

Prenatal and Cardiovascular Outcome in Pregnant Patients With Dyspnea

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Background: Pregnancy is a physiologic phenomenon in women, which leads to significant hemodynamic changes in cardiovascular system. Many patients reach reproductive age due to improvements in diagnosis and treatment of cardiac diseases. Dyspnea is a common complaint in pregnant women and can be a sign to refer patients for an easy and feasible workup such as echocardiography.

Objectives: We aimed to evaluate dyspnea as a common complaint in pregnant women and its prenatal outcome.

Patients and Methods: Pregnant patients with dyspnea NYHA class > II were included. A thorough physical examination and routine lab tests were performed. Echocardiography was performed to rule out previous cardiac and lung diseases, anemia and thyroid disorders. It was repeated monthly till one month after delivery. Collected data was analyzed after one year.

Results: Fifty patients were enrolled with a mean age of 30.49 ± 6.34 years. 58% of them, had NYHA class II, 40% III and 2% IV. Pulmonary rales were diagnosed in 8% and palpitation in 80%, while all had normal lab tests. Mean EF value was 52.26 ± 6.80 ; 54% had valvular diseases and 12% had pulmonary hypertension. Cesarean section was performed in 26, preeclampsia occurred in 7 and 21 had preterm labor. Three neonates had anomalies and six had an Apgar score below six. Mean birth weight was 2897 ± 540.00 grams. A significant association was found between NYHA Class with valvular disease ($P = 0.007$) and sys PAP ($P = 0.036$); however, it had an inverse correlation with LV EF ($P = 0.06$).

Conclusions: Dyspnea may coincide with cardiac dysfunction and poor prenatal outcome in pregnant patients. In such cases echocardiography is a feasible screening tool.

Keywords: Pregnancy; Dyspnea; Echocardiography

1. Background

Pregnancy is a physiologic phenomenon in women, which may lead to significant hemodynamic changes in cardiovascular system. Volume overload, anemia and hem dilution, changes in coagulation system and emergence of specific antibodies in blood circulation can each affect the life of even healthy individuals in certain ways (1). The prevalence of heart disease has been increased which is probably due to improvements in diagnosis and treatment; therefore, many patients reach to reproductive age. Some cardiovascular diseases such as congenital heart disease, pulmonary hypertension and ventricular dysfunction can affect prognosis of both pregnant women and their newborns (2).

2. Objectives

Dyspnea is a common complaint in pregnant women. Physiologic and hemodynamic changes can result in a significant dyspnea in such cases (1). In some patients dyspnea in normal daily activities can be a sign of heart

or lung disease and may be associated with poor perinatal and cardiac outcome in which early detection can prevent adverse events during pregnancy and delivery (3). This study aimed to investigate prognosis of patients with pregnancy-induced dyspnea in routine daily activities from cardiovascular point of view. In addition, the role of echocardiography as a cheap, simple and available modality was evaluated in screening patients with dyspnea in the second trimester.

3. Patients and Materials

In this prospective cross-sectional study, 50 pregnant women (estimated based on previous studies) with a live fetus confirmed by ultrasound imaging and chief complaint of dyspnea starting from the second trimester and a NYHA class > II were enrolled (NYHA class is explained in Table 1). Patients were outpatients referred to perinatal clinic of Omolbanin and Imam Reza Hospitals with no history of heart disease, previous heart surgery,

asthma or pulmonary disease, renal or hepatic disease, no wheezing in lungs indicative of asthma and no history of drug use due to cardiac involvement. Regarding the significance of anemia and thyroid disease in the occurrence of dyspnea, patients with anemia and Hb level below 10.5 mg/dL and those with hyper or hypothyroidism (TSU < 0.01 or > 3 IU/dL) were excluded from the study. The study goals and protocol were fully explained and an informed consent was obtained from each participant prior to study enrollment. For each participant a thorough physical examination was performed, an ECG was taken and an echocardiography was performed by a single cardiologist with the vivid S5 device and a 4MHz probe. Echocardiography parameters including ejection fraction volume (EF), valvular function, pulmonary pressure and ventricular function were investigated and certain recommendations were given wherever appropriate. Patients were then supervised and followed up monthly during pregnancy till one month after delivery by a single perinatologist. Post-delivery data including age of pregnancy, type of delivery, neonate's Apgar score and general condition were recorded. After data collection, the correlation between dyspnea and perinatal outcome and cardiovascular problems were evaluated in 50 patients within a one-year interval.

Table 1. NYHA (New York Heart Association) Functional Capacity Classification for Dyspnea

Class	Patient Symptoms
Class I (Mild)	No limitation in physical activity. Ordinary physical activity does not cause undue fatigue, palpitation or dyspnea (shortness of breath).
Class II (Mild)	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea.
Class III (Moderate)	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation or dyspnea.
Class IV (Severe)	Unable to perform any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased.

3.1. Statistical Analysis

Analysis was performed using SPSS software, version 11.5 for windows. Absolute number and percentage were computed to better describe data. Data was expressed as mean \pm SD for continuous variables and median and interquartile range for ordinal variables. Mann Whitney test and Spearman's rho correlation were used for data analysis when appropriate. A $P < 0.05$ was considered statistically significant.

4. Results

The mean age of pregnant women was 30.5 ± 6.034 years (ranged 20 to 42 years). Gestational age at echocardiography study was 31.5 ± 3.3 weeks (ranged 22-34 weeks). The functional capacity of participants at study enrollment was class II in 58% and class III in 40%; whereas, only 2% had a NYHA class IV (based on the American Society of Cardiology staging for dyspnea). In total, 8% of cases had pulmonary rales in physical examination. About 80% of cases had used supplementary drugs during pregnancy. The mean creatinine level was 0.73 ± 0.11 (min: 0.5, max: 1 mg/dL) and mean TSU level was 0.74 ± 0.34 mg/dL (0.4-2.5 mg/dl). In echocardiography data analysis, the mean ejection fraction was $56.25 \pm 6.8\%$ (25-65%). Regarding valvular disease, 54% of cases had at least one type of such involvement, whereas other 46% had normal heart valves. Table 2 shows the distribution of valvular disease in the studied population. On the other hand, 88% of cases did not have pulmonary hypertension, whereas PAP ≥ 30 mmHg was detected in 12% by echocardiography.

4.1. Mother and Fetus Prognostic Study

Among the studied mothers (Table 3) 7 (14%) experienced preeclampsia, whereas preterm labor occurred in 21 (42%). Congenital anomalies were diagnosed in three (6%) newborns. No maternal mortality occurred during the study. Cesarean section (CS) was performed in 26 (52%), whereas 24 (48%) had a normal vaginal delivery (NVD). Cesarean section indications were previous CS in 15 cases and obstetrical issues such as sufferance or preeclampsia in other 11 ones. The mean gestational period was 36.88 ± 2.94 weeks ranging from 28 to 41 weeks. Neonates mean birth weight was 2897 ± 540 grams (ranged 1000-3850 grams). In total, 13 (26%) neonates were hospitalized in NICU and the mean Apgar score was 7.64 ± 2.1 . All newborns had an Apgar ≥ 2 . There was no significant correlation between NYHA class and neonatal and obstetrical outcomes (preterm Apgar < 6 and preeclampsia).

4.2. Cardiovascular Outcome

Studying NYHA class regarding cardiovascular outcomes revealed a significant correlation between NYHA class and valvular disease ($P = 0.007$), especially mitral valve disease (MS, MR and MVP; $P = 0.095$) and increase in pulmonary pressure ($P = 0.036$); whereas, an inverse association was found with LV EF ($P = 0.06$) (Table 4). Increased prevalence of preterm labor and preeclampsia and low Apgar score were found in patients with valvular diseases ($P = 0.3, 0.22, 0.06$), but it was not statistically significant, which can be due to low number of studied patients. In addition, we considered the association between increased systolic Pulmonary pressure (PAP) and prenatal outcome, which was not significant ($P = 0.58, 0.57, 0.68$).

Table 2. Distribution of Cardiac Diseases in the Studied Participants^a

Type of cardiac disease	Results
Mitral regurgitation (MR)	17 (34)
Mitral stenosis (MS)	5 (10)
Tricuspid valve regurgitation (TR)	7 (14)
Aortic valve regurgitation (AR)	7 (14)
Mitral valve prolapsed (MVP)	6 (12)
Pulmonary valve regurgitation	2 (4)
Aortic valve stenosis (AS)	1 (2)
Pericardial Effusion	2 (4)
Pulmonary hypertension	6 (12)

^a Data are presented as No. (%).**Table 3.** Prevalence of Perinatal Outcomes in Pregnant Patients With Dyspnea^a

Prenatal Outcome	Results
Preeclampsia	7 (14)
Cesarean	26 (52)
Apgar of neonates < 6	6 (12)
NICU admission	13 (26)
Preterm labor	21 (42)
Neonates anomaly	3 (6)

^a Data are presented as No. (%).**Table 4.** Correlation of NYHA Functional Class to Cardiologic Problems in Pregnant Patients With Dyspnea

Spearman's Correlation Coefficient	PAP	Valvular Disease	Mitral Disease	EF
P Value	0.036	0.007	0.095	0.06

5. Discussion

In the study by Zeldis et al. it was shown that dyspnea is a common finding even in normal pregnancies, while many cardiac and pulmonary diseases manifest with this symptom (4). Weinberger stated that dyspnea in a pregnant woman brings up the question whether the patient has certain degrees of an underlying cardiac or pulmonary disease or if is an isolated symptom induced by pregnancy (5). In total, 60-70% of pregnant women experience dyspnea during pregnancy, which is most commonly occurred during the first and second trimesters, while the frequency of dyspnea remains constant up to the third trimester (6, 7). The exact mechanism of dyspnea during pregnancy is not yet known; however, it may be due to increased metabolic needs or mechanical causes during pregnancy (8). In pathologic situations, 85% of patients with dyspnea are related to one of the following etiologies: asthma, pneumonia, cardiac ischemia, pulmonary

disease, heart failure, obstructive airway disease and psychological problems (9, 10). Regarding the great importance of cardiac diseases and their related morbidity and mortality, mainly during pregnancy and due to unknown nature of many such diseases, the European Cardiac Society Guideline on cardiac disease in pregnancy recommended precise evaluation in pregnant women with dyspnea or an induced dyspnea following pregnancy (2). In the current study, women with dyspnea in the second and early third pregnancy trimesters who mostly had a NYHA class of II or III were evaluated. Most patients (92%) had no pulmonary rales but palpitation was a common finding (80%). Lab tests including routine blood and thyroid function tests were in the normal range; therefore, renal and endocrine etiologies were ruled out for dyspnea. In 54% of participants, valvular disease was diagnosed by echocardiography, which was either a mild MR or MVP. Pulmonary hypertension was detected in 12% of cases, which is of high significance. Faghizade Piri et al. (11) reported the rate of preeclampsia in pregnancy as 5% and 5.4%. The rate of preeclampsia in mothers with dyspnea was 14% in our study, which is significantly higher than the mean prevalence in normal pregnant women of our society. Based on Rahimi et al. study, preterm labor occurred in 11.7% of pregnancies in the normal population, whereas 42% of our study population had preterm labor (12). Congenital anomalies were observed in 6% of the neonates, while it was reported as 2.4% in the study by Akbarzadeh et al. (13). The mean weight of newborns was 2897.93 ± 540 grams in the present study, which was less than the mean expected weight. The same value was reported as 3232 ± 449.6 grams in a similar study (14). The mean Apgar score in the first five minutes of life was 7.64 ± 2.19 , which is less than most similar studies reporting the same score (15). Drenthen et al. studied prognosis of 2491 pregnant women with congenital heart diseases (CHD). The most common complications of pregnancy in this study population were abortion (5%), preterm labor (15%) and maternal heart complications (11%). These adverse events were more common in those with more severe cardiac involvement (16, 17). Balint studied delayed cardiac events in 405 pregnant women with CHD within a 5-year interval (18). Occurrence of such events during pregnancy was 12% and were more common in severe cyanotic disease and in cases with aortic stenosis or sub pulmonary stenosis (relative risk of 3.9 and 3.2%, respectively) (19). In the current study, only congenital anomalies were studied and delayed events were not assessed. Siu et al. studied neonatal and maternal cardiovascular events in 302 Canadian pregnant women. They observed that women with CHD were at a greater risk of maternal complications (17% vs. 1%, mainly including preterm labor and cardiac and neonatal complications (18% vs. 7%, mostly as low birth weight) compared to the control group (20). Moreover, the risk of CHD was higher in patients younger than 20 and those older than 35 years, smokers and those using anticoagulant drugs (21). Our results

were also compatible with Siu study regarding the rate of preterm labor and LBW neonates. In the study by Naghshbandi et al. in Sannandaj, prognosis of 3125 pregnant women was studied. The rate of cardiac disease was 1.6%. Therefore, the interaction between pregnancy and heart disease was evident as four cases of abortion, two cases of intrauterine fetal death (IUFD) and two neonatal mortalities were recorded (22). In another study, weight gain during pregnancy was less in women with heart disease compared to controls. Moreover, the mean weight of neonates born from mothers with heart disease was 2300 grams compared to 2730 grams among controls (23, 24). The most common types of cardiac disease among mothers were MS (22%) and MVP (20%). As the delivery method of choice in pregnant women with heart disease is NVD, 64.4% of the deliveries were performed (25, 26). Our results regarding neonates birth weight of mothers with heart disease was in accordance with these findings. In the present study, it was observed that more than 50% of patients with dyspnea had valvular disease; however, 80% of such cases were not significant clinically and did not require any intervention during pregnancy. A significant correlation was revealed between NYHA class and valvular disease, especially mitral valve involvement and increased pulmonary pressure, whereas a no significant inverse association was found with LVEF and no significant correlation with prenatal outcome, although increased prevalence in those with high NYHA class (more than II), which can be due to low number of patients. In addition, there was an increased prevalence of preterm labor, preeclampsia and Apgar < 6 in those with mitral valve disease and high sys PAP. As dyspnea is a common complaint in pregnant women, valvular disease and other important cardiovascular problems and high risk prenatal outcome should be considered, especially in those with NYHA class more than II even when other clinical findings are normal. Moreover, higher rate of valvular disease in patients with dyspnea highlights the need for more precise care and follow-up in such cases (27, 28). In addition, high prevalence of pulmonary hypertension which can be potentially life threatening if not diagnosed early, confirms this approach. On the other hand, considering the high rate of preeclampsia, preterm labor and LBW neonates in such cases, more precise follow-up of patients with valvular disease even clinically insignificant ones should be considered. This could be due to hypoxia and release of inflammatory mediators in the context of cardiac disease and fetal injury (29). Due to excluding women with thyroid or pulmonary involvement and anemia, the role of such causes in inducing dyspnea was excluded. It seems that excessive shortness of breath during pregnancy despite normal lab tests is accompanied by a high rate of valvular disease, pulmonary hypertension, ventricular disorders and congenital disease and with a poor prognosis for both mother and her fetus. As echocardiography is a simple and cost-effective modality for screening, its application in such cases and precise follow-up in those

diagnosed with valvular disease even of clinical insignificance, can be beneficial to both mother and her newborn (28). It seems that dyspnea during pregnancy especially in normal daily activities (NYHA class more than II) even with no abnormal physical findings or lab tests can be predictor of valvular disease increased prevalence of increased sys PAP and low LVEF. It also correlates with poor perinatal outcome, preterm labor, preeclampsia, low Apgar score and LBW. Screening and close follow-up of such cases is highly recommended. Echocardiography can be an easy, available and efficacious screening tool.

Authors' Contributions

Study concept and design: Dr. Tara, Vakilian; acquisition of data: Dr. Moosavi, Vakilian; analysis and interpretation of data: Dr. Salehi; drafting of the manuscript: Dr. Mogiman, Vakilian; critical revision of the manuscript for important intellectual content: Dr. Tara, Vakilian; statistical analysis: Dr. Salehi; administrative, technical and material support: Dr. Moosavi, Vakilian; study supervision: Dr. Tara.

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