

## ABSTRACTS OF SOCIETIES

### Scottish Programme for Clinical Effectiveness in Reproductive Health

#### Features associated with time to diagnosis and subsequent management of ectopic pregnancy.

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**Introduction:** Although refinement of transvaginal ultrasonography has improved the early detection of ectopic pregnancy, diagnosis can be difficult and is often delayed. The aim of this study was to assess whether specific risk factors for ectopic pregnancy and level of human chorionic gonadotrophin (beta-hCG) are associated with length to diagnosis and subsequent management of ectopic pregnancy. **Methods:** Review of case histories of women presenting with ectopic pregnancy to the Royal Infirmary of Edinburgh over a one-year period. **Results:** In 2004, 79 patients presented to the Royal Infirmary of Edinburgh with ectopic pregnancy. The mean age of the women examined was 31.3 years (range, 18 to 45 years). The mean number of days of amenorrhoea was 47 (range, 13 to 88). Risk factors included smoking (30%), previous abdominal surgery (22%), previous ectopic pregnancy (17%), previous pelvic inflammatory disease (4%) and sterilisation (2.5%). 60 of the patients were managed by a laparoscopic approach (76%) and the remainder had medical management with methotrexate (24%). None of the patients required a laparotomy. 56% of women had a diagnosis of ectopic pregnancy made at the first visit, 23% within 2-3 visits, and 21% required more than three hospital visits prior to diagnosis. Two out of the 79 patients with a final diagnosis of ectopic pregnancy had this excluded at the first visit and the diagnosis was confirmed at subsequent presentations. The most common symptoms at first presentation were pelvic pain (38%) and vaginal bleeding (74%). Both symptoms varied with each subsequent visit but nearly half of the women requiring a third hospital visit had no symptoms at this stage. Women who had their diagnosis made within the first three visits were more likely to be regular smokers (47%). No other risk factor seemed to be associated with time to diagnosis. Beta-hCG levels varied considerably. Median beta-hCG at first visit was 789 but ranged between 2 to 40,505 iu/L. A lower beta-hCG level was associated with prolonged diagnosis (mean beta-hCG 542 iu/L, range 18-3134 for greater than three visits, versus 2615 iu/L, range 56-22411 for one visit) but this was not statistically significant. Neither the association of risk factors or beta-hCG levels were associated with type of management. **Conclusion:** The early diagnosis of ectopic pregnancy is difficult. Up to one fifth of patients presenting to our unit require over three visits to make the diagnosis of ectopic pregnancy. Although the presence of symptoms and a history of smoking are associated with an early diagnosis of ectopic pregnancy, the absence of risk factors or level of beta-hCG does not appear to be associated with multiple visits and delayed diagnosis. Similarly, there does not appear to be a link between specific risk factors or beta-hCG levels and type of management of ectopic pregnancy.

#### Substance abuse in pregnancy and maternal & neonatal outcome - five year study.

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**Introduction:** Our main aim was to study the maternal and neonatal outcome in women with substance abuse in pregnancy following the establishment of a dedicated multidisciplinary clinic in 2001. **Materials and Methods:** Seventy (70) women who abused substances attended the multidisciplinary clinic held at Dumfries & Galloway during the period between 2001 and 2005 and their case notes were analysed retrospectively. **Results:** The incidence of substance abuse in pregnancy was 0.11%. 71% (51) had used heroin, 62% (44) had used heroin and methadone, 46% (32) used benzodiazepines, 67% (47) smoked cannabis, and all of them smoked tobacco (70) 100%. The mean age of women was 25 years and the average gestational age at booking was 13.9 weeks. Amongst the women who were screened [(67) 95% coverage] 35% (25) tested positive for hepatitis C and none was positive for hepatitis B, HIV and syphilis. Only 47% (33) attended the multidisciplinary clinic without any default. Antepartum complications such as pre-eclampsia (1) and DVT (1) was 2% respectively and in 58% (41) fetal growth was 50th centile on growth scans. 83%(58) went into spontaneous labour, and compared to women without substance abuse 84% (59) in the substance abuse group had spontaneous vaginal deliveries (84% vs 64%), 2% (1) had instrumental deliveries (2% vs 6%) and 14% (10) had emergency caesarean sections (14% vs 29%). The incidence of preterm deliveries was high at 12.8% (9) (12.8% vs 5%). 87% (61) of babies in the substance abuse group had an appgar of 9/10 at 5 minutes and the average birth weight was 2.87 kgs. 70% (49) of the babies needed neonatal admission, and 46% (32) developed neonatal abstinence syndrome; in 36% (25) morphine had to be administered. 61% (43) of the babies spent about two weeks in the neonatal unit and the incidence of neonatal death was 0.08%. 94% (66) of the mothers went home with their babies with support. **Conclusion:** Though with multidisciplinary clinic and dedicated care a favourable outcome has been observed, in the majority of women, preterm deliveries, low birth weight and neonatal admissions are still high, placing a huge burden on the NHS. Every effort should be undertaken to further improve the outcome in these women. Setting up of a computer database is vital to enable learning between centres to plan care in these mothers who need great help.

#### Outcomes in women undergoing induction of labour with prostaglandins

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**Background:** Induction of labour (IOL) is a standard practise in modern obstetric care. It aims to expedite delivery if the risk of continuing the pregnancy outweighs the benefits. It is commonly used when pregnancies are prolonged and labour has not commenced spontaneously.<sup>1</sup> The protocol in our unit states that IOL for post dates should not routinely be offered before 41 weeks. In our hospital prostaglandin tablets or gel are used for cervical ripening.<sup>2</sup> The licensed dose of the tablets is two doses of 3mg. Further doses are at the discretion of medical practitioners.

**Aim:** To assess women requiring prostaglandins for induction of labour (IOL) including how many doses they received, which formulation was given and labour outcomes. **Methods:** A database search was undertaken to identify patients who were given vaginal prostaglandins for IOL over a two month period and case notes were reviewed to identify number of doses and formulation of drugs given. We also recorded parity, gestation, indication for IOL and body mass index (BMI). The mode of delivery, and indication if instrumental or operative delivery, were recorded. Two patients were excluded as they were undergoing IOL for intra-uterine death and two were excluded as they did not receive prostaglandins. Data regarding prostaglandins was unavailable for one patient. **Results:** There were 673 deliveries over the study period. 79 had elective caesarean sections. 25% of the patient population underwent induction of labour and 15% were given prostaglandins for cervical ripening. 98 patients were included in the study. Parity (delivered) ranged from 0 to 5 children, with a mean value of 0.91, mode 1 and median 0. BMI ranged from 16.3 to 44.3, with a mean value of 26.5, mode 24.8 and median 25.7. 48% of patients were overweight or obese. 59% of women were induced for post dates, 29% for obstetric or maternal indications and 3% for fetal indications. 9% were social inductions. 9% (n=5) of women being induced for post dates pregnancies delivered before 41 weeks. 77% delivered between 41 and 42 weeks and 14% delivered after 42 weeks. The patient characteristics of the 5 patients who delivered before 41 weeks were assessed. 4 had a spontaneous vertex delivery (SVD) and 1 had an emergency caesarean. Those who delivered after 41 weeks were significantly more likely to require an operative delivery (p=0.02). 91% of women required 2 or less doses of prostaglandin, 8% required 3 doses and 1% was unknown. Of the 8% (N=8) who required a 3rd dose, 87% (N=7) were primigravida and 75% (N=6) required delivery by emergency caesarean section. Only one woman achieved an SVD. Women who required a third dose were significantly more likely to require operative delivery (p<0.02). Operative delivery rate was 11%, 18% and 75% for those receiving one, two or three doses of prostaglandin respectively. Overall 66.3% delivered by SVD, 16.3% had an instrumental delivery and 17.3% required an emergency caesarean section. For primigravida the proportions were 35%, 32.5% and 32.5% respectively, and for parous women 91%, 4% and 5% respectively (p<0.001). **Conclusion:** The IOL rate was 25% overall and 15% with prostaglandins. 1) Almost half of patients were overweight or obese; 2) Majority of inductions were for 'post dates'; 3) A third were for obstetric, maternal or fetal indications; 4) A tenth were social inductions; 5) 91% of women who had induction for post dates delivered after 41 weeks 6) Less than 10% of women required a third dose of prostaglandin: those who did were significantly more likely to require operative delivery; 7) Primigravid women were significantly more likely to require instrumental or operative delivery than parous women

For references refer to [www.smj.org.uk](http://www.smj.org.uk)

### **Krukenberg tumours of unknown origin presenting with Sister Mary Joseph's nodule.**

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**CASE REPORT:** A 45-year-old, parous, pre-menopausal woman, presented to her GP with a 2-month history of an

inflammatory, firm, 4-cm, umbilical nodule causing local abdominal discomfort. She had no other complaints and no other findings on physical examination and was reassured that it was not a worrying lesion. However, she returned to her GP another three times and was prescribed antibiotic therapy, which was unsuccessful. Three months later she was referred to a general surgeon, who thinking it was primarily a skin lesion, referred her on to a dermatologist. The dermatologist found the lesion to be highly suspicious and requested further investigations. Biopsy revealed metastatic adenocarcinoma, confirming the lesion to be a Sister Mary Joseph's nodule. Computed tomography (CT) scan showed bilateral ovarian tumours and multiple soft tissue deposits within the peritoneal cavity. Serum carcinoembryonic antigen (CEA) was elevated to 8.2, whereas cancer antigen 125 (CA125) and Alpha-fetoprotein (AFP) were within normal range. She was prescribed chemotherapy for colonic cancer (oxaloplatin and 5-Fluorouracil), based on her CEA levels and histopathology, with no improvement. The nodule acquired a warty appearance and began to discharge mucus. A repeat CT scan indicated that the ovarian masses had continued to grow. She was then changed to an ovarian cancer chemotherapy regime (cisplatin and paclitaxel), with her umbilical nodule healing and decreasing in size after only three weeks. However, the ovarian masses started causing symptoms as they grew to a maximum of 11 x 9 cm on the right and 10 x 6 cm on the left, measured by CT. Twelve months after her initial presentation, she underwent palliative resection of the ovarian masses, sub-total hysterectomy, and bilateral salpingectomies with appreciable symptomatic improvement. The ovarian masses were fixed to the bowel posteriorly, and extensive omental disease was seen. Additionally, the surgeon felt the stomach was abnormal on palpation. Pathology showed the presence of mucinous carcinoma with signet-ring cells, confirming the diagnosis of ovarian Krukenberg tumours and suggesting a gastric primary. Further investigation with upper GI endoscopy failed to identify a primary lesion, with normal gastric and duodenal biopsies. The prognosis of Krukenberg tumours is poor with an average survival of less than two years.<sup>1</sup> A Sister Mary Joseph's nodule also carries a poor prognosis with an average survival of less than one year. It would be important to determine the site of the primary malignancy in order to formulate an adequate management plan. This lady was referred to the upper GI team for further investigation, despite lack of pathological evidence of the source of the primary tumour. **Discussion:** Krukenberg tumours, named after the German gynaecologist and pathologist Friedrich Krukenberg (1871-1946), are metastatic adenocarcinomas of the ovaries, displaying mucin producing neoplastic signet-ring cells involving the ovarian stroma.<sup>2</sup> They should be diagnosed solely on histological criteria, even when clinical suspicion is high. They are solid tumours, usually bilateral and more commonly originate from primary malignancies of the stomach, although primaries of the colon, breast and other sites have been implicated. In many instances the primary tumour may be very small and go unrecognised. A retrograde lymphatic spread is likely to originate these tumours. Krukenberg tumours account for 1-2% of all ovarian tumours. However, incidence is directly proportional to the incidence of gastric carcinoma, and in countries with a high incidence of this type of malignancy such as Japan, they can represent up to 17% of all ovarian tumours.<sup>3</sup> "Primary" Krukenberg tumours have been described, although it is currently accepted that these were likely to be cases of undetected primary cancers, rather than a primary tumour. The possibility of gastric or breast neoplasms occurring in very small sizes and remaining silent for many years could be the basis of such reports.

Additionally, the patients may not survive long enough, following Krukenberg tumour resection, for the primary cancer to manifest itself, and the presence of the classical signet-ring cells can also occur within some types of primary ovarian tumours. All efforts should, therefore, be put in place to find the primary tumour when faced with a diagnosis of Krukenberg. This may be challenging and only evident on laparotomy or months after tumour resection.<sup>4</sup> Krukenberg tumours occur in young women, on average at 45 years of age. Symptoms can be limited to unspecific gastrointestinal complaints, or may be completely absent. Ascites may be present in 50% of cases. Gross pathological features include asymmetric bilateralism, solidity, and the presence of a smooth capsular surface, which is free of adhesions. Microscopically, the tumour has an epithelial and a stromal component. The former is composed of mucin-laden signet ring cells. The latter is formed from benign reactive ovarian stroma. CA125 levels may be elevated indicating a poor prognosis, but are expected to decrease after surgical resection, which makes this marker useful for follow-up. Krukenberg tumours must be differentiated from other metastatic or from primary ovarian tumours containing signet ring cells, based on both clinical, pathological, and immunohistochemical differences.

Immunohistochemistry is based on immunoreaction both to cytokeratin 7, which is commonly seen in primary ovarian carcinomas, and to cytokeratin 20, observed in gastric, intestinal, and appendiceal primaries. Levels of CEA, Ca125, and Ca19.9 may also aid in identifying the primary cancer. Curiously, this lady first presented with a Sister Mary Joseph's nodule, a metastatic lesion of the umbilicus, most commonly from primary gastric or gynaecological malignancies. Sister Mary Joseph (1856-1939) was a surgical assistant of Dr. William Mayo, and the first to establish the association between the umbilical lesion and underlying abdominal malignancy.<sup>5</sup>

**Conclusion:** Krukenberg tumours are rare metastatic tumours of the ovaries, which spread by lymphatic route. They characteristically present bilaterally, and commonly originate from a primary gastric malignancy. Krukenberg tumours with unknown primary demands thorough investigation of the GI tract and other possible sources. There is no curative treatment, and the prognosis of Krukenberg tumours is very poor. Sister Mary Joseph's nodule is a clinical sign of metastatic adenocarcinoma of gastric or ovarian origin, carrying an ominous prognosis. This lady presented with two uncommon metastatic manifestations of primary GI tract malignancy: Sister Mary Joseph's nodule and Krukenberg tumours. Furthermore, the primary malignancy remains undeclared.

For references refer to [www.smj.org.uk](http://www.smj.org.uk)