Original Article

Evaluation of the cardiac function using GLS in speckle tracking echocardiography in preeclampsia and IUGR patients

Najmieh Saadati[1], Sara Masihi[1], Narges Abouali[2*], Nehzat Akiash[3], Razieh Mohammad Jafari[1], Yasaman Tahmasebi[4]

[1]Fertility, Infertility and Perinatology Research Center, Jundishapur University of Medical Sciences, Ahvaz, Iran. [2]Department of Obstetrics and Gynecology, Faculty of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran. [3]Department of Cardiology, School of Medicine, Atherosclerosis Research Center, Imam Khomeini Hospital, Jundishapur University of Medical Sciences, Ahvaz, Iran. [4]Department of Cardiology, Faculty of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran.

Correspondence: Narges Abouali, Department of Obstetrics and Gynecology, Faculty of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran. dr.narsis@hotmail.com

ABSTRACT

A higher chance of maternal cardiovascular disease in later life is linked to pregnancies complicated by preeclampsia and foetal growth restriction. Before significant cardiovascular illness manifests itself, subclinical cardiac abnormalities are discernible. An elegant way to evaluate subclinical cardiac dysfunction is to use strain measurement in conjunction with speckle-tracking echocardiography (STE). The current study sought to assess the subclinical cardiac dysfunction in mothers with preeclampsia and intrauterine growth restriction (IUGR) by measuring Global Longitudinal Strain (GLS) using the 2D STE technique). This cross-sectional research was done on pregnant individuals with preeclampsia (n=29), IUGR (n=26), or both (n=20) who were referred to the prenatal department of Imam Khomeini Hospital in Ahvaz between January 2021 and June 2022. Demographic and clinical characteristics of the patients were recorded and the patients underwent 2D STE to evaluate the cardiac function and measure GLS using 2D speckle tracking echocardiography. In the current research, seventy-five pregnant women having a mean age of 31.37 ± 6.69 years (range of 19 to 45 years) participated. The mean GLS was a significant difference between preeclampsia, IUGR, and Preeclampsia + IUGR groups (-19.97 ± 2.02 vs. -20.59 ± 1.90 vs. -18.56±0.57; P=0.001). There was no significant difference between the three groups regarding other echocardiography parameters (LVEF, LVEDD, LVESD, RVD, LAD, PWD, IWD, and PAP) (P > 0.05). The current literature results revealed that Preeclampsia with or without IUGR may be related to subclinical myocardial LV dysfunction. Thus, accurate evaluation of cardiac function by STE echocardiography is recommended for proper management of possible cardiac dysfunction in preeclampsia. Long-term follow-up with a larger sample is required to evaluate the changes in GLS during and after pregnancy.

Keywords: Preeclampsia, IUGR, Speckle tracking echocardiography, Global longitudinal strain (GLS), LV function

Introduction

Preeclampsia is a pregnancy-related disorder affecting 2 to 15% of pregnancies. It is one of the primary causes of complications including heart disease and maternal and fetal mortality [1].

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Intrauterine growth restriction (IUGR) also affects about 3-7% of pregnancies and can cause the occurrence of diseases and cardiovascular problems for the mother [2]. Since pregnancies with preeclampsia and IUGR are associated with diastolic dysfunction and subclinical changes in maternal cardiovascular function [2, 3]. Subclinical cardiac alterations can mostly be identified before major cardiovascular disease. Hence, it is crucial to examine the mother's heart function accurately in complex pregnancies using preeclampsia and IUGR [4, 5].

There are numerous non-invasive methods for assessing cardiovascular parameters in expectant mothers. There isn't a gold standard in place at the moment, and the evaluation method is chosen based on many aspects such operator training, technique availability, and cost [6]. Measurements of longitudinal, radial, and circumferential myocardial strain, as well as two-dimensional speckle tracking echocardiography (2D-STE), are sensitive and precise techniques for assessing subclinical myocardial dysfunction [4]. Fibers with sub-endocardial longitudinal arrangement are directly exposed to intra-ventricular blood pressure and have a much more sensitive coronary circulation anatomy [7]. Thus, longitudinal function is damaged in coronary artery diseases in the initial stages. Previous studies have indicated that longitudinal strain is more sensitive in diagnosing myocardial dysfunction, and it is disturbed earlier than radial and circumferential functions [7, 8]. Evaluation of global longitudinal strain (GLS) by STE is a sensitive marker for changes in LV function in pregnancies with preeclampsia and IUGR [9-11].

Low GLS in women with preeclampsia has been useful for diagnosing subclinical LV systolic dysfunction [12]. Reports also indicate that GLS is more sensitive to identifying left ventricular function than LVEF in women with IUGR, so the mean GLS in women with IUGR is lower than that in normal pregnancies. However, the left ventricular volumes and LVEF did not differ between IUGR and normal pregnancy groups [9]. Thus, given the significance of identifying cardiac dysfunction in pregnant women with preeclampsia and IUGR to prevent cardiovascular diseases in the future, the present study evaluated the subclinical myocardial function in patients with preeclampsia and IUGR using GLS measurement by 2D STE.

Materials and Methods

This descriptive-analytical resaerch was done from January 2021 to June 2022 on pregnant patients referred to the prenatal department of Imam Khomeini Hospital in Ahvaz and diagnosed with either IUGR, preeclampsia, or both. The Jundishapur University of Medical Sciences, Ahvaz Research Ethics Committee gave its approval before it could be carried out (Code of Ethics: IR.AJUMS.HGOLESTAN.REC.1401.030). Informed consent was attained from all patients before starting the study. Furthermore, the Helsinki Research Ethics Statement's rules and the patient information confidentiality guidelines were followed during the entire investigation. Census sampling was employed in this investigation, and all patients who satisfied the inclusion criteria were included in the research. Inclusion criteria included pregnant women with a definite diagnosis of preeclampsia and/or IUGR, age 18 to 45 years, and having consent to participate in the study. Exclusion criteria also included suffering from cardiovascular diseases, chronic hypertension, smoking any type of tobacco, pregnancy with a fetus with a chromosomal disorder or other structural disorders, and twin or multiple pregnancies.

Data collection

First, the demographic and clinical features of the mother, including maternal age, BMI, gestational age, gravid (number of pregnancies), parity (number of deliveries), history of infertility, history of abortion and stillbirth, and type of delivery were collected and recorded in the patient's medical record. Gestational age was determined according to the measurement of crown to rump length (CRL) in the initial ultrasound (before the 12th week of pregnancy). Preeclampsia was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg with proteinuria (≥ 300 mg of protein in 24-hour urine, or a result of at least +1 on dipstick) after 20 weeks of gestation in women with normal blood pressure before pregnancy. Additionally, blood pressure was measured at least 2 times with an interval of at least 4 hours and after 10 minutes of rest [13]. Intrauterine growth restriction (IUGR) was defined based on fetal weight estimation in ultrasound assessment as a fetal weight below the 10th percentile (<10th percentile) relative to gestational age along with pathophysiological evidence, especially abnormal Doppler [14].

Echocardiography

Patients underwent 2D echocardiography by STE method to evaluate cardiac function and measure GLS. All echocardiography examinations were performed by a cardiologist who did not know the clinical characteristics of the patients. The images were taken digitally and were reported in at least three consecutive beats. Then, they were analyzed offline by an operator using specialized software. Finally, 2D echocardiography measurements and their variables were performed based on the latest guidelines. To measure left ventricular GLS, peak systolic strain values were used in a 17-segment model. The longitudinal strain was measured in three standard apical views (2-chamber, 4-chamber, and long-axis) in two continuous cardiac cycles at rest separately for all subjects. The sum of the results of them was used to calculate the mean GLS.

Statistical analysis

For statistical analysis, SPSS-22 software (SPSS Inc., Chicago, IL, U.S.A.) was utilized. The data were described using mean, standard deviation, frequency, and percentage. The Kolmogorov-Smirnov test was used to determine whether the data were normal. The means of the quantitative variables were compared between groups using the independent t-test and one-way analysis of variance (ANOVA). Tukey's HSD test was also used for the pairwise comparison of the means of the groups. The significance level in the tests was considered to be less than 0.05.

Results and Discussion

in the current research, seventy-five pregnant women with a mean age of 31.37 ± 6.69 years (at a range of 19 to 45 years) participated. Also, their mean gestational age at the time of echocardiography was 31.68 ± 2.70 weeks **(Table 1)**. Patients were examined in three groups including 29 cases of preeclampsia (38.67%), 26 cases of IUGR (34.67%), and 20 cases with both preeclampsia and IUGR (20.67%).

Table 1. Basic characteristics of the studied patients

Variable	Group	
Mean±SD, Age (year)		31.37 ± 6.69
BMI (kg/m²), S.D±Mean		30.58 ± 3.64
BSA (m²), S.D±Mean		1.82 ± 0.12
Mean± S.D, gestational age		31.68 ± 2.7
History of infertility, frequency(%)		3.03 ± 1.61
Gravidity, frequency (%)	1 pregnancy	33 (44.0%)
	2-3 pregnancies	21 (38.0%)
	4-6 pregnancy	21 (38.0%)
Parity, frequency (%)	Nulliparous	37 (49.3%)
	Multiparous	38 (50.7%)
History of abortion, frequency (%)		15 (20.0%)
History of stillbirth, frequency (%)		9 (12.0%)
Type of previous birth, frequency (%)	vaginal	23 (60.5%)
	Cesarean section	15 (39.5%)
Doppler ultrasound results, frequency (%)	Right/left notch	34 (45.3%)
	Increased UtA-PI	59 (78.7%)
Pregnancy complications, frequency(%)	Preeclampsia	29 (38.7%)
	IUGR	26 (34.7%)
	Preeclampsia + IUGR	20 (20.7%)

BMI: Body mass index; BSA: Body surface area; UtA-PI: Uterine artery Pulsatility index; IUGR: Intrauterine growth restriction

According to the analysis of variance in **Table 2**, the mean GLS was significantly different between the three groups of preeclampsia, IUGR, and preeclampsia + IUGR (P=0.001). The results of Tukey's post-hoc test for pairwise comparison of the means of studied groups revealed no significant difference between the two groups of preeclampsia and IUGR (P=0.374). However, the mean GLS in both groups of preeclampsia and IUGR showed a significant difference only with the Preeclampsia + IUGR group (P=0.017 and P<0.0001, respectively). Other echocardiographic parameters (LVEF, LVEDD, LVESD, RVD, LAD, PWD, IWD, and PAP) were not significantly different between the three groups of preeclampsia, IUGR, and preeclampsia + IUGR **(Table 2)**. According to the echocardiography results, LVEF was normal in all patients (LVEF ≥ 50%).

Table 2. Results of 2DSTE echocardiography indices in three groups

Parameter	Preeclampsia (29 people)	IUGR (26 people)	Preeclampsia + IUGR (20 people)	*P-value
GLS (%)	-19.97 ± 2.02	-20.59 ± 1.90	-18.56 ± 0.57	0.001
LVEF (%)	54.48 ± 1.54	54.23 ± 1.83	54.46 ± 1.1	0.537
LVEDD (mm)	4.19 ± 0.26	4.06 ± 0.19	4.27 ± 0.22	0.117
LVESD (mm)	3.11 ± 0.41	3.24 ± 0.48	3.23 ± 0.40	0.609
RVD (mm)	2.68 ± 0.22	2.76 ± 0.26	2.77 ± 0.20	0.252
LAD (mm)	3.17 ± 0.51	3.15 ± 0.22	3.34 ± 0.09	0.128
PWD (mm)	0.67 ± 0.17	0.72 ± 0.18	0.64 ± 0.16	0.261
IWD (mm)	0.72 ± 0.16	0.75 ± 0.18	0.69 ± 0.14	0.524
PAP (mmHg)	22.52 ± 2.65	23.52 ± 1.55	21.85 ± 3.82	0.126

IUGR: Intrauterine growth restriction; 2DSTE: Two-dimensional speckle tracking echocardiography; GLS: Global longitudinal strain; LVEF: left ventricular ejection fraction: LVEDD: Left ventricular end-diastolic diameter; LVESD: left ventricular End Systolic Diameter; RVD: Right ventricular Diameter; LAD: Left Atricular Diameter; PWD: Posterior Wall Diameter; IWD: Interventricular Wall Diameter; PAP: Pulmonary artery pressure

* Analysis of variance test

The findings of comparing the mean GLS between two groups with and without **Table 3** displays IUGR and consequences related to preeclampsia. The mean GLS of patients with preeclampsia was considerably lower than that of patients without preeclampsia, according to the findings of the independent t-test used to compare the means between the two groups (P=0.008). Furthermore, there was a significant difference (P<0.0001) in the mean GLS between patients with preeclampsia + IUGR and those without preeclampsia + IUGR. However, the mean GLS in patients with and without IUGR was not significantly different (P=0.565).

Table 3. Comparison of mean GLS evaluated by 2D STE echocardiography

Group	Yes	No	*P-value
Preeclampsia	-19.39 ± 1.73	-20.59 ± 1.90	0.008
IUGR	-19.71 ± 1.78	-19.97 ± 2.02	0.565
Preeclampsia + IUGR	-18.56 ± 0.57	-20.26 ± 1.97	<0.0001

* Independent t-test
2DSTE: Two-dimensional speckle tracking echocardiography; GLS: Global longitudinal strain; IUGR: Intrauterine growth restriction

The findings of the current research showed that the mean GLS was different between the three groups of preeclampsia, IUGR, and preeclampsia + IUGR, so the mean GLS in the preeclampsia + IUGR was significantly lower in this group as compared to compared to two preeclampsia and IUGR groups combined. However, the mean GLS did not show any significant difference between the two groups of preeclampsia and IUGR. Additionally, the data showed that preeclamptic individuals had a significantly lower mean GLS than non-preeclamptic patients. Nonetheless, there was no discernible difference in the mean GLS between patients with and without IUGR. Furthermore, there was no discernible difference in the three groups' ventricular diameters, LVEF, or PAP, among other echocardiographic characteristics. These findings suggest that in women with preeclampsia and IUGR, GLS assessment can be utilised as a sensitive marker to identify the early stages of LV dysfunction even in the presence of normal LVEF. Other studies have also reported that preeclampsia is associated with subclinical myocardial dysfunction in the form of abnormal strain (GLS reduction) in STE [15, 16].

GLS assessment by STE is a new and accurate technique to identify left ventricular systolic function disorders. GLS indicates longitudinal myocardial contractions and is used to assess ventricular systolic function [17]. GLS measurement is an accurate, repeatable, and operator-independent method. In the general population, GLS is superior to LVEF for predicting cardiac events and all types of mortality [18]. The normal rate of GLS has been reported between -15.9 and -22.1 in different studies [19, 20]. Recently, GLS less than -20 in pregnant women has been used as an accurate marker to predict myocardial dysfunction and cardiac events during the postpartum period [21]. Other studies have also indicated that preeclampsia significantly affects the cardiac function of pregnant mothers. In the study by Paudel *et al*. the evaluation of echocardiography by speckle tracking revealed that patients with preeclampsia have less left ventricular GLS than normal pregnant women (-0.18 vs. -19.8). Also, patients with preeclampsia had larger left atrium, thicker interventricular walls, higher pulmonary artery systolic blood pressure, and higher mitral E/e index than the control group, but the LVEF of the two groups was similar [22].

In the study by Cong *et al*. women with preeclampsia had thicker left ventricular walls and higher left ventricular mass index (LVMi) compared to normal pregnant women. Also, in Speckle tracking, LVEF, tissue Doppler, and strain indices including GLS were significantly lower in the preeclampsia group [23]. In the study by Mostafavi *et al*. 2D-STE evaluation showed that pregnant women with preeclampsia have lower systolic function than normal pregnant women, which is detected as a reduction in GLS and GCS of the left ventricle [24]. The study by Ajmi *et al*. also reported that the GLS of the left ventricle is significantly reduced in the preeclampsia group [25]. These results indicate that preeclampsia can cause significant heart damage in pregnant women, which can be identified as a reduction in GLS in STE echocardiography during pregnancy.

The results of a study by Domínguez also revealed that pregnancies with IUGR fetuses were associated with a significant reduction in GLS in 2D-STE echocardiography, indicating subclinical cardiac dysfunction in these patients [26]. In the study by Orabona *et al*. the examination of cardiac function and echocardiography of three groups of pregnant women with preeclampsia, FGR, and preeclampsia + FGR revealed that the rate of left ventricular hypertrophy in the two preeclampsia groups with and without FGR was higher than the FGR alone group. However, the FGR normotensive group had smaller left ventricular mass (LVM), less EDV and ESV, and less LVM than the other two groups. The rate of GLS in the three groups did not show any significant difference. Finally, both groups of women with a history of preeclampsia or FGR showed abnormal myocardial function in speckle-tracking echocardiography. Thus, both groups of women with preeclampsia and normotensive FGR have the risk factor of clinical myocardial dysfunction and should be examined for the control of cardiovascular disorders [4]. However, in the present study, GLS in the preeclampsia group was significantly lower than in the IUGR group. However, other echocardiographic parameters were not different between the three groups. Thus, the results of our study indicate that the risk of left ventricular dysfunction is higher in preeclampsia women.

Both preeclampsia and IUGR are characterized by chronic inflammation, oxidative stress, and hypertension (in the case of preeclampsia) [27, 28]. Afterload can be the reason for the difference in the rate of left ventricular dysfunction (abnormal LV strain) in IUGR patients with or without preeclampsia (hypertension) [4]. In various clinical areas, chronic inflammation has been associated with subclinical cardiovascular changes [29, 30]. Coronary microvascular changes are the primary cause of three-quarters of cases of heart failure with preserved LVEF [31]. Inflammation and oxidative stress lead to heart failure through disruption of the nitric oxide (NO) pathway, which is an effective factor in the proper functioning of endothelial elasticity of arteries [32].

Finally, the present study revealed that the mean GLS in patients with preeclampsia with and without IUGR is significantly lower than in patients without preeclampsia. Since there is a direct association between myocardial strain parameters and left ventricular GLS reduction, despite normal LVEF, it is associated with negative pregnancy outcomes such as gestational hypertension, preeclampsia, gestational diabetes, preterm delivery, postpartum hemorrhage, premature rupture of membranes (PROM), and maternal death [33]. Therefore, 2D STE echocardiography examination of GLS can be employed as a low-cost, non-invasive, and practical means for the early detection of subclinical cardiac impairment, particularly in patients with preeclampsia. It can also be used to control and avoid other pregnancy-related issues. The minimal number of examined samples and lack of a control group (normal pregnancy) to compare echocardiogram results were two of the study's shortcomings. Also, the lack of echocardiography evaluation before and after pregnancy makes it impossible to investigate the cause-and-effect relationship between preeclampsia, IUGR, and cardiac function. Also, it is not clear whether the subclinical myocardial dysfunction is directly associated with preeclampsia and IUGR or caused by other factors such as genetic predisposition and other cardiovascular risk factors (obesity and dyslipidemia]. Thus, more accurate results can be obtained by conducting more studies with a larger sample size.

Conclusion

The findings proved that the mean GLS of the three groups was substantially differ, so the mean GLS in patients with preeclampsia with or without IUGR was considerably lower than that of patients with IUGR alone. However, other echocardiography parameters were not substantially different amongst the 3 groups. These results indicate that preeclampsia with or without IUGR can be related to subclinical myocardial LV dysfunction. Thus, accurate assessment of maternal cardiac function by STE echocardiography is recommended for proper management of possible cardiac disorders in preeclampsia. It is also recommended to conduct a study with a larger sample size and long-term follow-up to investigate and determine the clinical association of GLS changes during and after pregnancies with preeclampsia and IUGR.

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Conflict of interest: None

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Ethics statement: This investigation is approved by Jundishapur University of Medical Sciences, Ahvaz Research Ethics Committee with Ethics code of IR. AJUMS.HGOLESTAN. REC.1401.030. Informed consent was attained from all patients before starting the study. Furthermore, the Helsinki Research Ethics Statement's rules and the patient information confidentiality guidelines were followed during the entire investigation.

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