Volume1|Issue 11|2020

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 Gynaecology.

This issue contains:

- Is there any association between low Body mass index with ectopic pregnancy following assisted reproductive techniques.
- Treatment of refractory immune thrombocytopenic purpura with Romiplostim- A case report.
- A novel biomarker to detect still birth

Should you require any article or, medical information, please feel free to contact us medicalservices@microlabs.in

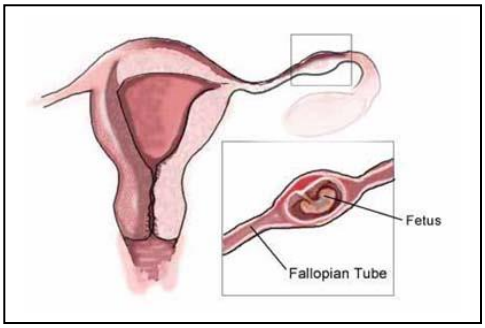
Looking forward to your valuable feedback.

Best Regards,

Medical Team, Micro Labs Limited

1. Is there any association between low Body mass index with ectopic pregnancy following assisted reproductive techniques.

Ectopic pregnancy (EP) is commonest acute abdominal emergencies a gynecologist has to meet in day-to-day practice.



Many pathological conditions present percentage of variables but only a few have greater disparity of symptoms, signs, opinions and reports as ectopic, which has made ectopic pregnancy both an interesting and challenging problem.

Methods:

A retrospective cohort study involving 20000 pregnancies derived from either fresh ET or frozen-thawed embryo transfer for 10 years.

Patients in included were cycles resulting in clinical pregnancies.

Patients excluded were those with cycles with missing data, cycles in women with uterine abnormalities (bicornuate, unicornuate, didelphic or septate uterus) and cycles in women with known diagnoses of metabolic disorders.

Pregnancy cycles were confirmed with visualization of a gestational sac under ultrasound

To analyze the association between BMI categories and EP generalized estimating equation (GEE) was used, as one patient may contribute to more than one pregnancy.

To demonstrate the non-linear association, Generalized additive models (GAMs) were used.

For age, parity, gravidity, previous history of ectopic pregnancy, duration of infertility, PCOS, endometriosis, diagnosis of tubal problem, ovarian reserve markers, ovarian stimulation parameters, insemination protocol, endometrial thickness, and embryo transfer policies, models were adjusted.

Recombinant FSH or hMG were used for the gonadotropin stimulation and the starting dosage was adjusted according to age, BMI and ovarian reserve markers.

Primary outcomes assessed were Ectopic pregnancy visualized on ultrasound or laparoscopy.

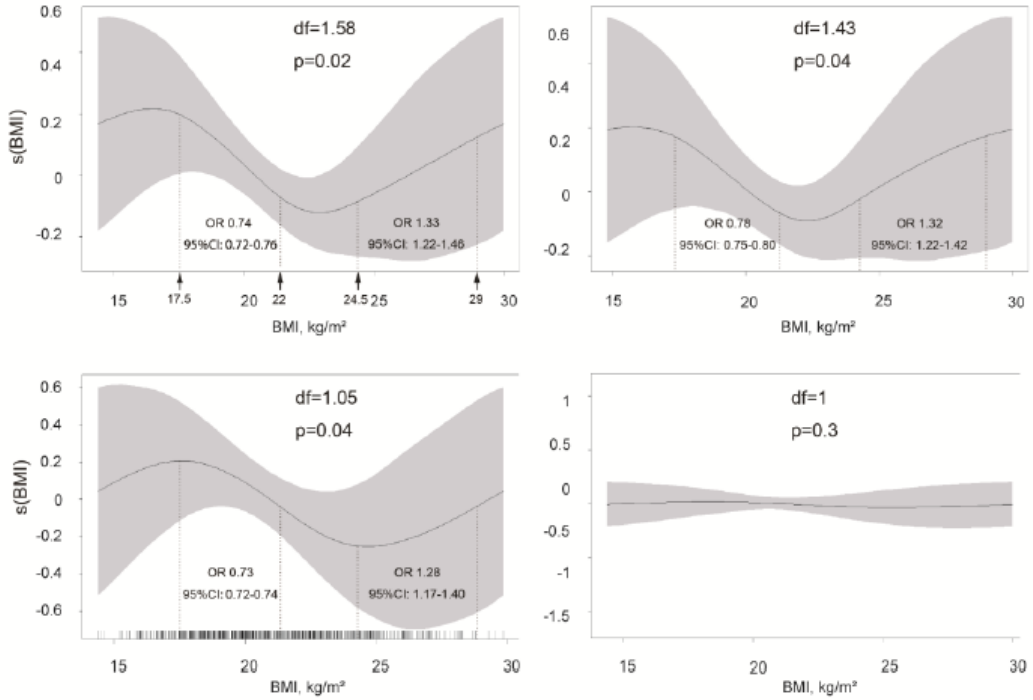
Results:

The rate of EP was significantly increased in the low BMI group (2.92% vs 2.02%, relative risk 1.45, 95%CI: 1.11-1.90) as compared to normal BMI group, but not in the high BMI group (2.84%, relative risk 1.41, 95%CI: 0.92-2.20).

The odds ratio for EP comparing low BMI versus normal BMI was 1.61(95%CI: 1.19-2.16) and that comparing high BMI versus normal BMI was 1.12(95%CI: 0.72-1.76) in GEE analysis.

No significant association between high BMI and EP was found. Other significant predictors

for EP in the multivariate models included diagnosis of tubal problem, use of GnRH agonist in ovarian stimulation, endometrial thickness and stage of embryo transfer.



Results of showed an U shaped association in the overall population (P=0.02). The tendencies were identical in fresh ET and FET (P=0.3). In either type of ET cycle, a decreasing trend was observed when BMI<22 kg/m2 and an increasing trend was observed in cycles with higher BMI.

In the decreasing range of the U-shaped curves (17.5-22 kg/m2), the ORs for EP were 0.74 (95%CI: 0.72-0.76), 0.78 (95%CI: 0.75-0.80) and 0.73 (95%CI: 0.72-74) in all patients, fresh cycles and FET cycles, respectively.

ICSI significantly increased the size of the association between low BMI and EP. On the other hand, tubal problems appeared to have no significant modification on the association between BMI and EP.

Discussion:

Hormones and growth factors, such as leptin and Insulin growth factor significantly alternate in low BMI women. These hormones and growth factors may participate in implantation and embryo development and their serum levels may predict the outcomes of ART.

Current study showed a significant association between low BMI and EP in the population. The OR for EP comparing patients with low BMI with patients with normal BMI is about 1.6.

Studies have shown that women with EP showed a significant reduction in IGF-1 level (4.2 ng/ml) compared with those with a live birth.

Conclusion:

A clear association between low BMI and Ectopic Pregnancy following Embryo Transfer was seen. Low BMI can be a risk factor for Ectopic pregnancy.

Reference:
Cai J et al. Low body mass index is associated with ectopic pregnancy following assisted reproductive techniques: a retrospective study. BJOG. 2020;10.1111/1471-0528.16378.

2. Treatment of refractory immune thrombocytopenic purpura with Romiplostim- A case report.

Common cause of thrombocytopenia in pregnancy is gestational thrombocytopenia, which accounts for 80% of cases and does not impose an increased risk of bleeding to the mother or fetus.

Causes other than this include severe pre-eclampsia/ HELLP (haemolysis, elevated liver enzymes and low platelets) syndrome, which occur in 5%–21% of cases and immune thrombocytopenic purpura (ITP) which occurs in 1%–4% of cases.

ITP during pregnancy can be managed conservatively with observation. First –line treatment includes corticosteroids and intravenous immunoglobulin (IVIG).

Current is a case presentation of case of chronic ITP refractory to first-line management successfully treated with romiplostim in the immediate postpartum period.

Case presentation:

A 40 year old multipara with chronic ITP and well-controlled chronic hypertension on labetalol was found to have severe thrombocytopenia with a platelet count of 37×109/L at 24 weeks of gestation.

Patient was started on oral prednisone (initially 40 mg/day, increased gradually to 90 mg/day) with poor response and then treated with IVIG (0.4 g/kg daily × 5 doses) with good response and her platelet count increased to 144×109/L.

During 28 weeks of gestation, the patient developed superimposed pre-eclampsia with severe features (elevation of liver enzymes). She received antenatal corticosteroids for the acceleration of fetal lung maturity (intramuscular betamethasone 12 mg × 2 doses, 24 hours apart), and labour was induced resulting in a successful vaginal delivery.

Course was uncomplicated with the exception of significant postpartum haemorrhage managed successfully with carboprost 250 µg intramuscularly , Bakri tamponade balloon placement and tranexamic acid (1000 mg intravenously).

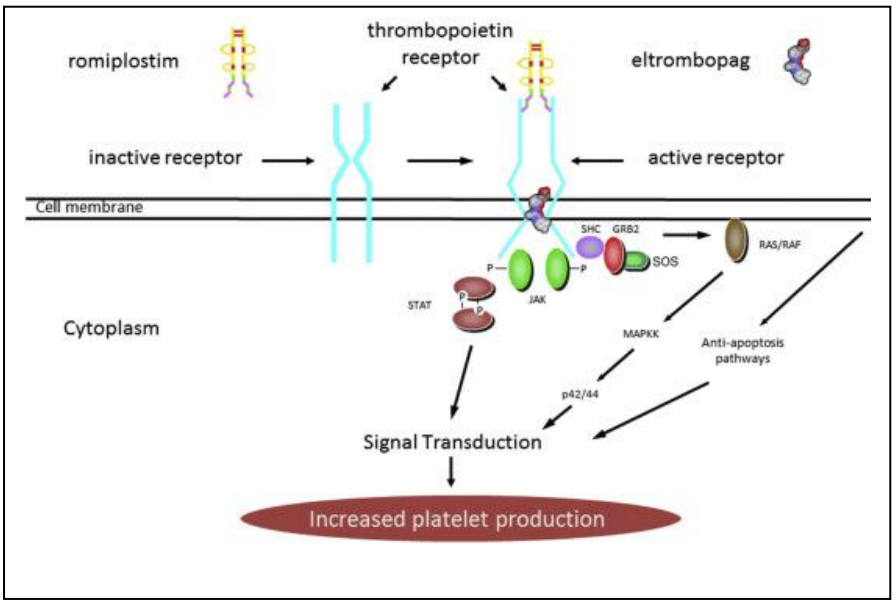
She had an elevation of liver enzymes (peak elevation alanine aminotransferase (ALT): 672 IU/L, aspartate transaminase (AST): 304 IU/L); her platelet count stayed stable ranging from 122×109/L to 150×109/L.

Post delivery, patient's liver enzymes progressively improved (ALT: 438 IU/L and AST: 102 IU/L on second postpartum day). Eventually her platelet count dropped from 112×109/L to 32×109/L 12 hours and to 9×109/L 24 hours.

Differential diagnosis included pre-eclampsia/ HELLP syndrome versus ITP.[1]

Treatment:

Patient did not actively bleed, due to her proximity to the immediate postpartum period, she was transfused with 5 units of platelets with no response.



Following transfusion, the platelet count was 8×109/L. She was started on high-dose intravenous methylprednisolone 500 mg/day for 2 days and was given IVIG 1 g/kg with poor response.

The next morning, platelet count had further dropped to 5×109/L (~60 hours after delivery). She received another 5 units of platelets and the platelet count increased to 12×109/L.

With patient's poor response to the first-line therapies, her proximity to the immediate postpartum period and the risks associated with extremely low platelet count, the decision was made to use romiplostim.

Romiplostim 2 µg/kg on the evening of postpartum day 2 (68 hours postdelivery) along with 90 mg oral prednisone.

Patient received the second dose of 2 µg/kg romiplostim n the third postpartum day. On the fourth postpartum day, her platelet count rose to 16×109/L.

On the fifth postpartum day, her platelet count had increased to 40×109/L and the patient was discharged home with instructions to follow-up with haematology and as an doctor's outpatient visit. Platelet count on the ninth postpartum day was 786×109/L. Platelet count 6 weeks post-partum was 184×109/L.

Discussion

Primary ITP is an autoimmune condition which is characterised by isolated destruction of platelets. IgG antiplatelet antibodies of mother sensitised to native maternal platelet antigens have the potential to cross the placenta placing the fetus and neonate at risk of thrombocytopenia.

Treatment is initiated when the patient has symptomatic bleeding, when platelet counts fall below 30×109/L, or to increase platelet counts to a level considered safe for procedures.

Management of ITP is based on an assessment of maternal bleeding risks associated with the delivery and epidural anaesthesia.

In patients with severe chronic ITP who are not responding to first-line treatments and splenectomy is not preferable, thrombopoietin receptor agonists (TPAs) pose a viable second-line therapeutic option. They do work by increasing the endogenous production of platelets.

Romiplostim and eltrombopag are TPAs approved by the Food and Drug Administration for patients with ITP.

Acccording to a study, evaluating romiplostim in patients with platelet level <50×109/L a positive platelet response was observed in 87% of the 142 patients with ITP enrolled in the study.[1]

Conclusion:

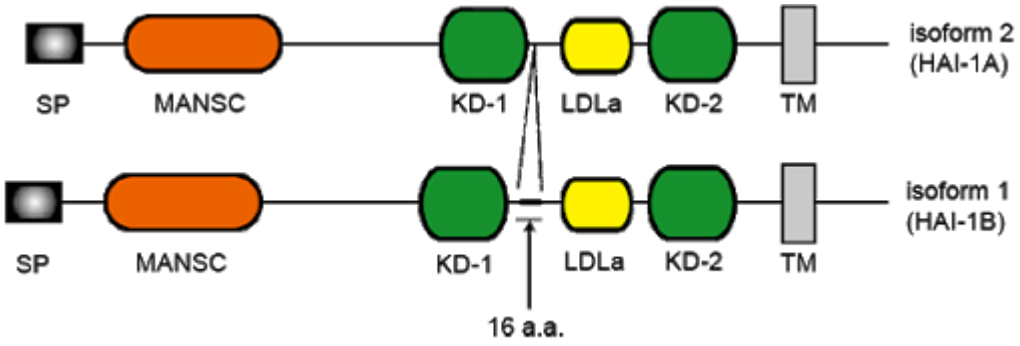
A case of idiopathic thrombocytopaenia was successfully managed with Romiplostim.

Reference:

1)Patras A et al. Romiplostim for management of refractory immune thrombocytopenic purpura in the immediate postpartum period. BMJ Case Rep. 2020;13(5):e234335.

IN FOCUS

A novel biomarker to detect still birth



Placental insufficiency can cause fetal growth restriction and stillbirth. The first sign that a placenta may be failing is poor growth of the baby, or fetal growth restriction. A poorly grown fetus is at 3-4 times increased risk of being born still compared to a well grown fetus.

Screening proteins released directly from the placenta into the mother's bloodstream, researchers have discovered a novel protein called **SPINT1** as a new biomarker of reduced growth of babies.

Risk of stillbirth increases at the end of pregnancy; a time at which expedited delivery of an at risk baby would invariably result in a live birth.

Focusing on blood samples collected from pregnant donors towards the end of pregnancy (36 weeks' gestation) researchers have shown that SPINT1 levels are significantly reduced in women carrying a small baby. [1]

The validation has been done in a study in UK. Remarkably, SPINT1 has considerably stronger associations with several indicators of poor placental function than previously reported biomarkers, and may be the first biomarker to predict women at risk of stillbirth.

Low SPINT1 is associated with antenatal ultrasound and neonatal anthropomorphic indicators of placental insufficiency. Results of the study concluded that. Low circulating SPINT1 is a marker of placental insufficiency and may identify pregnancies with an elevated risk of

stillbirth[2]

Researchers are planning to use artificial intelligence to produce a sophisticated multi-marker blood test that could be offered to women around the world.

Reference:

1)Available at : https://www.mercyhealth.com.au/wp-content/uploads/sites/61/2020/05/Mercy-Health-Media-Release-New-diagnostics-to-prevent-stillbirth-FINAL.pdf. Accessed on 29-06-2020.

2) Kaitu'u-Lino TJ et al. Circulating SPINT1 is a biomarker of pregnancies with poor placental function and fetal growth restriction. Nat Commun. 2020;11(1):2411.

.