Introduction

The pregnancy is a physiological metabolic syndrome and women have to pass this stress test to continue a safe life journey, otherwise consequences of this failure will put harmful burden on cardiovascular system of these women. We have chosen the main critical high risk changes affecting pregnant women which are the preeclampsia, gestational Diabetes Mellitus, giving birth to low weight babies and developing peripartum cardiomyopathy and decided to follow them for a period of 5 years of post-partum. The research group managed to monitor the Arterial stiffness and Non dipping BP development in these women and comparing them with a normal control group of women who passed through similar pregnancies without having any complications. The research group have defined this particular high risk pregnancy as "the development of preeclampsia, gestational DM, giving birth to low weight babies and Non dipping BP development in these women and comparing them with a normal control group of women who passed through similar pregnancies without having any complications. The research group have defined this particular high risk pregnancy as "the development of preeclampsia, gestational DM, peripartum cardiomyopathy and giving birth to low weight babies during the pregnancy period", also the definition of preeclampsia was "mild preeclampsia - is the presence of hypertension of $> = 140/90$ mmHg on 2 occasions at least 6 hours apart, without evidence of end organ damage, in women who were normotensive before 20 weeks gestation. In women with preexisting essential hypertension, preeclampsia is diagnosed if SBP has increased by 30 mmHg or the DBP has increased by 15 mmHg.

Severe preeclampsia will be the presence of one of the following in the presence of preeclampsia: The BP $= 160/110$ mmHg, 3+ proteinuria, pulmonary edema or cyanosis, Oliguria of $< 400$ ml/24hrs , persistent headaches, epigastric pain and/or impaired liver function, Thrombocytopenia or Oligohydramnios, decreased fetal growth or placenta abruption'. Low birth babies were defined as "birth weight of a live born infant of less than 2,500 g, regardless of gestational age". The peripartum cardiomyopathy was defined as "left ventricular systolic dysfunction presenting in the last month of pregnancy or the 5 months post-partum. There should be no existing LV dysfunction and no alternative cause of patient's heart failure". Echocardiography study should reveal the LVEF < 45%, FS < 30% and Left ventricle dilatation (and may be the 4 chambers will be dilated). Gestational Diabetes Mellitus is defined as "Any degree of glucose intolerance, with onset or diagnosis during pregnancy". The Non Dipper is defined as "A decline in the nocturnal BP of < 10% but > 0% and reverse dipping was defined as a decline in nocturnal BP of < 0%. Arterial stiffness has a more pathophysiological definition: "The reduced capability of an artery to expand and contract in response to pressure changes. The ABP Monitoring was done by sing the new technology of "TensionMED Ltd. From Hungary to detect the 24 blood pressure changes and using its Arteriography to detect the Arterial stiffness. The follow up of patients of both groups i.e. the high risk group and normal control pregnancy group, was at the end of the first year post-partum and at the end of the fifth year of the studied pregnancy, starting from the end of the year 2009. All subsequent pregnancies, complications and events were recorded and put into actual consideration.

Methods

Our research group had selected 100 female patients aged between 18 to 35 years of age from the Gynecology and Obstetrics Clinics of main 2 public Hospitals in Tripoli Libya. Both groups
were of Libyan women, Caucasians of Arab and Berber origin and some are of African origin. Group 1 was consisting of 50 women who had a high risk pregnancy with no previous cardiovascular diseases. The group 2 consists of 50 women who had also normal pregnancies without any complications and they have no cardiovascular diseases. All women with any cardiovascular diseases like hypertension, diabetes mellitus, metabolic syndrome, Dyslipidemia, valvular heart diseases and congenital heart diseases were excluded from the study. Also we excluded females who are on oral contraception and we kept those using safe period, husband using condom, or have done Tubal ligation. Measurement of 24 blood pressures and estimation of Arterial stiffness was performed using the “TensioMed Arteriography Method” which measures the “PWV”, Augmentation Index (Aix), the central systolic blood pressure (SBPao), it is a manufacture of Hungary with highest technology standards. The blood pressure is measured from the brachial area (SBP, DBP, MAP, PP and HR). Cuff size was chosen on the basis of arm circumference, the cuff was fixed to non-dominant arm. Three BP readings were obtained in the morning (7:00 to 10:00 am) comitant with sphygmonanometric measurements to ensure that the mean of the two sets of values differ by <5 mmHg. BP was recorded every 15 minutes from 7:00 am to 10:00 pm, and every 30 minutes from 10:00 pm to 7:00 am. The Arteriograph was studied at the end of the monitoring to detect the Arterial stiffness. Strenuous physical activity was discouraged in all patients during the monitoring period. The measurements were taken for a continuous 48 hours, once at the start of the study (year 1) and the other at the end of study (year 5).

Dipping and Non Dipping BP

Daytime and nighttime systolic blood pressure predicted all-cause and cardiovascular mortality, coronary heart disease and stroke, independent of office blood pressure and confounding variables. Although nighttime blood pressure predicts all outcomes, daytime blood pressure did not add prognostic precision to nighttime pressure. The systolic night-day blood pressure ratio predicts all outcomes, which only persists for all-cause mortality after adjusting for 24-hour blood pressure. These findings are similar in men and women, in young and older patients, and in treated and untreated patient’s. Nocturnal blood pressure present in resting conditions, sleeping and repose, represent minimal BP that the subject needs for adequate organ perfusion. The non-dipping pattern, once excluded bad quality of sleep, reflects an inadequate of the mechanisms regulating BP. It can be a consequence of baroreflex or autonomic dysfunction, relative nocturnal volume overload or abnormal sodium handling. In the majority of cases the pattern represents the consequences of an underlying disease. The presence of non-dipping pattern indicates that the patient is at more advanced stage of organ damage.

ABPM and arterial stiffness

Ambulatory arterial stiffness index (AASI), a novel index which is derived from ambulatory blood pressure (BP) recordings, has been suggested recently as an index of arterial stiffness. AASI has been shown to strongly correlate with classic measures of arterial stiffness, such as central and peripheral augmentation indexes, central pulse pressure (PP), carotid-femoral pulse wave velocity (PWV), and carotid intima-media thickness. It also demonstrated that there is a close correlation between AASI and PWV in normotensive volunteers; the correlation was stronger in women vs. men, and the correlation was significant when analyzing adults under age 40 years. Moreover, in subjects under age 40, AASI but not PP correlated with systolic augmentation index, suggesting AASI might be an indicator of arterial dysfunction at a much younger age. Finally, AASI has also been postulated to be a predictor of cardiovascular mortality, even in normotensive subjects. In addition to AASI, other markers derived from ambulatory blood pressure monitoring may have diagnostic, prognostic, and therapeutic relevance. Exaggerated ambulatory BP variability (BPV) has been proposed to be a risk factor for cardiovascular disease in hypertensives. Ambulatory BPV, PP, nocturnal dipping, and morning BP surge have all been shown to be predictive of end-organ damage and cardiovascular disease. Growing evidence suggests that the degree of cardiovascular reactivity to laboratory stressors may be predictive of future development of cardiovascular disease. Four of the most common laboratory provocations of sympatho-excitatory stress target different integrative pathways: orthostatic stress, emotional stress, cold stimuli, and the exercise pressor reflex. Normotensive individuals who show a robust pressor response to sympatho-excitatory stimuli like mental stress (MS) and cold pressor test (CPT) are at increased risk for developing hypertension. Therefore, it seems reasonable to predict that healthy individuals with markers of increased arterial stiffness might also generate greater pressor responses to sympapto-excitation. These “pre-clinical” characteristics are important because socioeconomic status, job strain, and chronic emotional stress have powerful widespread implications on cardiovascular health and wellness in general [1-10].

Results

This is a 2 group comparison study over a period of 5 years to evaluate both groups during this period and to discover if the offensive risk pregnancies is affected against the control group with normal pregnancies. We managed to follow up the 100 women at the end of year 1 and at the end of year 5. All the 100 females were having no evidence of any cardiovascular disease, no dipping nocturnal pattern or arterial stiffness at the beginning of the study. We have excluded all females with established cardiovascular diseases from the start of the study. In group 1 with high risk pregnancy (n=50), some got pregnant again during the 5 years (n=34) and the rest did not (n=16). Out of the pregnant group 22 had no any cardiovascular disease, 5 females got essential hypertension, 2 females developed diabetes mellitus type2 and 5 females got Dyslipidemia. 21 females had non-dipping nocturnal pattern and 4 showed arterial stiffness positive results. The risk group with no re-pregnancy (n = 16), 10 females had no cardiovascular diseases, 1 female developed essential hypertension, 3 females developed diabetes mellitus type2 and 2 females developed Dyslipidemia. 7 females developed non dipping nocturnal pattern and none had positive result for arterial stiffness. Group 2, the control group (n=50), 41
females got pregnant during the 5 years and 9 females did not get pregnant. From the pregnant group 38 had no cardiovascular disease, 3 females had diabetes mellitus type 2, and 2 females were having non-dipping nocturnal pattern and none had any evidence of arterial stiffness. From the non-pregnant group, none had any cardiovascular disease or evidence of arterial stiffness. None of the whole group showed any event (heart failure, MI or stroke) during the studied period.

Discussion

It is obvious from the data we have collected that most of the women with high risk pregnancies had developed a clear progressive cardiovascular disease process in the form of the non-dipping blood pressure pattern and an established arterial stiffness, especially those who got pregnant again. It was clear that the re-pregnancy made more burdens on these women to develop cardiovascular dysfunction. The opposite was seen in the control group with no high risk pregnancy, the cardiovascular diseases were not common in this group and almost none had the non-dipping blood pressure pattern or arterial stiffness.

The pregnancy with development of preeclampsia, birth of low weight babies, gestational diabetes and peripartum cardiomyopathy (the latter was the least affecting the pregnant females, with only 1 female had left ventricular dysfunction and no heart failure was detected) have obvious impact on women with high risk pregnancies in the long run leading to cardiovascular dysfunction and if not controlled from the beginning the patients will gradually establish a cardiovascular decompensation and generate future events. It is expected to develop more morbidity and mortality than the other normal pregnancy group (control group). There should be strong cooperation between the Gynecological doctors and Cardiologist to follow this sort of pregnant females who had a failure of the pregnancy stress test and expected to face a serious future with morbid and fatal events. Also the study proved that high risk pregnancy with established complications will be exaggerated with multiple pregnancies and reduced with fewer or no consequent pregnancies. After 5 years from the first critical stress the clinical diseases observed were an established hypertension, Diabetes and Dyslipidemia, but if still we continue to lose prevention control parameters in these women, clear cut events will develop and permanent damage consequences will be inevitable. Recently in a cohort study done in US has showed that normal females who developed gestational DM are likely to have subclinical atherosclerosis, this atherosclerosis was detected by the measurements of CIMT changes. Pregnancy has been under recognized as an important time period that can signal a woman’s risk for future cardiac disease. In this recent study GDM will initiate early signs of heart disease before they develop T2DM or metabolic syndrome after pregnancy. Our study has included three other risk factors they will initiate this early atherosclerosis in these women with the risky pregnancies [11-14].

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