Objective:
Silhouette ultrasound can demonstrate both outer and inner structure in a single image (Figure 1). The objectives of the present study are to determine the prevalence of LSE in human fetuses in the first trimester between 11 and 13 weeks of gestation by three-dimensional ultrasound, to analyze relationship between fetal LSE in the first trimester and genetic cause, and between LSE and associated congenital abnormalities.

Patients and Methods:
Between October of 2013 and December of 2017, a total of 12,671 cases visited our institute for first trimester scan (FTS) were enrolled in this study. The ultrasound equipment used in this study was Voluson E8 and E10 (GE healthcare, Milwaukee, USA) with three-dimensional transabdominal and transvaginal transducers. Fetal profile was demonstrated by 3D ultrasound and the ear position was confirmed. LSE was defined when the upper end of ear pinna is located below the line between the canthus and occiput. In borderline cases, silhouette ultrasound was used for determination of external ear position (Figure 2). The ear-position evaluation line was determined as and extension line connecting the anterior center of the lens and the end of hyaloid and LSE was defined when the upper end of ear pinna was below the evaluation line. In LSE group, ratios of genetic abnormalities and morphological abnormalities were retrospectively investigated.

Results:
Results of this study was summarized in Figure 3. In 12,671 cases, LSE was detected in 948 cases (7.5%) as shown in Figure 7. In a group of LSE, genetic tests (CVS or amniocentesis) were done in 791 cases (83.4%). Results of genetic test, abnormal G-band karyotype was found in 292 cases (36.9%), including 281 aneuploidy and 11 chromosomal structural abnormality. SNP microarray was done in 123 cases (24.6%) out of negative G-band group, and abnormal copy number variation (CNV) was found in 12 cases including nine pathogenic CNVs and three likely-pathogenic CNVs. In a total of negative LSE, genetic tests (CVS or amniocentesis) were done in 5,396 cases (46.0%). Results of genetic test, abnormal G-band karyotype was found in 232 cases (4.3%), including 220 aneuploidy and 12 chromosomal structural abnormality. SNP microarray was done in 90 cases (1.7%) out of negative G-band group, and abnormal copy number variation (CNV) was found in 5 cases including three pathogenic CNVs. Figure 4 shows the significance difference of genetic aberration ratio between LSE(+) group and LSE(-) group. LSE(+) group contained 38.4% of abnormal genetic results and LSE(-) group contained only 4.4%. Itemised genetic results in a total of 304 cases with genetic aberration in LSE(+) group (Figure 4), showing 118 cases of Trisomy 21(38.8%), 105 cases of Trisomy 18 (34.5%), 25 cases of Trisomy 13 (8.2%), 17 cases of 45,X, 16 other aneuploidy (5.3%) 11 chromosomal structural abnormality (3.6%) and abnormal CNVs (3.9%). In 499 cases of normal genetic test with LSE(+), morphological abnormalities were confirmed by ultrasound in 49 cases (10.1%) containing congenital heart disease (42.9%), central nervous system (14.3%), multiple anomalies (28.6%), skeletal dysplasia (10.2%) and facial anomalies (4.1%). From our data in this study, in total of congenital diseases including genetic and morphological abnormalities were confirmed in a total of 44.6% of LSE group as shown in Figure 5. Furthermore, cases of LSE with micrognathia had significantly higher incidence of abnormal genetic result than cases of LSE without micrognathia as shown in Figure 6. Lastly, isolated LSE without any morphological abnormality case was found in 31 cases in our study. Ten cases did not appear for a subsequent ultrasound scan and follow-up scan was performed in 21 cases and confirmed normalized ear position at 18-20 weeks of gestation in all cases.

Conclusions:
In this study, we discovered the new method using recent advanced ultrasound application of silhouette ultrasound for detecting landmarks of exact evaluation line for assessment of ear position. From our results, it was obvious that fetal LSE in the first trimester should be strongly associated with congenital abnormalities of both genetic aberration and morphological abnormalities. Our results indicated that LSE in the first trimester can become one of useful ultrasound markers for screening fetal congenital diseases.

P20.01 Lowset ear detected by three dimensional ultrasound in the first trimester and genetic cause
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Figure 3. Lowset ear positive and negative groups in 12,671 cases with first trimester scan

Figure 4. Abnormal genetic results in lowest ear (LSE) positive and negative groups. Table shows the itemised genetic aberration and ratio in a total of 304 lowest ear positive cases.

Figure 5. Congenital abnormality ratio in lowset ear positive group Totally 44.6% had congenital abn. in LSE positive group.

Figure 6. Genetic aberration ratio in micrognathia (MGN) positive and negative group in lowest ear (LSE) cases.