# **Original Article**





**DOI:** 10.4103/pjog.pjog\_10\_24 **Association of global cardiac sphericity index and neonatal outcomes of appropriate for gestational age fetuses, small for gestational age fetuses, and growth-restricted fetuses delivered at term in Dr. Jose Fabella Memorial Hospital: A prospective cohort study**

**Brenan Ian De Claro Capuno1 , Roberto M. Montaña1**

#### **Abstract:**

**OBJECTIVE:** The objective of this study was to evaluate and compare the global cardiac sphericity index (GCSI) of appropriate for gestational age (AGA) fetuses, small for gestational age (SGA) fetuses, and growth-restricted fetuses scanned at term in a government tertiary hospital, maternal high risk (MHR) and to determine the association between the GCSI of these three groups of fetuses and their neonatal outcomes.

**METHODOLOGY:** The study prospectively evaluated and compared the GCSI of AGA, SGA, and growth-restricted fetuses. Pregnant women at term seen at the outpatient department and scanned at the MHR clinic then eventually delivered in the same hospital from March to May 2022 were included in this study.

RESULTS: GCSIs were measured with 147 fetuses (106 AGA, 38 SGA, and 3 growth-restricted fetuses). The result indicated that the GCSI of AGA fetuses was higher than that of the SGA and growth-restricted fetuses. This study found that there is a significantly higher frequency of abnormal GSCI among SGA and growth-restricted fetuses. This study also found that there is no statistically significant correlation between the GCSI measurements of these three groups of fetuses and their neonatal outcomes.

**CONCLUSIONS:** Abnormal GCSIs were found in fetuses with an estimated fetal weight <10<sup>th</sup> percentile (more specifically in growth-restricted fetuses than in those who are just SGA) as compared with AGA fetuses. However, the correlation between an abnormal GCSI in any of these three groups of fetuses and their neonatal outcomes needs further investigation.

#### **Keywords:**

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Fetal growth restriction, global cardiac sphericity index, neonatal outcomes

# **Introduction**

Fetal growth restriction (FGR) is the second-leading cause of perinatal

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morbidity and mortality, surpassed only by prematurity.[1] About 3%-7% of all pregnancies are affected by FGR.<sup>[2]</sup> The incidence of intrauterine growth restriction (IUGR) is estimated to be approximately 5% in the general obstetric population. The prevalence, on the other hand, varies based on the population studied (as well as its geographic location) and the standard growth curves used as a reference. Infants that weigh <2500 g at term have a perinatal mortality risk that is 5–30 times higher than infants whose birth weights are in the 50th percentile when perinatal outcome is measured by weight. Infants weighing <1500 g have a mortality rate that is 70–100 times higher. Perinatal asphyxia involving multiple organ systems is one of the most significant problems in growth-restricted infants.<sup>[3-5]</sup>

The determination of the optimal delivery time is a critical clinical challenge in the management of early FGR fetuses, as it requires a balance between the risks of prematurity and stillbirth, as well as the risks of severe intrauterine hypoxia and organ damage due to insufficient tissue perfusion. Once early FGR is diagnosed, management of this pregnancy should be close to fetal monitoring in a tertiary‑level fetal medicine and neonatal unit. Doppler velocimetric evaluation of the umbilical artery, middle cerebral artery and ductus venosus, biophysical profile scoring, and cardiotocographic assessment of fetal heart rate short-term variation are used for surveillance and timing of delivery of early growth-restricted fetuses.<sup>[6]</sup>

The global cardiac sphericity index (GCSI) is a measurement of the shape of the four-chamber view of the heart. The heart is normally an ellipsoid-type shape and when it becomes more globular it suggests to have a potential cardiac dysfunction. It is derived by calculating the ratio between the basal–apical length (BAL) and transverse width during the end‑diastolic phase. The sphericity index has been examined in adult and pediatric patients and found to be a useful tool for detecting abnormal cardiac function resulting from remodeling of the ventricular chamber.[5]

Screening fetuses at risk for ventricular dysfunction of the fetal heart have focused primarily on alterations of the anatomy and size of the four-chamber view, followed by further evaluation using pulsed Doppler ultrasound, speckle tracking, and other imaging modalities. However, recent studies have suggested that the shapes of the right and left ventricles and atrial chambers are abnormal when FGR is present because the fetal heart may adapt by altering the size of the atrial and ventricular chambers as well as increasing the thickness of the ventricular and septal walls in various disease states.<sup>[5]</sup>

The aim of the study is to find out if the size and shape of the four‑chamber view of the fetal heart (measured as GCSI) is altered or affected in small for gestational age (SGA) fetuses (i.e., those whose sonographic estimate of fetal weight [SEFW] is  $<10<sup>th</sup>$  percentile but  $>3^{rd}$  percentile), more so in growth-restricted fetuses (i.e., those whose SEFW is  $\langle 3^{rd}$  percentile or  $\langle 10^{th}$  percentile but accompanied by abnormal umbilical artery pulsatility index (PI) or cerebroplacental ratio). It will also investigate if the GCSI associates with other neonatal outcomes such as low Apgar score or birth depression, neonatal intensive care unit (NICU) admission, and presence of any neonatal cardiac abnormality of complication

# **Objectives**

### *General objective*

This study is designed to determine and compare the GCSI and neonatal outcomes of appropriate for gestational age (AGA) fetuses, SGA fetuses, and growth-restricted fetuses scanned at term  $(\geq 37$  weeks' gestation) in a government tertiary hospital, maternal high risk (MHR) Clinic from March to May 2022.

# *Specific objectives*

- 1. To determine and compare the demographic and clinical profile of pregnant patients included in the study and grouped according to whether their fetus is AGA, SGA, or growth-restricted fetus
- 2. To compare the mean and range GCSI of the fetuses scanned in a government tertiary hospital MHR at term (≥37 weeks' gestation) and grouped according to whether they are AGA, SGA, or growth-restricted fetuses
- 3. To compare the incidence of the following adverse neonatal outcomes among the abovementioned three groups of fetuses (AGA, SGA, and FGR) on their delivery:
	- Birthweight  $<$ 10<sup>th</sup> percentile
	- Apgar score <7 at 1 min
	- Apgar score <7 at 5 min
	- NICU admission
	- Any cardiac abnormality or complication diagnosed before discharge.
- 4. To determine if there is an association between the GCSI measurement and the incidence of each of the above‑mentioned neonatal outcomes among the three groups of fetuses.

# **Methodology**

# **Study design and study period**

This was a prospective cohort study done among pregnant women at term (≥37 weeks' gestation) seen at the outpatient department (OPD) and scanned at the MHR Clinic in a government tertiary hospital and then eventually delivered in the same hospital from March to May 2022.

# **Study setting**

The study was conducted in a government tertiary hospital with a 500-implementing bed capacity where many low-risk and high-risk pregnant patients within Metro Manila and neighboring provinces seek prenatal consultation.

# **Study subjects**

### *Inclusion criteria*

- 1. Pregnant patients 18 years old and above
- 2. Carrying singleton pregnancies >37 weeks age of gestation
- 3. Consulting at the OPD and referred to the MHR Clinic for third-trimester ultrasound
- 4. Who consented to participate in the study.

# *Exclusion criteria*

- 1. Those carrying fetuses with aneuploidy, congenital, or structural anomalies
- 2. Those carrying multiple gestations
- 3. Those with uncertain gestational age (unsure of last menstrual period (LMP), irregular menses, no first-trimester scan, etc.)
- 4. Those who are in labor.

### *Withdrawal criteria*

- 1. Patients who consented to participate and underwent third-trimester ultrasound but did not deliver in the same hospital
- 2. Patients who initially consent but later request to withdraw from the study.

### **Data collection, methods, and tool**

The sample size was computed based on the 2021 Hospital Neonatal Statistics showing that 9093 births were AGA and 521 were SGA and was determined using Cochran's formula. The sample size was computed to be 92 patients for AGA fetuses and 55 for SGA fetuses. All pregnant patients consulting at the OPD who met the inclusion and exclusion criteria were included in this study.

The demographic, age of gestation, presence of medical complications, biometric parameters, Doppler velocimetry studies, and measurement of the GCSI were done. Neonatal outcomes (birthweight, Apgar score, and NICU admission) were collected. These data were divided into three groups  $-$  (1) AGA, (2) SGA, and (3) growth‑restricted fetuses —‑ based on the SEFW and fetal Doppler velocimetry findings during ultrasound.

### **Study procedure**

The study protocol was reviewed by the technical and ethics committee of the hospital. The primary investigator oriented the OB‑GYN residents rotating at the DJFMH OPD on the objectives and methods of the study. They were instructed to refer to the primary investigator or any perinatology or maternal-fetal medicine (MFM)

fellow on-duty at the OPD MHR Clinic any patient who qualified to the study based on the inclusion/exclusion criteria mentioned above.

Subsequently, the demographic and clinical data of the patient required for the research were obtained by the primary investigator or by any perinatology or MFM fellow on-duty at the MHR Clinic and documented using the data collection form.

The information collected from this research was kept confidential. The name and other identifying information were not written in the data collection form. The patients were represented by an alphanumeric code whose identity was only known to the primary investigator. In addition, the information contained in the data collection form will be stored for 3 years in a cabinet with a lock and key and in a computer protected by a password which is only known primary investigator after 3 years all the data collection forms will be shredded and the data in the computer will be deleted.

The primary investigator also oriented the other perinatology or MFM fellows regarding the study including demonstrating how to take the fetal GCSI.

Figure 1 shows the procedure for taking and measuring the GCSI.

- 1. An image of the four-chamber view of the fetal heart during end diastole was obtained by reviewing the frame-by-frame clip of the scan of the said view until the first downward systolic motion at the junction of the annulus of tricuspid and mitral valve occurred. The frame just before this view was identified for measurement of the GCSI
- 2. On the identified frame, the BAL was measured by identifying the longest length from the base of the atrial chambers to the apex of the ventricular



**Figure 1:** Measurement of global cardiac sphericity index as described by Hobbins *et al*. [7]

chambers (as shown in the image above, Figure 1)

- 3. Then, the transverse length (TL) was measured orthogonally to the BAL from the epicardial borders at the widest part of the four-chamber view [Figure 1]
- 4. Finally, the GCSI was computed using the following formula: BAL/TL
- 5. An image of the four‑chamber view of the fetal heart during end diastole was obtained by reviewing the frame‑by‑frame clip of the scan of the said view until the first downward systolic motion at the junction of the annulus of tricuspid and mitral valve occurred. The frame just before this view was identified for measurement of the GCSI
- 6. On the identified frame, the BAL was measured by identifying the longest length from the base of the atrial chambers to the apex of the ventricular chambers (as shown in the image below)
- 7. Then, the TL was measured orthogonally to the BAL from the epicardial borders at the widest part of the four-chamber view [Figure 1]
- 8. Finally, the GCSI was computed using the following formula: BAL/TL.

Then, the requested ultrasound procedures were performed by the primary investigator or by any perinatology or MFM fellow on‑duty at the MHR Clinic. The procedures were done using a Samsung WS80A ultrasound machine equipped with S‑Vue convex transducer. Measurement of the GCSI was only done once on the patient and was checked by the MFM consultant on‑duty at the MHR Clinic.

Finally, the neonatal outcomes of all patients or subjects included in the study were followed up also by the primary investigator or by any perinatology or MFM fellow on-duty after delivery.

### **Data analysis**

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) software (version 24) (IBM Inc., Chicago, IL, USA). Mean and standard deviation were used to present continuous variables. The normality distribution of the continuous variables was checked using the Kolmogorov–Smirnov test. Analysis of variance was used to compare the continuous variables between the groups. Categorical variables were presented using frequency and percentage. The Fisher's exact test was used to compare the distribution pattern of categorical variables between the groups. Finally, the relationship between FGR and SGA sphericity indices with reference to the control group was assessed using multivariate logistic regression *P* < 0.05 was considered statistically significant.

### **Results**

A total of 147 subjects consented to participate and were assessed in this study. AGA fetuses were observed in 106 (72.10%) of the subjects, SGA fetuses in 38 (25.85%), whereas 3 subjects (0.02%) were fetal growth-restricted (FGR). Thus, meeting the required sample size of at least 92 subjects for the AGA group, whereas falling short by 14 for the SGA group which is only 41 subjects instead of the required 55.

The mean maternal age of the AGA group, SGA group, and FGR group was  $27.58 \pm 5.86$ ,  $27.13 \pm 7.61$ , and  $27.67 \pm 6.03$  years, respectively. There was no significant difference between the groups in terms of maternal age (*P* value: 0.7415) [Table 1]. In terms of parity, the AGA and SGA groups had the highest median parity of 1. In terms of the mean, AGA had the highest parity of 1.33. However, statistical tests using the nonparametric Kruskal–Wallis test showed that the median parity across groups was equal. Parity did not significantly differ across groups (*P* = 0.1754) [Table 1].

In terms of gestational age, the SGA group had the highest median of 38 weeks AOG. Similarly, the SGA group also had the highest mean gestational age of 37.97 weeks AOG. However, statistical tests using the nonparametric Kruskal–Wallis test also showed that the median gestational age across groups was equal. Gestational age did not significantly differ across groups (*P* = 0.1701) [Table 1].

Medical complications were observed in 54 of the subjects. Out of which, 4 had chronic hypertension, 6 had preeclampsia with severe features, and 44 had gestational diabetes mellitus. The proportion of those with chronic hypertension, preeclampsia, and gestational diabetes mellitus did not significantly differ across groups  $(P = 0.084)$  [Tables 2-7].

A GCSI value of <1.08 is considered abnormal as cited in the study of DeVore *et al*., wherein 55 out of 300 fetuses had

### **Table 1: Different parameters across the study groups**



AGA: Appropriate for gestational age, SGA: Small for gestational age, FGR: Fetal growth restriction, SD: Standard deviation

a GCSI of below the  $5<sup>th</sup>$  percentile (<1.08), of whom  $96\%$  (53 of 55) had abnormal ultrasound findings.[8] If we consider a GCSI value of <1.08 as abnormal based on this previous study and apply this to this study, the frequency of abnormal GCSI among AGA, SGA, and growth‑restricted fetuses is shown in Table 8. Analysis revealed that there is an increased incidence of abnormal GCSI among SGA and FGR fetuses. As a matter of fact, all three fetuses identified to be FGR in this study have abnormal GCSI.

Comparing the GCSI measurements itself across groups, AGA had the highest median GCSI of 1.17. In terms of the mean, the AGA group also had the highest GCSI of 1.19. The differences from other groups were proven to be significant by the Kruskal– Wallis test. It showed that at least one group had a different median  $(P = 0.0017)$  [Tables 9 and 10]. Further tests showed that the AGA group's mean GCSI was significantly different from the mean GCSI of SGA and FGR. Meanwhile, FGR's and SGA's mean GCSI were statistically equal [Table 11].

The neonatal outcomes of the three groups of fetuses (AGA, SGA, and FGR) were also compared in this study. In terms of the proportion of fetuses with APGAR <7 at 1 min, FGR had the highest percentage at 66.67%. The differences from other groups were proven to be significant by Fisher's exact test. It showed that the percentages across

### **Table 2: Occurrence of chronic hypertension among groups**



AGA: Appropriate for gestational age, SGA: Small for gestational age, FGR: Fetal growth restriction

### **Table 3: Proportion of chronic hypertension among groups**



### **Table 4: Occurrence of preeclampsia among groups**



AGA: Appropriate for gestational age, SGA: Small for gestational age, FGR: Fetal growth restriction

#### **Table 5: Proportion of preeclampsia among groups**



groups were not equal. The proportion of those with APGAR <7 at 1 min significantly differed across groups (*P* = 0.025) [Table 12].

In terms of the proportion of fetuses with APGAR <7 at 5 min, AGA had the highest percentage at 0.94%. It was not observed among SGA and FGR groups. The difference from other groups was proven to be not significant by Fisher's exact test. The proportion of those with APGAR <7 at 5 min did not significantly differ across groups  $(P = 1.000)$  [Table 13].

In terms of the proportion of NICU admissions, the FGR group had the highest percentage at 100.00%. The differences from other groups were proven to be significant by Fisher's exact test. It showed that the percentages across groups were not equal. The proportion of those admitted to NICU significantly differed across groups  $(P = 0.003)$  [Table 14].

Correlating between the GCSI measurement and the incidence of each of the neonatal outcomes among the

### **Table 6: Occurrence of gestational diabetes mellitus among groups**



GDM: Gestational diabetes mellitus, AGA: Appropriate for gestational age, SGA: Small for gestational age, FGR: Fetal growth restriction

### **Table 7: Proportion of gestational diabetes mellitus among groups**



### **Table 8: Frequency of abnormal global cardiac sphericity index among groups**



GCSI: Global cardiac sphericity index, AGA: Appropriate for gestational age, SGA: Small for gestational age, FGR: Fetal growth restriction

### **Table 9: Comparison of global cardiac sphericity index among groups**



GCSI: Global cardiac sphericity index, AGA: Appropriate for gestational age, SGA: Small for gestational age, FGR: Fetal growth restriction, SD: Standard deviation

three groups of fetuses (AGA, SGA, and FGR) showed that the association was found to be not statistically significant [Tables 15-17].

### **Discussion**

This prospective study evaluated and compared the GCSI of AGA fetuses, SGA fetuses, and growth‑restricted fetuses. The result indicated that the GCSI of AGA fetuses was higher (mean of 1.19) than that of the SGA and FGR fetuses (mean of 1.13 and 1.05, respectively). If a value of <1.08 is used as the criteria for an abnormal GCSI based on previous studies of DeVore *et al*., this study found that there is a significantly higher frequency of abnormal GCSI among SGA and FGR fetuses. As a matter of fact, in this study, all FGR fetuses had abnormal GCSI.

In the study of Pérez-Cruz M, Cruz-Lemini M, Fernández MT, Parra JA, Bartrons J, Gómez-Roig, *et al*., which included the measurement of GCSI among 150 FGR fetuses, results showed that the sphericity indices

### **Table 10: Kruskal–Wallis Test of global cardiac sphericity index among groups**



#### **Table 11: Difference of global cardiac sphericity index among groups**



FGR: Fetal growth restriction

#### **Table 12: Proportion of APGAR score of <7 at 1 min among groups**



AGA: Appropriate for gestational age, SGA: Small for gestational age, FGR: Fetal growth restriction

#### **Table 13: Proportion of APGAR score of <7 at 5 min among groups**



AGA: Appropriate for gestational age, SGA: Small for gestational age, FGR: Fetal growth restriction

were significantly lower in FGR fetuses compared with the AGA fetuses which were in line with the findings of this study wherein the GCSI among SGA and FGR fetuses were lower than the AGA fetuses.

In a similar study by Devore *et al*., which included 300 fetuses, a GCSI below the 5<sup>th</sup> percentile was observed in 55 fetuses. They reported that the measurement of the TL was significantly higher in FGR fetuses compared to AGA fetuses, whereas the BAL was lower than the AGA fetuses resulting in a lower GCSI and a more globularly shaped heart. This finding was also in line with the findings current study.

Conversely, the study of Borna *et al*., where 160 subjects were assessed, reported that the measurements of the BAL, TL, and GCSI had no significant effect on FGR and SGA, which was in contrast with the findings of this study. The difference in the results may be due to differences in the gestational ages of the fetuses included in the two studies which were lower in the study of Borna *et al*. (mean AOG of 32 weeks) as compared to term fetuses in this study. This can be explained by the mechanism of adaptation of the fetal heart which becomes globular in the presence of adverse conditions including IUGR,

### **Table 14: Frequency of neonatal intensive care unit admission among groups**



AGA: Appropriate for gestational age, SGA: Small for gestational age, FGR: Fetal growth restriction





GCSI: Global cardiac sphericity index, SD: Standard deviation

### **Table 16: Correlation of global cardiac sphericity index with APGAR score of <7 at 5 min**



# **Table 17: Correlation of global cardiac sphericity index with neonatal intensive care unit admission**



GCSI: Global cardiac sphericity index, SD: Standard deviation, NICA: Neonatal intensive care unit

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diabetes, or other congenital heart diseases which are usually diagnosed later in pregnancy.[9]

This study also found that there is no statistically significant correlation between the GCSI measurements of these three groups of fetuses (AGA, SGA, and FGR) and their neonatal outcomes. No other cardiac abnormalities were documented in any of the newborn babies included in this study. However, follow‑up echocardiographic evaluation needs to be done later for babies with abnormal GCSI (who are usually those with FGR) to determine the possible effects (if any) of the cardiac remodeling that transpired in these fetuses, whereas they were in utero. Perhaps also, because of the rarity of FGR, more so of cardiac abnormalities, there is a need to investigate a larger sample size to determine the correlation between these two.

The strength of this study, aside from its prospective design, is that measurement of the GCSI only involves the computation of the ratio of the BAL and the TL and can be easily obtained by trained sonologist. Furthermore, the measurement can be used as a screening examination of the fetal heart. This can be applied to patients being seen in this tertiary government hospital to identify and monitor fetuses with abnormal GCSI findings.

# **Summary, Conclusion, Limitations, and Recommendations**

This prospective study demonstrated that abnormal GCSI was found in fetuses with an estimated fetal weight  $<$ 10<sup>th</sup> percentile (more specifically in growth‑restricted fetuses than in those who are just SGA) as compared with AGA fetuses. However, there is no significant statistical correlation between an abnormal GCSI in any of these three groups of fetuses (AGA, SGA, and FGR) and their neonatal outcomes. Mothers of babies with abnormal GSCI were advised of lifestyle modifications and regular monitoring of their babies for the possibility of cardiac dysfunction during infancy, childhood, and adulthood. Further study with a bigger sample is warranted to identify which of these fetuses is at risk of developing cardiac dysfunction during neonatal, infancy, and childhood periods.

This study had some limitations. First, is that, as mentioned above, the required sample size for SGA fetuses were not met. During the data collection period, only 41 patients were identified as SGA, out of which only 3 were FGR fetuses. The correlation of GCSI with estimated fetal weight can be assessed more robustly if there are more subjects. Second, only the GCSI was measured for all the subjects. Abnormal GCSI, as mentioned above, must warrant further examination in the form of a detailed fetal echocardiogram to assess the possible presence of adverse cardiac neonatal outcomes. Third, neonatal outcomes which include the possibility of a cardiac abnormality are not further assessed beyond mere physical examination of the heart of the newborn after delivery.

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# **Authorship contributions**

Brenan Ian De Claro Capuno - Involved in the conceptualization, methodology, validation, formal analysis, data curation, writing of the original draft, review and editing.

Roberto Montojo Montaña - Involved in the conceptualization, methodology, validation, formal analysis, data curation, writing of the original draft review and editing.

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# **Conflicts of interest**

There are no conflicts of interest.

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