months and 83 (51.9 \%) had interpregnancy interval more than 1 year. Mean gestational age at the development of pre-eclampsia was 33.12 ± 2.54 weeks and pre-eclampsia was noted in 125 (78.1\%) of our study cases. Pre-eclampsia was
stratified with regards to gestational age, age, residential status, obesity, parity, gravidity, family history, previous history and interpregnancy interval.

| Confounding Variables | Preeclampsia | P–Value |
|-----------------------|-------------|---------|
|                       | Yes (n =125) | No (n =35) |
| Gestational Age (In weeks) | Up to 23 (n=89) | 71 18 | 0.701 |
|                        | More than 23 (n=71) | 54 17 |
| Age groups (In Years) | Up to 30 (n=137) | 102 35 | 0.005 |
|                        | More than 30 (n=23) | 23 00 |
| Residential status | Rural (n=72) | 49 23 | 0.007 |
|                        | Urban (n=88) | 76 12 |
| Family History | Yes (n=42) | 42 00 | 0.001 |
|                      | No (n=118) | 83 35 |
| Previous history | Yes (n=41) | 41 00 | 0.000 |
|                     | No (n=119) | 84 35 |
| Obesity | Yes (n=30) | 24 06 | 1.000 |
|                   | No (n=130) | 101 29 |
| Parity | Up to 3 (n=113) | 84 29 | 0.093 |
|           | More than 3 (n=47) | 41 06 |
| Short Interpregnancy | Up to 12 (n=77) | 53 24 | 0.007 |
| interval     | More than 12 (n=83) | 72 11 |

Table-I. Cross-tabulation of preeclampsia with regards to different confounders. (n = 150)

DISCUSSION
Abnormal trophoblastic distribution of the spiral arteries is linked with increased risks associated with the higher proportions of pre-eclampsia, Intrauterine growth restriction (IUGR) and various other adverse perinatal outcomes. Globally, uterine artery Doppler has gained popularity as a screening test in middle stages of pregnancy. In our study, uterine artery Doppler was planned in 22-24 weeks of pregnancies which is contrary to many other studies who conducted it in the first trimester and early second trimester based upon hypothesis that this timing was unlikely to influence fetal growth and well-being.

Of these 160 study cases, 89 (55.6 %) had gestational age up to 23 weeks patients while 71 (44.4 %) had gestational age more than 23 weeks. Mean age was 25.44 ± 4.77 years ranging 20–38 years and 137 (85.6 %) were aged up to 30 years. Ebrashy et al has reported mean age as 28.5 ± 5.9 years. Schwarzman et al has also reported mean age as 27.30 ± 6.44 years while Talari et al has reported it to be 27.8 ± 4.5 years.

Family History of pre-eclampsia was noted in 42 (26.3%) of our study cases. Previous history of pre-eclampsia was noted in 41 (25.6%). Ebrashy et al has also reported 28.4 % previous history of pre-eclampsia while 20.4 % family history of pre-eclampsia; close to our results. Talari et al has also reported similar results.

Mean parity of our study cases was 2.24 ± 1.06 and 113 (70.6%) had parity up to 3. Mean gravidity of our study cases 3.87 ± 1.16 and 89 (55.6%) had gravidity up to 4. Schwarzman et al has also reported 2.76 ± 2.33 mean parity while mean gravidity was 3.32 ± 2.84. Talari et al has also reported that 37.5 % patients with abnormal uterine artery Doppler had parity equal/more than 3.

Obesity was present in 30 (18.8 %) having mean body mass index 25.23 ± 1.92 kg/m² which is quite close to that reported by Talari et al (25.1 ± 3.2 kg/m² mean BMI.)

Mean gestational age at the development of pre-eclampsia was 33.12 ± 2.54 weeks. Barati et al has...
has also reported that 17% patients developed preeclampsia before 32 weeks of gestation.

Pre-eclampsia was noted in 125 (78.1%) while Verma et al. has reported 41% preeclampsia which is quite lower than our study results. Barati et al. has reported 88.2% preeclampsia, close to our study results.

CONCLUSION

Very high frequency of pre-eclampsia was noted in our study in pregnant women presenting with abnormal uterine artery Doppler at 22 – 24 weeks of gestation. Pre-eclampsia was significantly associated with age, family history of pre-eclampsia, previous history of pre-eclampsia and interpregnancy interval.

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| 3     | Asiya Fayyaz             | Study collection, Study design, Interpretation.                                             |                     |
| 4     | Faiza Suman              | Data collection, Study design, Interpretation, Final reading.                                |                     |
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