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GYNAE SPECTRUM

Dear Doctor,
Greetings from Micro Labs. We are happy to bring you "Gynae Spectrum", which contains latest and interesting news in the field of Obstetrics and Gynecology.

This issue contains:

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1) Postoperative Respiratory Compromise Associated with Obesity and systemic opioids after cesarean birth

Introduction:

Obesity is linked to poor pregnancy outcomes, such as cesarean delivery and maternal mortality caused by anesthesia. Although the risk of obesity-related respiratory depression as well as its link to postoperative opiate usage has been extensively reported in the general surgical literature, there has been little research in obstetric literature. [1] Although one study found no cases of respiratory depression among post-cesarean women receiving morphine, the route of administration was neuraxial, which has been found to be associated with clinically relevant respiratory depression only in a small number of cases. [2]

Respiratory events can range from minor respiratory depression to life-threatening hypoxia. The aim of this study was to determine the percentage of women who had at least one composite respiratory event during the first 24 hours following cesarean delivery, as well as to assess the effects of obesity (by BMI class) and opioids on the incidence of these respiratory events. The focus on maternal respiratory incidents within the first 24 hours was chosen since this has previously been proven to be the time period when a respiratory event as a result of opiate usage is most likely to occur. The researchers hypothesized that when BMI and opioid dosage increased, post-cesarean respiratory episodes would rise.

Methods:

The women in this retrospective cohort research were opioid-naive women who had a cesarean. The primary outcome was the percentage of women who had at least one composite respiratory outcome within 24 hours post cesarean (oxygen saturation less than 95% for 30 seconds or requirement for respiratory assistance). Obesity and total systemic opioid dosage in 24 hours (measured in morphine milligram equivalents [MMEs]) were investigated for their effects on the composite respiratory compromise result.

Result:

790 women experienced at least one composite respiratory incident out of 2,230 cesarean deliveries. Body mass index (BMI) as a continuous variable (odds ratio=1.063 for every one-unit increase in BMI [95 percent confidence interval (CI): 1.021–1.108], p=0.003), and MME (odds ratio =1.005 [95 percent confidence interval (CI): 1.002–1.008], p = 0.003), after adjusting for magnesium sulphate use, were predictors of the composite respiratory outcome. The odds ratio for the interaction of obesity and opioid dosage was 1.000 (95 percent CI: 0.999–1.000, p =0.030) (Fig.1).

Discussion:

Women with obesity, as well as those getting larger opioid dosages, had a higher risk of respiratory impairment in the first 24 hours after cesarean delivery. Mild desaturation events accounted for the bulk of the episodes of respiratory compromise. Despite the fact that an episode needing extensive respiratory assistance was not linked to obesity, the number of

women who experienced one were tiny. Women with a BMI of 50 kg/m2 had a 3.43 times greater risk of the composite respiratory outcome than women with a BMI of 30 kg/m2, according to the multivariate logistic regression model.

Prior studies, which were often conducted in an older population with more comorbidities, did not provide the same results. Numerous studies in the general surgical literature have looked at how obesity and opiate usage might exacerbate unfavourable respiratory outcomes. [3] There was a link between respiratory impairment and BMI, but the link between opioid dosage and BMI was less strong. It's likely that obstetric patients are less affected by opioids since they're typically younger, healthier, and physiologically different from the overall post-surgical population, but this is speculation.

Predictor	Linear predictors estimate (SE)	OR (95% CI)	Pr (> |z|)
Intercept	−1.188 (0.172)	0.305 (0.217–0.426)	< 0.001
MME by unit increase of 1 mg	0.005 (0.002)	1.005 (1.002–1.008)	0.003
BMI by unit increase of 1 kg/m^2	0.062 (0.021)	1.063 (1.021–1.108)	0.003
Magnesium sulfate use	0.918 (0.203)	2.505 (1.687–3.751)	< 0.001
MME: BMI interaction	−0.0004 (0.0002)	1.000 (0.999–1.000)	0.03

Fig. 1 Predictors of the composite respiratory outcome in the first 24 hours post cesarean birth

The findings of this study have a number of major clinical implications. Although many hospitals have improved respiratory monitoring of obese postoperative women, this is not consistent. [4] When employing systemic opioids vs neuraxial opioids as a major method for post-cesarean analgesia, this study has implications for the safety and intensity of postoperative monitoring.

This is an important contrast to the results of frequent clinically meaningful respiratory depression when utilizing systemic hydrophilic opioids rather than neuraxial opioids. When used in a multimodal strategy for post-cesarean analgesia, neuraxial opioids are not only more effective but also likely safer than systemic opioids, according to the findings of the study. This is also in line with newer guidelines that allow for less supervision after neuraxial hydrophilic opioids. [4]

The study's strengths include the large number of women who were included, which provided enough statistical power for the computations. Because the hospital did not employ prolonged-release intrathecal morphine during the research period, the systemic opioid dosages administered in the population were higher than those found in the obstetric population. While this limits the study's generalizability, it does allow researchers to investigate the effects of greater parenteral opioid dosages than are often used in the post-partum population. Other

populations with less systemic opiate usage may have less dramatic findings.

Conclusion:

Obesity, and to a lesser extent, systemic opioid dose, were found to be positively correlated with the occurrence of respiratory events in the postoperative period after cesarean birth in this study. It was also discovered far more clinically significant respiratory depression in the population than has been documented in post-cesarean women treated with neuraxial morphine, and we're utilizing these findings to help us make improvements to the post-cesarean analgesia protocol. Other studies have found a link between obesity and respiratory impairment in non-obstetric patients.

- **With the degree of obesity and opiate dosage, the proportion of women reporting respiratory problems after cesarean birth rises.**

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2) Preservation of fertility with hematological disorders in female patients.

Introduction:

Malignant tumours are becoming more common in young individuals, according to local and international epidemiological statistics. Malignant tumors, particularly those of hematological origin, are most common in adults of reproductive age, including teenagers. Leukemia ranks sixth and eighth in males and females, respectively, in terms of mortality from malignant tumours, and first in children and people under 35. [1] Because of recent advancements in therapeutic technology, particularly early diagnosis, and successful chemotherapy, as well as the development of bone marrow stem cell transplantation (BMT) technology, patients' post-treatment survival rates have improved and their surviving span has been prolonged. While efficient chemotherapy saves lives, it can also harm the gonads, and in women, this harm to the ovaries results in the loss of fertility and endocrine functions that create sex hormones. The alkylating agents, such as cyclophosphamide, are clearly gonadotoxic, and even in patients who do not experience premature ovarian failure as a result of chemotherapy, recovery of ovarian function has been shown to be delayed, and response to superovulation reduced, in patients receiving these drugs compared to those in the control group (age-matched women with male factor infertility undergoing the same treatment protocol). [2]

Methods:

Prior to the planned BMT, preoperative fertility counselling was provided to 29 individuals with hematologic diseases (Fig. 2), ranging in age from 12 to 38 years. 16 of these patients, ranging in age from 22 to 38 years old, elected to have their oocytes extracted and then their ovum or embryos frozen.

Results:

Following the random-start controlled ovarian hyperstimulation (COH), an average of 8.2 oocytes were recovered, as the patients were in immediate need of chemotherapy or BMT. The average number of oocytes frozen in ten patients was 6.9, whereas the average number of embryos frozen in six individuals was 3.2. There were no intraoperative or postoperative problems, while two of the 11 transfused patients had a blood transfusion reaction. (Fig.1)

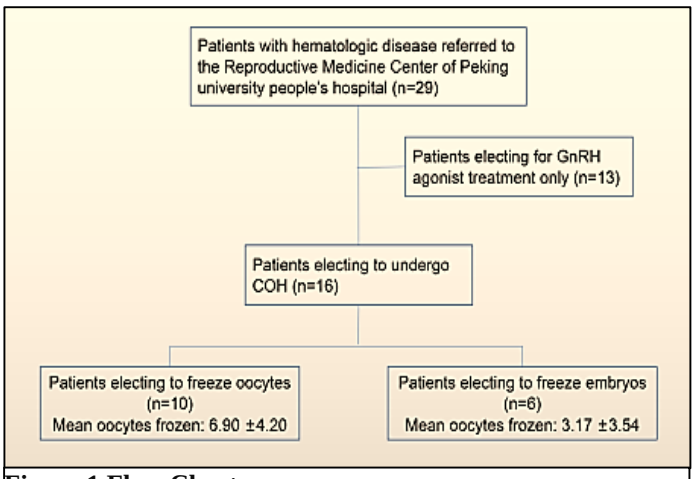

Figure 1 Flow Chart

Discussion:

Due to the specificity of hematological disorders, several non-malignant diseases, such as myelodysplastic syndrome and

aplastic anaemia, require HSCT in addition to acute and malignant diseases. Prior to HSCT, systemic chemotherapy has been demonstrated to substantially affect fertility in the treatment of several disorders. However, unlike patients with acute, malignant illness, these individuals do not require rapid chemotherapy, and most will have a significant wait between making the choice to undergo a BMT and commencing treatment. In the contrary, all of the patients in this research came to the Fertility Center for normal physical exams before BMT and at a period quite near to when they were scheduled to begin treatment. Oocyte or embryo cryopreservation is a well-established procedure for adults and post-pubertal patients now.

They could also use donor sperm or gestational carriers if it's legal and required. Ovarian tissue cryopreservation is an experimental therapy for those who do not have adequate treatment time. Ovarian tissue cryopreservation is the sole way to preserve ovarian tissue for pre-pubertal females. In terms of ovarian protection, there isn't enough data to back up GnRH agonist's usefulness in preserving fertility. [3]

Patient No	Age (years)	Diagnosis	Years of diagnosis (Year)	Times of chemotherapy (Times)	Day 1 of ovarian stimulation in the menstrual cycle (Day)	AFC (Number)	COS days (Day)	Obtained oocytes (Number)	Number of oocytes of MII (Number)	Number of frozen oocytes (Number)	Number of frozen embryos (Number)
1	25	Myelodysplastic syndrome (MDS)	4	0	17	8	5	7	1	4	
2	22	Chronic granulo-cytic leukemia	8	0	18	10	11	7	5	6	
3	38	Chronic aplastic anemia	15	0	2	4	5	2	1		1
4	23	Myelodysplastic syndrome (MDS)	4	0	20	10	17	9	5	5	
5	28	Acute non-lymphoblastic leukemia (M4)	2	10	3	10	9	9	6		4
6	31	Acute non-lymphoblastic leukemia (M5)	2	4	2	11	12	9	5	5	
7	23	Chronic aplastic anemia	3	0	2	10	7	18	13	13	
8	29	Acute lympho-cytic leukemia	1	3	4	6	9	5	4		2
9	28	Myelodysplastic syndrome (MDS)	4 months	0	1	12	12	12	10		10
10	19	Chronic aplastic anemia	7	0	15	9	12	15	15	15	
11	27	Chronic aplastic anemia	7	0	16	10	9	7	7	7	
12	29	Acute lympho-cytic leukemia	5 months	4	4	4	7	2	2		1
13	32	Acute lympho-cytic leukemia	2	10	23	3	11	10	9		1
14	23	Chronic aplastic anemia	7	0	3	7	11	6	5	5	
15	25	Acute lympho-cytic leukemia	5 months	4	3	5	12	9	8	8	
16	26	Acute myelog-enous leukemia	3 months	2	2	5	9	4	0	1	

Fig 2 General condition and ovulation promotion in patients with oocytes retrieval

Oocyte or embryo cryopreservation is a well-established procedure for adults and post-pubertal patients now. They could also use donor sperm or gestational carriers if it's legal and required. Ovarian tissue cryopreservation is an experimental therapy for those who do not have adequate treatment time. Ovarian tissue cryopreservation is the sole way to preserve ovarian tissue for pre-pubertal females. In terms of ovarian protection, there isn't enough data to back up GnRH agonist's usefulness in preserving fertility. When the dominant follicle had expanded to 18mm, hCG or a GnRH agonist was used to stimulate oocyte maturation, which was followed by luteal phase COS 2–3 days later. If the patient was in the luteal phase when they came in, i.e., P>3ng/ml, ovarian stimulation might be initiated right away without the use of GnRH

antagonists. GnRH antagonists might be given to the patient in the mid-luteal phase to cause luteal atrophy, following which the blood P level would decline and menstruation would begin 2–4 days later. As a result, rather than waiting for natural mensuration, the COS might be begun sooner. [4]

Vitrification is a very effective approach for freezing oocytes, and it is connected with a higher survival rate of frozen oocytes than slow programmed freezing. The recovery rate, fertilization rate, and clinical pregnancy rate utilizing frozen oocytes have all increased dramatically with the steady maturity of oocyte freezing technology. [5]

Conclusion:

Oocyte or embryo freezing prior to chemotherapy or BMT may give hope for fertility preservation in female patients with hematologic diseases. However, in order to do so, a consistent, realistic, and successful treatment approach is required, which should incorporate all aspects of patient selection as well as ovulation promotion, perioperative care, and postoperative surveillance protocols.

- **Oocyte or embryo freezing prior to chemotherapy or BMT may give hope for fertility preservation in female patients with hematologic diseases.**

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3) Disseminated Blastomycosis in pregnancy: a case report

Introduction:

Blastomyces dermatitidis is a dimorphic fungus that primarily affects immunocompromised people, although it can also impact immunocompetent individuals. Blastomycosis can manifest in a variety of ways and affect numerous organ systems. [1] The lungs and skin are the most usually afflicted organs, although infection can also spread to the CNS, bone, genitourinary, liver, and spleen. Despite the fact that the disease may be transmitted to immunocompetent hosts, case studies show that people with a compromised immune system are more likely to have disseminated severe disease. [2]

Case Report:

A 24-year-old woman who was 11 weeks pregnant, presented with dizziness, shortness of breath, chest discomfort that radiated to the right arm and increased when sleeping on the right side, and vomiting from 5 days. A respiratory virus panel (RVP) including SARS-CoV-2 was sent after the presentation and came back negative. A CT-PE scan was also performed, which revealed a mass-like consolidation in the anterior left upper lobe with a localized region of necrosis, indicating necrotizing pneumonia (Fig. 1)

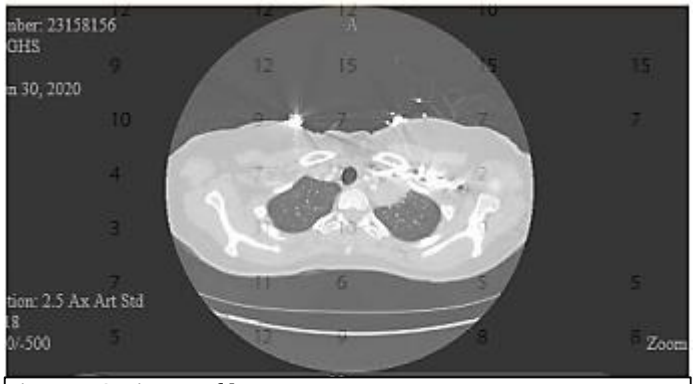

Figure 1 CT image of lung

Blood and respiratory cultures were taken at the time, but both came back negative. The patient was put on piperacillin-tazobactam and vancomycin for 4 to 6 weeks, with a plan to repeat the CT chest scan in 6 weeks and see a thoracic medicine specialist for a potential bronchoscopy. Her blood creatinine level climbed from 0.4 to 0.5 mg/dL to 1.5 mg/dL about a week after she was discharged, and she was told to stop using piperacillin-tazobactam and vancomycin. Antibiotics were stopped for roughly a week while the patient's acute kidney damage (AKI) healed, and then piperacillin-tazobactam monotherapy was restarted. Our patient was re-admitted one day after beginning her medication due to hemoptysis, a lack of appetite, and a lesion on her right hip. Bronchoscopy and biopsy of the lung mass were performed on the

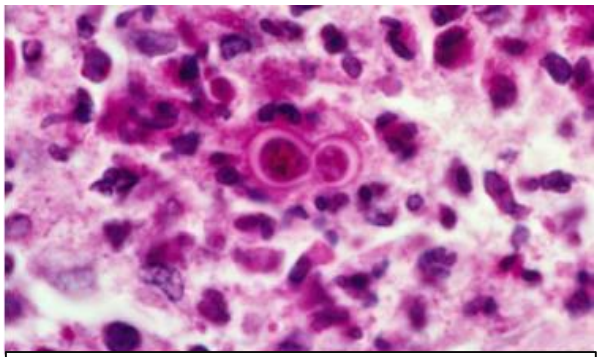

Figure 2 Pathology image from biopsy of lung mass

patient (Fig.2). The lung biopsy revealed benign lung parenchyma with active chronic inflammation and multinucleated large cells, suggesting non-necrotizing granuloma, as well as fungal organisms (budding yeast type). Rare broad-based budding yeast forms measuring 12 - 15 m, consistent with fungal organisms, were detected using special fungus and acid-fast bacteria stains, with Blastomyces species being the most prevalent.

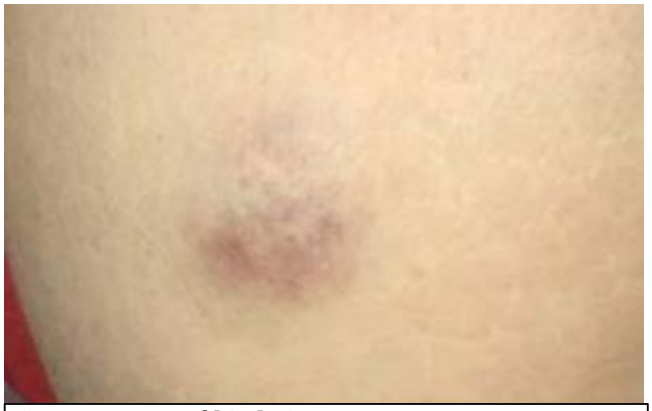

Figure 3 Image of hip lesion

A punch biopsy of the right hip lesion (Fig. 3) revealed yeast-like organisms within multinucleated large cells, which was consistent with blastomycosis. B. dermatitidis was identified from a fungus tissue culture taken from the lesion.

Following confirmation of B. dermatitidis by biopsy and tissue culture, piperacillin-tazobactam was stopped, and a multi-disciplinary decision was made to start the patient on amphotericin B lipid complex infusion 300 mg (5 mg/kg) once daily for two weeks, followed by itraconazole 200 mg twice daily for a total of 12 months of treatment. The patient had nausea, vomiting, chills, and rigors around an hour into the first amphotericin infusion. The first infusion was halted, and the patient was given IV diphenhydramine, which brought the symptoms under control. The next day, the infusion period was slowed down, and pre-medication with IV diphenhydramine, IV prochlorperazine, and acetaminophen was prescribed along with the next infusion.

In addition, the patient was recovering from an acute kidney impairment caused by the administration of vancomycin and piperacillin/tazobactam earlier in this case. The patient was informed of the hazards of itraconazole to the fetus once again, and a multidisciplinary decision was taken to proceed with a 12-month treatment regimen of itraconazole monotherapy. She handled the regimen well and gave birth to a healthy baby boy by spontaneous vaginal delivery. At her follow-up consultation with infectious disease, the patient was assessed and the 12-month itraconazole regimen was planned to be finished.

Discussion:

In pregnancy, blastomycosis is uncommon. Azole antifungal medications should be avoided, according to the 2008 IDSA guideline guidelines for blastomycosis therapy, and despite its well-known toxicity, amphotericin B remains the preferred systemic drug. Nephrotoxicity rates in pregnant and non-pregnant patients were similar, according to the data. Liposomal and lipid complex formulations of amphotericin B have also been demonstrated to be safe and effective during pregnancy, and are often preferred over traditional versions due to their low risk of adverse effects. Although amphotericin B crosses the placenta, animal tests have shown that it has no teratogenic consequences. [3]

Itraconazole is an additional standard-of-care drug for non-pregnant individuals with blastomycosis. In contrast to the amphotericin B lipid complex, which is approved during pregnancy, itraconazole is not suggested owing to the potential of teratogenicity. In animal tests, itraconazole was found to induce a dose-related increase in maternal toxicity, embryotoxicity, and teratogenicity, and it should be avoided during pregnancy, particularly in the first trimester. [4]

In 2020, a meta-analysis looked into the effects of oral fluconazole and itraconazole on prenatal outcomes. Oral itraconazole or fluconazole was not linked to an increased incidence of overall birth abnormalities, spontaneous abortion, or stillbirth, according to the study. However, the agents may be associated to an elevated risk of various birth malformations (e.g., eye, limb, neurological, digestive, and urinary system disorders). [5]

Despite the increased safety evidence, itraconazole is still not indicated for usage during pregnancy, particularly in the first trimester. Contraception is also recommended throughout itraconazole therapy and for at least two months afterward, according to the manufacturer's instructions.

Conclusion:

While there hasn't been much research on the treatment of disseminated blastomycosis during pregnancy, the general agreement is that amphotericin is the best option. This technique is not always possible, as in the instance of our patient, who was identified in her first trimester and would have been on amphotericin for another 6 months if she had been able to take it. She was unable to take amphotericin, leaving the medical team with a difficult decision to make about how to treat her, especially because azoles are embryotoxic and teratogenic, making them contraindicated during pregnancy. Itraconazole had a good outcome, but additional study into acceptable alternative therapy for pregnant individuals with disseminated blastomycosis is needed.

- **Amphotericin B is a safer choice in treating blastomycosis in pregnant women but when the treatment fails, Itraconazole may be considered for treatment despite the studies suggesting teratogenic effects which in this study did not occur**

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