A Retrospective Comparison of Prenatal Diagnosis of Congenital Heart Defects

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A. Study Purpose and Rationale

Congenital Heart Defects (CHD) make up a major component of all recognized congenital anomalies. Cardiac anomalies are the most common birth defects worldwide with an incidence of 4 to 8 per 1000 live births. These anomalies, despite medical and surgical advancements, continue to represent significant morbidity and mortality (approx. 20% of neonatal deaths). Specific factors that increase a mother's likelihood of carrying a fetus with CHD include: a family history of CHD, maternal age >35, coexisting maternal disease, exposure to teratogens and rubella infection.

In the US, screening for congenital cardiac abnormalities is a part of the routine ultrasonographic assessment made during the 2nd trimester. This ultrasound is usually completed between weeks 18 and 22 of gestation. This transvaginal ultrasound is routinely used to detect fetal number, location of gestational sac, gestational age, amniotic fluid volume, presentation, generalized fetal anatomy and detection of fetal heart motion. Improvements in obstetric sonographic cardiac assessment in the last 10 years have been expanded to include the four chamber view as well as detection of rate and rhythm. These improvements as well as others have lead to the increase in prenatal sonographic diagnosis of potentially critical CHD.

Once the obstetric sonogram has been described as abnormal and a flag has been raised to the possibility of a cardiac anomaly, fetal echo is often done. This can be completed by obstetric fetal-medicine physicians or pediatric cardiologist. This technology is particularly more time consuming, but boasts 2D and even 3D imaging as well as Doppler flow techniques. While there is literature describing fetal echo performed as early as week 13, adequate assessment is not usually possible until at least week 18. Even then, accurate assessment is dependent on fetal activity and position, maternal size, amniotic fluid volume, availability of equipment and expertise. For many of those infants suspected of having abnormalities, a fetal echo is the modality of choice to provide a detailed look and further prognostic data.

Since most of the cardiac abnormalities will be detected in women with low risk, (i.e. no family history, history of teratogenic or infectious exposure, and without maternal comorbidities) the question has been raise as to whether fetal echo should be routinely performed. However, given the relatively low population incidence it has become abundantly clear that implementing this technique as a part of the routine screening exam is unnecessary. It is very costly and will in most cases confirm a normal diagnosis. In those high risk cases, however, the literature describes an increase in prenatal detection and a more accurate diagnosis. In these high risk cases and low risk cases with identified lesions, early, accurate detection is important for counseling as to postnatal prognosis, immediate postnatal care coordination, and the option of termination.

Few studies have examined in utero diagnosis of suspected cardiac defects as compared to postnatal echocardiography, clinical examination and/or autopsy. Several studies, however, have suggested that collaborative efforts with pediatric cardiologists are beneficial for diagnosis. Thus with this collaborative spirit, the purpose of this study is to determine retrospectively the accuracy of ultrasonographic and fetal echocardiogaphic diagnosis of congenital heart defects. We will compare diagnosis in a non selected population of women seen in conventional obstetric clinics to those seen in the newly formed multidisciplinary center, the Center for Prenatal Pediatrics, by comparing prenatal diagnosis with postnatal outcomes at one major institution in the US.

B. Study Design and Statistical Analysis

This will be a retrospective study evaluating the accuracy of diagnosis of congenital heart defects (CHD) via prenatal ultrasound and in many cases concomitant fetal echocardiography of pregnant women who received prenatal testing and delivered at this institution in one calendar year. The primary outcome of this study is to compare accuracy of diagnosis between those women seen in 1 calendar year, 2004, by the general obstetrics clinics and those referred to the Center for Prenatal Pediatrics for a multidisciplinary approach.

The study population is to consist of all women seen at this institution, including referrals, whose fetuses were diagnosed prenatally or postnatally with a congenital heart defect that could have theoretically been detected in utero. Diagnosis will be considered the final prenatal diagnosis, by sonogram *or* echo, in cases where there is discrepancy. This diagnosis will be compared to the postnatal clinical, autopsy, or fetal echo findings.

CHD outcomes will be categorized into 2 separate groups- critical and noncritical lesions. The critical lesions will consist of those requiring surgical repair or catheterization to preserve function within the 1st month of life. The noncritical lesion will be classified as that which requires no intervention. When multiple lesions are present, the lesion most important for survival will be the identifier; however the other lesions will be reported.

The proposed method of analysis is to include all pregnant women seen at Columbia Presbyterian Sloan Hospital for Women in New York City including those at both low and high risk for fetal CHD. Our goal is compare prenatal diagnosis data yielded from transvaginal ultrasound and fetal echocardiogram with the postnatal diagnosis determined clinically with postnatal echocardiography, clinical assessment and autopsy. This data will be compiled as discrete data as proportions. Sensitivity, specificity, positive predictive value and negative predictive values will be calculated from this data. From this information a comparison will be made between those subjects seen in the regular obstetrics and gynecology practice and those referred specifically to be seen by the Center for Prenatal Pediatrics, for a multidisciplinary approach. The chi-square test with statistical significance set as $p<0.05$ will be used to evaluate if there is a significant change in accuracy of diagnosis between the two study groups.

If power analysis is calculated via the chi-square test at 80% power to detect a 25% difference in accuracy, the proposed sample must include at least 130 study subjects; groups: 65 regular patients and 65 patients seen in the CPP.

C. Study Procedure

All fetuses diagnosed with CHD by transvaginal ultrasonography and transabdominal fetal echo seen at this institution in the 2004 calendar year will be included in this study. The study groups will be divided into those seen in the CPP and those seen by the conventional methods (seen by obstetrics with referral to pediatric cardiologist for complicated lesions at the discretion of the physician). The prenatal and postnatal records of the mother and infant up until 1 month will be searched for cases with a prenatal and/or postnatal diagnosis of cardiac abnormality to include both false positives and false negatives.

The transvaginal ultrasound was performed by many obstetric sonographers of varying experience levels. Fetal heart scans were performed by pediatric cardiologists using conventional echocardiographic equipment. In the CPP all transvaginal ultrasounds were read by an experienced maternal-fetal medicine physician. For all referral cases to the CPP all outside sonograms were repeated.

D. Study Drugs

There were will be no drugs used in this study.

E. Medical Device

No medical devices will be used during the course of this study

F. Study Questionnaires

No study questionnaires will be used in this study.

G. Study Subjects

The study population is to include pregnant women who received some or all of their prenatal obstetric care at the Columbia Presbyterian Sloan Hospital for Women. These subjects had fetuses and/or infants who were diagnosed either prenatally or as newborns with a congenital heart disease. Exclusion criteria includes women who were never seen at this institution for prenatal scan prior to conception or abortion (elective and spontaneous).It also includes abnormalities that one could not diagnose prenatally, including patent foramen ovale (PFO) and patent ductus arteriosus (PDA). Arrhythmias detected prenatally are also excluded.

There will be two groups of study patients upon which comparison will be made. Group one will include those seen in the Center for Prenatal Pediatrics (CPP), a multi-disciplinary center for women with potentially complicated diagnosis to have available access to pediatric specialists in every field. The other group will be comprised of all other women who were followed in other prenatal clinics, who were at no time followed by the CPP, but received their prenatal care and delivered at this institution.

H. Recruitment of Subjects

As this is a retrospective trial, no active recruitment will be done. All of the data that will be used in this study will be elicited from the subjects' prenatal, delivery records and the infant neonatal records until day of life 30. The infant records will be obtained as need to discern whether a new or previously identified defect was detected via scan or on clinical assessment. It will also be used to determine if surgical or medical intervention was required.

I. Confidentiality of Study Data

HIPAA regulations will be strictly adhered. All study data will be de-identified. All study subjects' protected information will be compiled in a password restricted data file and all paper records will be stored under lock and key.

J. Potential Conflict of Interest

There are no conflicts of interest in this study. No one involved has a proprietary interest or will stand to gain financially from the information elicited in this study.

K. Location of Study

This study will take place at Columbia Presbyterian Medical Center's Department of Obstetrics and Gynecology at the Center for Prenatal Pediatrics.

L. Potential Risks

As this study is being conducted retrospectively there is no risk for the study subjects.

M. Potential Benefits

No individual benefits will be reaped through the conduct or publication of this study but there are potential long term benefits for prenatal screening and diagnosis.

N. Alternative Therapies

No alternative therapies will be given in this study.

O. Compensation to Subjects

There will be no compensation provided to individuals used in this study.

P. Costs to Subjects

Participation in this study is of no cost to the subjects.

Q. Minors as Research Subjects

Since this study is to be conducted on a population that includes minors, it is likely that women under the age of 18 will be included in this study.

R. Radiation or Radioactive Substances

While the scanning techniques assessed do include minimal radiation, there will be no radiation or radioactive substances used during the course of this study.

S. References

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