



University at Buffalo

The State University of New York

School of Medicine and Biomedical Sciences

**DEPARTMENT OF
GYNECOLOGY-OBSTETRICS**

Annual
RESIDENT RESEARCH DAY

Visiting Professor:

Gautam Chaudhuri, M.D, Ph.D.

Distinguished Professor of
Molecular and Medical Pharmacology,
Distinguished Professor and Executive Chair
Department of Obstetrics and Gynecology
David Geffen School of Medicine at UCLA
University of California at Los Angeles

Wednesday, May 27, 2009

8:00am – 12:00pm

Gyn-Ob Classroom, 3rd Floor
239 Bryant Street
Buffalo, New York

**Resident Research Day Schedule
Wednesday, May 27, 2009**

- Moderator:** Glenna Bett, Ph.D.
- 8:00 – 8:10 a.m.** “Comparison of Topotecan Myelosuppression in Differing Dosing Schedules”
Nina Strollo, M.D.
Mentor: Joshua Kesterson, M.D.
- 8:15 – 8:25 a.m.** “Finding A Correlation Between Placental Dopplers and Estimated Fetal Weights In Monochorionic Diamniotic (MCDA) Twin Gestations.”
Ashwini Pandit, M.D.
Mentor: Kofi Amankwah, M.D.
- 8:30 – 8:40 a.m.** “Are multiple tests for Chlamydia, Gonorrhea, Syphilis and Herpes Simplex necessary in the pregnant population?”
Toinette O. Chin, M.D.
Mentor: **Kofi Amankwah, M.D.**
- 8:45 – 8:55 a.m.** “Assessing the Histopathological Findings of Morcellating the Uterus”
Azeema Moosa, M.D.
Mentors: Ali Ghomi, M.D. and Tamera Paczos, M.D.
- 9:00 – 9:10 a.m.** “Assessing quality of life following colpocleisis performed at the time of transobturator tape sling for stress urinary incontinence.”
Nita Thapa, M.D.
Mentors: Ali Ghomi, M.D. and Moeen Abu-Sitta, M.D.
- 9:15 – 9:25 a.m.** “Prediction of Proteinuria and Microalbuminuria in Diabetic Pregnancies with a Random Single Void”
M. Baraa Allaf, M.D.
Mentors: Abeer Eddib, M.D. and Bruce Rodgers, M.D.
- 9:30 – 9:40 a.m.** “Fertility and Birth Rates After Hydrotubation with Corticosteroid at Hysterosalpingogram in Patients Experiencing Unexplained Infertility”
Jeremy A. Kalamarides, D.O.
Mentor: Anthony R. Pivarunas, D.O.
- 9:45 – 10:00am** BREAK

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- 10:00 – 10:10 a.m.** “Prediction of Preterm Labor by Fetalfibronectin (FFN) in Multiple Gestation.”
Afshan Samad, M.D.
Mentor: Chad Strittmatter, M.D.
- 10:15 – 10:25 a.m.** “Comprehensive Aneuploidy Screening of Single Cells: A Comparison of Methods of DNA Amplification.”
Olubunmi Alo, M.B.B.S.
Mentors: Norma Nowak, Ph.D., Bruce Holm, Ph.D., and Michael Bianchi, M.S.
- 10:30 – 10:40 a.m.** “Post-ablation-tubal-sterilization syndrome after global endometrial ablation techniques: A clinical pathologic correlation”
Margaret Mulvihill, M.B.Ch.B.
Mentors: Ali Ghomi, M.D. and Tamera Paczos, M.D.
- 10:45 – 11:30am** “Hormone Therapy and Cardiovascular Disease: The Estrogen Paradox”
Gautam Chaudhuri, M.D., Ph.D.
Distinguished Professor of Molecular and Medical Pharmacology, Distinguished Professor and Executive Chair Department of Obstetrics and Gynecology,
David Geffen School of Medicine at UCLA
University of California at Los Angeles

11:45 a.m. Presentation of Awards

Research Awards - Dr. Gautam Chaudhuri & Dr. John Yeh

Buffalo Gynecologic-Obstetric Society Award - Dr. Amol Lele

Wayne Johnson M.D. Award - Dr. Bruce Rodgers

Robert J. Patterson, M.D. Award - Dr. Ali Ghomi

AAGL Award - Dr. Ali Ghomi

Chairman's Award Group – Dr. John Yeh

ABSTRACTS

"Comparison of Topotecan Myelosuppression in Differing Dosing Schedules"

Nina Strollo, M.D.

Mentor: Joshua Kesterson, M.D.

Objective: Topotecan is a topoisomerase I inhibitor used to treat chemotherapy patients who are platinum-sensitized or platinum-resistant. The selected study group had a known, limiting side effect of myelosuppression. The object of this study was to compare the degree of patient myelosuppression resulting from three different Topotecan dosing regimens over their treatment course.

Methods: A retrospective chart review assessed data from patients between 2006 and 2008. The full data set was not available, but the charts for 20 patients receiving Topotecan during this time period were analyzed. The data fell into three subgroups, according to the frequency of their chemotherapy regimen. Patients received either a 3D (chemo every 3 days), 5D, or weekly (W) regimen depending on physician preference. Patients had blood-lab analysis performed prior to the administration of each cycle of Topotecan.

Results: Values were tracked for Hemoglobin, Platelets, and Absolute Neutrophil Count (ANC), as specific indicators of change in the degree of myelosuppression. The number of patients within the three subgroups were: 3D (n = 9), 5D (n = 7), and W (n = 4). A portion of the analysis included calculating the difference between the Week 0 and Week 15 values (differential). For ANC, the mean \pm SD for Week 0 versus Week 5 of treatment were: 4.45 ± 1.8 versus 4.22 ± 3.2 ($p > 0.05$). All 9 differentials for the Weekly cases were Negative --- perhaps indicating that women in the Weekly group were receiving treatment to support better immune competence.

Conclusion: The data revealed that, over a 15-week treatment period, there was no statistical difference in myelosuppression between the three different administration regimens

"Finding A Correlation Between Placental Dopplers and Estimated Fetal Weights In Monochorionic Diamniotic (MCDA) Twin Gestations."

Ashwini Pandit, M.D.

Mentor: Kofi Amankwah, M.D.

Introduction/Objective: MCDA is present for 20% of all twin gestations and 15% of them get Twin To Twin Transfusion Syndrome (TTTS). We have asked whether there could be an alternative pathogenesis in early Quintero (Q) stages which may not involve overt blood transfer between the twins via surface arteriovenous shunts. Discordance may be due to imbalance in placental sharing, and the true incidence of TTTS may be far less than currently estimated. Our purpose was to measure Placental Dopplers on MCDA twins without TTTS in order to establish a correlation. We would then evaluate whether this correlation applied to a new case of severe TTTS.

We hypothesized that non-TTTS cases and early Stage I and II cases would demonstrate Doppler data having no correlation; the severe TTTS patients should reflect a negative correlation between the gestational age and S/D and PI indices (presence of true vascular pathological shunt).

Design: Prospective study based on MCDA twins from the WCHOB Regional Perinatal Center.

Methods: Placental Doppler studies are conducted in the arterial blood vessels on the chorionic plate in the vicinity of the umbilical cord. To control for the variation in fetal weights (318g to 2100g), we use the percent difference – i.e. (Twin B – Twin A)/Twin A. The actual P/I and S/D ratios between the smaller and larger twins were compared by t-test.

Results: We have collected data thus far on 9 twin cases (19 visits with ultrasound measurements). To date, there has been no case with documented TTTS. These preliminary data show a trend towards a negative correlation between percent difference in P/I index and the percent difference in fetal weight (borderline significance with $r = -0.616$ and $p=0.077$). There is no significant correlation between percent difference in S/D index and the percent difference in fetal weight ($r = -0.377$, $p=0.317$). Results changed when we excluded one outlier case. By "t- test" there was no association between S/D indices and EFW, or P/I index and EFW.

Conclusion: These preliminary data show no correlation between estimated fetal weights (EFW) and Placental Doppler indices in MCDA twins.

“Are multiple tests for Chlamydia, Gonorrhea, Syphilis and Herpes Simplex necessary in the pregnant population?”

Toinette O. Chin, M.D.

Mentor: Kofi Amankwah, M.D.

Objective: To assess the relevance of testing pregnant women for Chlamydia, Gonorrhea, Syphilis and Herpes Simplex types 1 & 2 multiple times or even once in pregnancy.

Methods: This chart review focused on 241 women who delivered in 2008 at WCHOB, focusing on the results of Herpes Simplex serology (HSV), Chlamydia & Gonorrhea cultures and Syphilis (RPR) serology. Data also included: patient's age, sexually transmitted disease (STD) history, gestation and parity, weeks of gestation at delivery, fetal weight, and HIV status. Chi-squared statistic was used to analyze the data.

Results: Gonorrhea and Chlamydia testing was performed for 204 women at their initial prenatal visit; 9.3% were positive for Chlamydia and 2% were positive for Gonorrhea. At 36 wks, 170 of these pregnant women were retested: 3.5% (n=6) were now positive for Chlamydia and zero were positive for Gonorrhea. Not surprisingly, 80% of women with positive Chlamydia results also had a history of STD. Sixty % of patients that had a positive Chlamydia test at 36wks had been positive initially. About 17% of women who had an initial positive test result remained positive at 36wks. Syphilis testing showed 0/217 were positive at the initial visit. None were positive at 28wks, nor on the day of delivery. HSV testing (type 1) was completed for 74/217 women and 54.1% were positive. Ninety-four out of 217 women received type 2 testing, and 40.4% were positive. For those with no STD history: 51.7% (n=15) showed type 1, and, 35.9% (n=14) were positive for type 2.

Conclusion: Based on these results, all pregnant women should be tested for Chlamydia at their initial prenatal visit and retested at 36 wks. Gonorrhea and syphilis testing should be performed once, at the initial prenatal visit. All women should receive serology testing for HSV, types 1 and 2. Our results show that a significant number of women with no STD history, about half, are positive for types 1 and 2.

“Assessing the Histopathological Findings of Morcellating the Uterus”

Azeema Moosa, M.D.

Mentors: Ali Ghomi, M.D. and Tamera Paczos, M.D.

Objective: To evaluate the difference in histopathologic findings of morcellated uterine specimens from laparoscopic supracervical hysterectomies (LSH) versus non-morcellated specimens from abdominal supracervical hysterectomies (ASH).

Methods: We conducted a retrospective chart review. 71 laparoscopic cases and 20 abdominal cases, identified over a one-year period, were evaluated. The slides and reports were examined by the same pathologist. Endpoints considered were: identification of endocervical tissue in specimen, preoperative and postoperative diagnosis correlation, presence of endometrial tissue in specimen and performance of a pre-operative endometrial biopsy.

Results: The only statistically significant finding was the identification of endocervix in 17/20 (85%) of ASH specimens, versus 7/71 (10%) of LSH specimens ($p < 0.05$). Upon evaluating other parameters, the two groups were found to be similar. Endometrium was identified in 20/20 (100%) of the ASH group, vs. 64/71 (90%) of the LSH group ($p > 0.05$). Preoperative and postoperative diagnoses were well correlated in both the ASH group 17/20 (85%) and the LSH group 55/71 (77%) ($p > 0.05$). Preoperative endometrial biopsy was not available for evaluation in 56/71 (79%) of LSH cases and 15/20 (75%) of ASH cases. There were 3 cases of simple and complex endometrial hyperplasia among the LSH group and none among the ASH group.

Conclusion: The histologic identification of the endocervix may not be as readily feasible in the morcellated uterine specimen compared to the non-morcellated uterine specimen. This finding may also suggest that with the LSH group amputation took place at a level superior to the internal os.

Although not statistically significant, several LSH specimens did not include an endometrial component. This highlights the importance of preoperative endometrial biopsy to avoid inadvertent morcellation of abnormal endometrium.

Level of Evidence: II-3

“Assessing quality of life following colpocleisis performed at the time of transobturator tape sling for stress urinary incontinence.”

Nita Thapa, M.D.

Mentors: Ali Ghomi, M.D. and Moeen Abu-Sitta, M.D.

Objective: The purpose of the study is to assess the quality of life in women who have undergone concomitant colpocleisis for severe pelvic organ prolapse and transobturator tape for the stress urinary incontinence.

Methods: Twenty patients were identified between 1998 and 2005 who underwent concomitant colpocleisis and transobturator tape. Patient characteristics were recorded including age, parity, BMI, tobacco use, history of hormone replacement therapy, prior hysterectomy, prior pelvic reconstructive surgery and pre-operative urodynamic parameters. Peri-operative variables including operating time, estimated blood loss, hospital stay, and peri-operative complications were recorded. Quality of life after and before the surgery was evaluated by the standard Urogenital Distress Inventory questionnaire.

Results: Sixteen patients (80%) out of twenty returned questionnaires with complete data on study outcomes. Mean age was 81 years (range 76-85 years), mean parity 2 (range 1-3), mean BMI 25.5 (range 18.8-32.2), 25% used tobacco and 5% were on hormone replacement. 65% had urodynamic stress incontinence preoperatively, 75% of the patients had uroflow pattern suggesting urinary obstruction, 65% had detrusor instability and mean post void residual was 200ml (range 5-400 ml). Mean hemoglobin difference before and after the surgery 1.9 gm/dl (range 1.18-2.62gm), mean estimated blood loss was 100 ml (range 30-200 ml), mean operating time was 117.5 minutes (range 80-159 minutes), and mean hospital stay was 1 day (range 1- 3 days). There were no intraoperative and postoperative complications. Urogenital Distress Inventory scores before and after surgery was analyzed using Wilcoxon Signed Ranks test. Mean Urogenital Distress Inventory scores were improved significantly postoperatively (5.3 vs. 3.6, $P < 0.05$).

Conclusions: Transobturator tape done at the time of colpocleisis for stress urinary incontinence results in improved urinary symptoms appears to be safe and is associated with low complications.

“Prediction of Proteinuria and Microalbuminuria in Diabetic Pregnancies with a Random Single Void”

M. Baraa Allaf, M.D.

Mentors: Abeer Eddib, M.D. and Bruce Rodgers, M.D.

Background: Diabetic nephropathy in pregnancy is associated with a significantly increased risk of maternal and perinatal morbidity and mortality. The most widely accepted method for the assessment of proteinuria and microalbuminuria is the 24-hour urine collection; however, these are inconvenient, and are subject to errors and noncompliance. The random spot microalbumin-to-creatinine (M:C) ratio correlates with the 24-hour urinary microalbumin (M) in non-pregnant diabetics, but this has not been validated in diabetic pregnancies. The random urinary protein-to-creatinine (P:C) ratio has also been shown to correlate with the 24-hour urinary protein excretion (P) for non-pregnant, healthy pregnant women, and those with preeclampsia. Limited data is available about its correlation in diabetic pregnancies.

Objective: To determine whether a single urine specimen, could replace the 24-hour urine collection in screening for microalbuminuria and proteinuria in pregnant women with pregestational diabetes.

Methods: A cohort study on 45 diabetic pregnant patients was performed. Cases complicated by multiple gestations or other autoimmune disease were excluded. Demographic and clinical variables were collected and analyzed. The 24-hour urine specimens were brought to the clinic at which time a random urine spot sample and a serum sample were obtained. Specimens were rejected if total creatinine excretion was < 10 mg/Kg/day. Urinary P:C ratio and M:C ratio were measured for the spot sample. Total urine (P) and total urine (M) were assayed for 24-hour. Linear regression was used to determine the correlation between the 24-hour urine (P) versus the spot P:C ratio. Likewise, the 24-hour urine (M) excretion was compared against the spot M:C ratio. The strength of the association was assessed with the Pearson correlation coefficient.

Results: Maternal age was 30.8 years (range, 18.5-41.5) and the mean gestational age at collection was 19.8 weeks (range, 6-36.6). A logarithmic relationship exists between the spot M:C value and 24-hour microalbumin, with a strong correlation ($r=0.85$; $P<0.0001$). Agreement between the spot P:C ratio and 24-hour protein was less optimal ($r= 0.56$; $P < 0.0001$).

Conclusions: A spot test using a random single void for the microalbumin-to-creatinine ratio appears to be reliable and also more practical for assessing microalbuminuria. The simplicity of a spot test will make possible large-scale surveys of diabetic pregnancies to identify patients who may be at risk.

"Fertility and Birth Rates After Hydrotubation with Corticosteroid at Hysterosalpingogram in Patients Experiencing Unexplained Infertility"

Jeremy A. Kalamarides, D.O.

Mentor: Anthony R. Pivarunas, D.O.

Objective: To determine if steroid hydrotubation at time of hysterosalpingogram (HSG) would decrease time to conception and increase birthrates in unexplained infertility.

Methods: Prospective, randomized, double-blinded, placebo-controlled study, institutional based, IRB approved. Inclusion criteria: infertility patients with normal tubal and uterine anatomy, normal semen analysis and having evidence of ovulation by either LH kits or follicular series. Subjects were not excluded if receiving assisted reproductive technology with intrauterine insemination (IUI) and oral ovulation induction agents (standard protocols). Couples with male factor infertility were excluded. Patients were consented to receive either water based contrast solution mixed with 100 mg of hydrocortisone or normal water based contrast solution alone (placebo) at time of HSG. Randomization was computer generated with sequential patient assignment. Participants and examiners were blinded to the solution. Subjects were then followed for pregnancy at 3 months and 6 months by telephone interviews.

Results: 76 patients were required to achieve statistical significance. Kaplan-Meier survival curves were used to compare outcomes along with odds ratios, confidence intervals, patient demographic data, and power calculations. Subgroup analysis was performed for data from patients using IUI with oral induction agents and separately for patients deferring any assisted reproductive technology immediately following HSG.

Conclusion: This ongoing study continues to produce blinded data. Participants and examiners will be unblinded when adequate sample size has been attained. Final tabulations will be complete in May 2010. To date, one of four patients has become pregnant.

"Prediction of Preterm Labor by Fetal Fibronectin (FFN) in Multiple Gestation."

Afshan Samad, M.D.

Mentor: Chad Strittmatter, M.D.

Introduction: Fetal fibronectin is a glycoprotein produced by chorionic membranes and is localized to deciduas basalis. FFN is one of the best predictors of preterm birth in singleton pregnancies.

Objective: Accuracy of predicting preterm deliveries in multiple gestation and additionally study the impact of FFN on hospital admissions and interventions.

Study Design: Retrospective

Methodology: To review all patients' charts with multiple gestations in Sisters Charity Hospital from July 2005 to December 2008 who had FFN testing done. Medical record demographics will be reviewed as well as FFN test results, gestational age at delivery, intervention with tocolytics, steroid use and length of stay in hospital.

Results: The results of the FFN test notified as either positive or negative. Sensitivity, Specificity, Positive predictive value and Negative predictive value of FFN in multiple gestation specifically within 14 days of testing will be analyzed.

The final tabulations anticipated by May 2010.

"Comprehensive Aneuploidy Screening of Single Cells: A Comparison of Methods of DNA Amplification."

Olubunmi Alo, M.B.B.S.

Mentors: Norma Nowak, Ph.D., Bruce Holm, Ph.D., and Michael Bianchi, M.S.

Objective: The combination of whole-genome amplification (WGA) and microarray technologies may provide an attractive solution to the many limitations of fluorescence in situ hybridization (FISH) based screening for pre-implantation genetic diagnosis (PGD). This study attempts to compare the methods involved in WGA and its effects on the quality of information obtained from the array comparative genomic hybridization (array CGH) technology which detects genomic imbalances in single cells.

Methods: Four aneuploid cell lines carrying trisomies for chromosomes 9, 15, 18 and 21 were utilized for the study. Single cells were isolated, and whole genome amplification (WGA) was performed on trisomy 18 using two kits (WGA-4 (Sigma) or REPLI-g (Qiagen) as directed by the manufacturer. The DNA was quantitated using a Nanodrop spectrophotometer. Test and reference DNA were labeled with Cy5 and Cy3 fluorescent dyes, respectively. The labeled DNAs were co-precipitated and hybridized to 3000 clone bacterial artificial chromosome (BAC) CGH arrays and then scanned, and Cy5/Cy3 intensity ratios calculated. A Lowess correction for unequal dye incorporation is applied normalizing the data.

Results: The GenomePlex WG4 provided superior results as determined by quality control metric for signal to noise ratio (SNR). Noise is defined as the weighted mean of the segmental standard deviation. The SNR values for chromosomes 9, 15, 18 and 21 were $0.13/0.24 = 1.85$, $0.16/0.17 = 1.06$, $0.12/0.26 = 2.17$, and $0.13/0.24 = 1.85$ respectively. Amplification of single cell DNA with REPLI-g failed to yield scorable array CGH results due to low signal to noise ratio. WG4 DNA in contrast produced genomic profiling of single cells that detected the known aneuploidies.

Conclusion: Conventional PGD techniques usually screen $<1/2$ of the human chromosomes and consequently many oocytes or embryos carrying lethal abnormalities are not identified. Array CGH together

with whole genome amplification allows comprehensive aneuploidy testing and detection of unbalanced translocations.

“Post-ablation-tubal-sterilization syndrome after global endometrial ablation techniques: A clinical pathologic correlation”

Margaret Mulvihill, M.B.Ch.B.

Mentors: Ali Ghomi, M.D. and Tamera Paczos, M.D.

Objective: To investigate post-ablation-tubal-sterilization syndrome (PATSS) after commonly performed global endometrial ablation techniques.

Methods: The medical records of seventy-two patients who underwent hysterectomy subsequent to an endometrial ablation, from 2000 to 2008 at three university-affiliated hospitals were reviewed. Patients without a tubal ligation, without pelvic pain and with an identifiable organic cause for failed ablation were excluded, resulting in twelve clinically selected cases of PATSS. The morphologic characteristics and pathologic findings as they relate to PATSS, were evaluated for each of the twelve cases.

Results: 5 patients underwent NovaSure ablation, 2 patients underwent thermal balloon ablation and 5 patients underwent rollerball ablation. The median age at hysterectomy was 39 (27-54) years. Histopathology specimens were examined from 4 to 28 months post ablation. All 12 patients had evidence of endometrial scarring. 8 of 12 patients (67%) had residual functioning endometrium. 6 of 12 (50%) had pigment-laden macrophages; granulomatous inflammation was identified in three of these patients. Adenomyosis was present in 5 cases (42%). In 50% of cases the fallopian tubes were not assessed, however 2 cases had morphologic evidence of hematosalpinx supporting the clinical diagnosis of PATSS. Time interval to hysterectomy following global ablation compared to rollerball ablation was not significantly different: 12.8+/-8.4 months versus 16.6 +/- 4.3, P=0.38.

Conclusion: This study confirms the occurrence of PATSS following global endometrial ablation, NovaSure specifically. In addition, the morphologic and histological appearance of the endometium and myometrium in PATSS following rollerball and global endometrial ablation techniques are similar. It is essential to inform the pathologist of the clinical history to facilitate the appropriate gross and histological examination.
