Abstract: Prediction of the viability of early intrauterine pregnancies by using ultrasound scan parameters - PEPU Study (A prospective cohort study)

Introduction: Ultrasound scan (USS) is the investigation of choice to diagnose the viability of an intra-uterine pregnancy. To confirm the viability, it is essential to demonstrate the cardiac activity of the fetus. But, in pregnancies of uncertain viability (PUV) to confirm the viability status, it needs serial ultrasound scan evaluations. There is no uniformity in the evaluation criteria used at present to discriminate viable from non-viable pregnancy by using the ultrasound parameters. Missing a viable pregnancy will unfortunately lead to a termination of one fetus, which may destine to be one human live birth in future. On the other hand, continuous surveillance without demonstrating desirable outcome will increase the anxiety over time; eventually will lead to a significant negative impact on woman's physical as well as psychological wellbeing.

Objectives: To determine the minimum ultrasound scan cut off values to predict the subsequent viability of an intrauterine pregnancy of uncertain viability.

Methods: This prospective cohort study was carried out in Castle Street Hospital for Women (Ward 7, Gynaecology Unit) and Colombo South Teaching Hospital (University Obstetrics and Gynaecology Unit). Women who presented in early pregnancy with pre-defined selection protocol were recruited to the study until the sample size (n = 348) is achieved. The Sample was categorized in to three groups as gestational sac only, gestational sac with yolk sac only and fetal pole without cardiac activity. The ultimate end point is to demonstrate the fetal cardiac activity in each group during the follow up. The sensitivity, specificity, positive predictive value and false positive rate (FPR) were calculated in each group by using Receiver Operating Characteristic curves with regard to the reference cut off values which used in different guidelines.

Results: Among the 348 women who were included in the study and diagnosed initially as having pregnancy of uncertain viability, 227 (65%) women were found to have viable pregnancies in subsequent scans, while 121 (35%) pregnancies were subsequently diagnosed as non-viable pregnancies. Presence of yolk sac, when

compared to gestational sac only group, improves the outcome by increasing the number of viable pregnancies ($p < 0.05$). In the gestational sac only group when the mean sac diameter (MSD) is 16 mm, the false positive rate (viable pregnancy) for a miscarriage was 21.9%. At the MSD of 20 mm the FPR declined to 1.9% and above 21 mm there was no misdiagnosis for a miscarriage where FPR is 0%. In the gestational sac with yolk sac group FPR for miscarriage was 20.5% at MSD of 16 mm, 1.3% at 20 mm and 0% beyond 21 mm. In fetal pole without cardiac activity group FPR for miscarriage was 51.4% at crown rump length of 4 mm, 17.4% at CRL of 5 mm. Above the CRL of 5 mm the FPR was 0% for a non-viable pregnancy.

Conclusions and Recommendations: The findings of this study support the current Royal College of Obstetricians and Gynaecologists recommendation in managing pregnancies of uncertain viability criteria. Even though we were unable to demonstrate fetal cardiac activity above MSD of 21 mm, given the consideration of intra and inter observer variability in obtaining USS parameters, it appears to be a safe option to adhere to the current cutoff of 25 mm to avoid any inadvertent interventions. Above 5 mm CRL there were no demonstrable fetal cardiac activity in subsequent scans suggests that inter and intra observer variability adjusted fetal pole cut off of 7 mm is the margin of choice to diagnose a miscarriage.

Key words: Pregnancy of uncertain viability, Mean sac diameter, Crown rump length, Miscarriage