Quest Journals
Journal of Medical and Dental Science Research
Volume 9~ Issue 4 (2022) pp: 44-49
ISSN(Online) : 2394-076X ISSN (Print):2394-0751
www.questjournals.org

Research Paper

Pregnancy after Successful Treatment of High-Risk Metastatic Choriocarcinoma- Case Report.

Boniface Uji Ago[1], Emmanuel Eyo Ekanem[2]
[1]*Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Calabar, Nigeria*
[2]*Department of Obstetrics and Gynaecology, University Hospitals of Leicester NHS Trust, UK*
Corresponding author: Boniface Uji Ago
Department of Obstetrics and Gynaecology, University of Calabar, Nigeria.

Abstract
A 40 year old HIV positive patient on highly active anti-retroviral therapy diagnosed and treated for high risk metastatic choriocarcinoma two years earlier became pregnant after successful treatment. She booked early and obstetric scan done showed an active fetus without anomalies detected. Baby was delivered at 39 weeks gestation through emergency Caesarean section because of prelabour rupture of fetal membranes and oblique lie. Type 2b placenta previa was an incidental finding. Placenta was grossly normal, but baby had bilateral talipes equinovarus. βhCG titre done at sixth week postnatal visit was normal and undetectable from eight weeks through to six months after delivery on follow-up. This case report was necessary to publish at least one of our successful pregnancies after chemotherapy for metastatic choriocarcinoma.

Keywords: Metastatic Choriocarcinoma, Pregnancy, Chemotherapy, Childbirth, Calabar

***R**eceived 04Apr, 2022; **R**evised 16 Apr, 2022; **A**ccepted 18 Apr, 2022 © The author(s) 2022.*
P**ublished with open access at **www.questjournals.org

I. Introduction

Pregnancy after choriocarcinoma presents a challenge to both the patient and the Obstetrician/Midwife. After successful treatment of choriocarcinoma, patients should use birth control to avoid pregnancy for at least one year of undetectable serum beta human chorionic gonadotrophin (βhCG). However, if pregnancy occurs, early diagnosis with ultrasonography is crucial to differentiate it from recurrence with rising βhCG titres. Ultrasonography has practically replaced all other methods of making preoperative diagnosis of molar pregnancy.[1]

Choriocarcinoma is at the extreme of a spectrum of trophoblastic neoplasia that are either gestational or non-gestational. Gestational choriocarcinoma does not appear to have a genetic mutation driving the malignancy, but epigenetic alterations probably allow the primitive trophoblastic cells of first trimester placenta to evade apoptosis and maternal immune system.[2] These cells undergo abnormal trophoblastic hyperplasia and anaplasia and directly invade the myometrium and blood vessels.[3] Non-gestational choriocarcinoma arises from pluripotent germ cells in the gonads or midline structures such as lungs, breasts, gastrointestinal tract, bladder, uterus, and cervix.[4] The most common presentation is prolonged vaginal bleeding.[5] Haemoptysis or seizure may indicate lung or brain metastasis respectively.[6] Diagnosis of choriocarcinoma depends on good clinical history and findings, in a dedicated specialist centre. Radiologic findings (Chest X-ray, CT scan of chest and abdomen, MRI of head and pelvis, and Doppler ultrasound scan of the pelvis) and the WHO risk score are crucial.[6]

It is very rare for choriocarcinoma to coexist with pregnancy, a condition reported to occur in 1:160,000 pregnancies.[7] A systematic review of published data on pregnancy outcomes after chemotherapy for trophoblastic neoplasia indicated an increase in some pregnancy complications such as miscarriages and stillbirths compared to the general population.[8] This is a source of worry for patients and midwives.

Our patient had been living with the human immunodeficiency virus (HIV) since diagnosis in 2006. She was enrolled in the United States President's Emergency Plan For AIDS Relief (PEPFAR) program. She was treated for her adult disease and was stable in health. However, between 2006 and 2016 while still on anti-retroviral treatment, her pregnancies were complicated by miscarriages, and preterm births, early neonatal deaths, postpartum haemorrhage and persistently positive Pregnancy tests and prolonged uterine bleeding.

Under our care in 2017, detailed history, physical examination and ancillary investigations confirmed the diagnosis of 'choriocarcinoma in a HIV positive patient'. Choriocarcinoma was treated using EMA-CO regimen comprised of Etoposide, Methotrexate, Actinomycin-D, Cyclophosphamide and Vincristine (Oncovin) for six cycles while she was co-managed by the PEPFAR team for her HIV control. She was disease free for two years before index pregnancy in 2019.

She had an early Ultrasound scan diagnosis following her first missed period and followed up during pregnancy at the prevention of maternal to fetal transmission (PMTCT) unit of our department where drug adherence, CD4 testing and drug side effects were monitored. The highly active antiretroviral therapy were provided by the United States President's Emergency Plan For AIDS Relief (PEPFAR).

Our patient delivered a baby with bilateral talipes equinovarus. Fetal lie was oblique before delivery, and fetal membranes ruptured before labour. Type 2b placental praevia was an incidental finding at caesarean section.

It remains unclear if the talipes equinovarus was related to the oblique lie and placental praevia since Congenital malformations are neither commonly attributable to chemotherapy in patients with choriocarcinoma,[8] nor to antiretroviral drugs in patients living with HIV.

This case report presents a successful outcome (a live baby) after a host of exposures (HIV, antiretroviral drugs, Choriocarcinoma and chemotherapeutics). We find the Talipes equinovarus deformity unusual.

II. Case Presentation

Mrs EA was a 40-year old Gravida 10 Para 4 plus 5 (2 induced abortions and 3 miscarriages) one stillbirth and one early neonatal death, and 2 living children.

She was Efik by tribe, a School Teacher married to a Banker in a monogamous setting. Both couple were diagnosed with HIV in 2006 and have been taking the highly active antiretroviral therapy.

Her first and second pregnancies were in 2003 and were terminated via dilatation of the cervix and curettage of the endometrium. In 2005, she had full term normal delivery of a female baby weighing 2.8kg. Baby is alive and well. In 2007, her pregnancy was complicated by preterm premature rupture of membranes and subsequent retained placenta at delivery. It was an early neonatal death. In 2010, she had a vaginal delivery of a male baby weighing 2.5kg complicated by postpartum haemorrhage. Baby is alive and well. In 2012, her pregnancy was complicated by premature rupture of fetal membranes, intrauterine fetal demise and retained placenta. She subsequently had successful manual removal of the retained placenta. In 2013, she had a complete miscarriage. In 2014, she had another miscarriage and a miscarriage yet again in 2016.

She was first referred to our facility in 2017 at the age of 38 years because of uncontrollable vaginal bleeding following excision of a vaginal mass. She was having haemoptysis and dyspnoea as well as cold clammy extremities. She had a prior history of pregnancy, and repeated evacuations for a failed pregnancy in which pregnancy tests had remained positive for 11 months prior to referral. At presentation on March 1, 2017, following the history of repeated evacuations and persistently positive pregnancy test after 11 months (from last miscarriage in 2016), and an 18-week sized uterine mass, we made a presumptive diagnosis of gestational trophoblastic disease. She had immediate resuscitation and vaginal packing to control the bleeding. We collected blood samples for investigation. Intravenous tranexamic acid was administered. Her Blood group was O RhD positive, Genotype AA, Hepatitis B and C negative. Her serum βhCG titre was 168,000 mIU/ml, and packed cell volume done was 17%. She received three pints of blood transfusion. Chest x-ray was done and it showed typical cannon ball metastases but the liver and renal functions were not impaired. Her WHO risk score was 11 necessitating her treatment with EMA-CO regimen.

She was counselled for chemotherapy and she consented.

After she had completed the first course of chemotherapy, she had another episode of vaginal bleeding for which examination under anaesthesia revealed three bleeding nodules 3cm sized on the posterior vaginal wall, anterior lip of cervix and the previous suburethral nodule. Only the nodule on the posterior vaginal wall was actively bleeding. Bleeding stopped after ligation and excision.

The patient had antibiotics, analgesics and haematinics, and repeat βhCG just before the second course of EMA-CO was 12,790 mIU/ml. Serum βhCG assay done before the third and fourth courses of EMA-CO were 326.9mIU/ml and 40.7mIU/ml. She tolerated six courses of chemotherapy following standard guidelines.

Subsequent βhCG assays were negative through follow up for 2 years. Normal menstruation had resumed 8 weeks after the last dose of chemotherapy.

She presented on the 29th of July 2019 with a last menstrual period (LMP) on the 2nd of May 2019 and a positive pregnancy test. A quick pelvic scan done showed a single active fetus with no obvious abnormality, crown rump length was 6.28cm, with an estimated gestational age of 12 weeks 5 days consistent with her LMP.

She was 1.79m tall, and weighed 82kg looking cheerful and healthy. General physical examination was normal. Blood pressure was 110/70mmHg. On vaginal examination, the vulva and vagina looked normal. The cervix was short and patulous, almost flush with vagina. A diagnosis of cervical insufficiency was made.

Investigations done and subsequent results include; PCV 31%. Urinalysis had no abnormalities detected. Hepatitis B and C as well as Venereal Disease Research Laboratory serology were non-reactive.

She was counselled and she gave consent for cervical cerclage, which was placed on 23.8.2019 (at gestational age of 16 weeks) under saddle block. Purse string suture was placed as high as possible with the knot at 12 O'clock. Estimated blood loss was 10 millilitres.

Anomaly scan was done 0n 4.09.2019 at a gestational age of 18 weeks. It showed an active fetus in breech presentation. Liquor was normal with a posterior low-lying placenta. The fetal biparietal diameter was 37.1mm, head circumference 153mm, abdominal circumference 128mm, femur length 28mm. No abnormalities were detected. Estimated gestational age was 18 weeks.

Her antenatal visits were fortnightly until 30 weeks and then weekly. She was also counselled for bilateral tubal ligation (BTL) as a form of permanent sterilization due to her age and past obstetric history.

The fetal lie and presentation had been longitudinal and cephalic from 30 weeks of pregnancy until her last antenatal visit at 38 weeks. She was requested to do an obstetric scan for placental localization since fetal head was two fingerbreadths above the pelvic brim. She did the ultrasound scan on the 3rd of February 2020. The obstetric scan noted an active fetus in transverse lie with a left postero-fundal placenta. The sonographer reported that the placenta was fundoposterior! She presented the following day (her clinic day), on the 4th of February 2020, at 39 weeks with spontaneous drainage of liquor. The fetus was alive and active. She was booked for emergency Caesarean section.

Intraoperatively fetal lie was oblique with the breech at the left iliac fossa. There was clean peritoneal cavity, but the lower uterine segment had prominent varicose veins. The fallopian tubes and ovaries looked normal. The liquor was clear but scanty, and a type 2b placenta praevia was noted. Outcome was a live male baby, 50cm in length, weighing 3.1 kg, APGAR 8 and 9 in one and five minutes respectively. Placenta was 0.6 kg and looked grossly normal. It was sent for histologic confirmation.

Baby was grossly normal except for bilateral clubbed feet. Pomeroy's bilateral tubal ligation was done intraoperatively while the cervical cerclage was removed vaginally after abdominal closure. Estimated blood loss was 1000 millilitres. The postpartum care was uneventful.

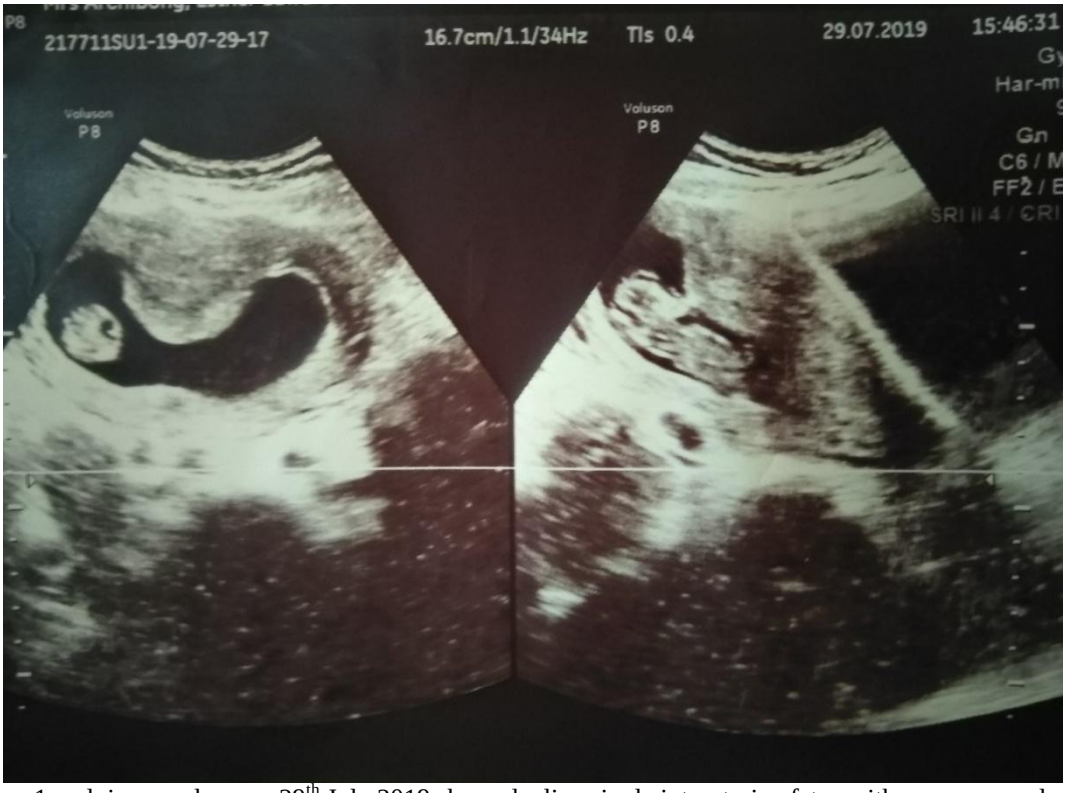

Figure 1: pelvic scan done on 29th July 2019 showed a live single intrauterine fetus with crown rumo length 6.28cm, estimated gestational age 12weeks 5days and expected date of delivery 5th February 2020. Amniotic fluid volume was adequate and no abnormal findings noted.

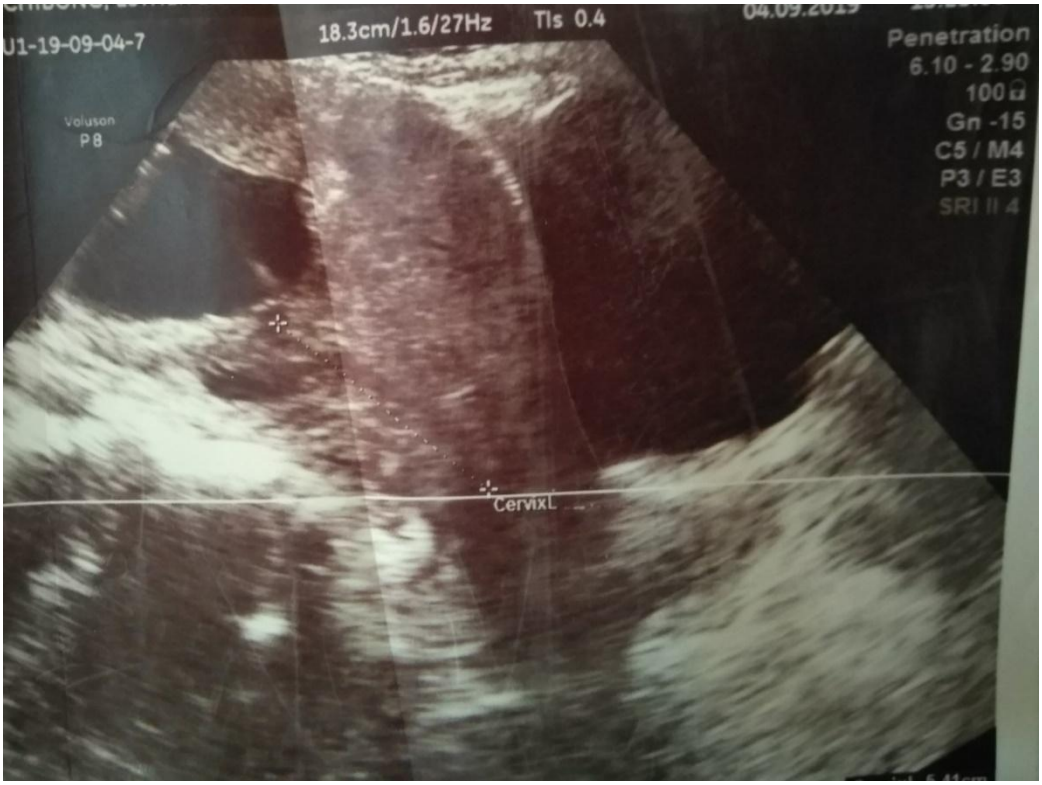

Figure 2: Anomaly scan done on 4.09.2019 at a gestational age of 18 weeks showed no gross fetal or placental anomalies. The placenta was low lying

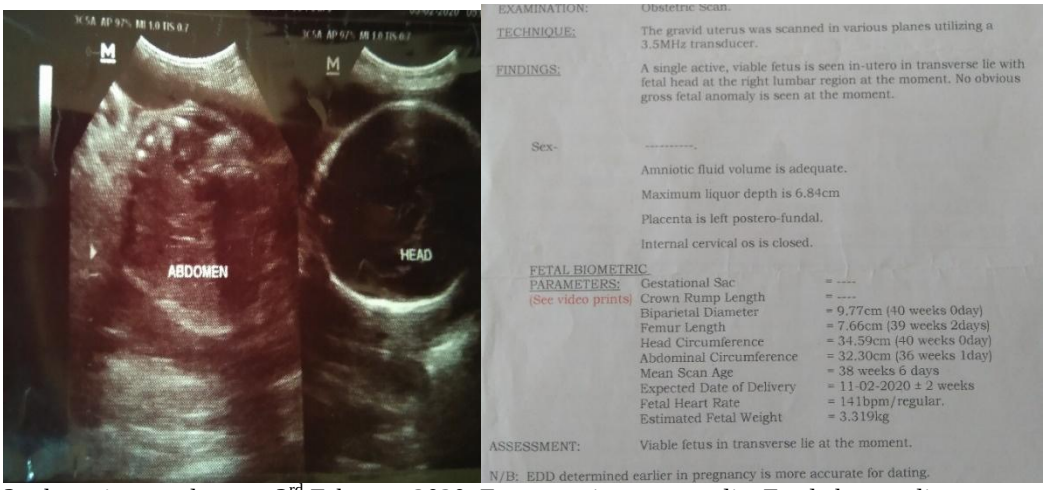

Figure 3: obstetric scan done on 3rd February 2020. Fetus was in tranverse lie. Fetal abnormality was not noted. Placenta was said to be posterofundal

Figure 4: bilateral clubbed feet noticed at delivery of the baby. Image taken by author's android camera.

Review at six weeks postnatal clinic, the histology of the placenta showed no abnormality. The baby had his feet in corrective plaster of Paris cast, the uterus had undergone complete involution, and the βhCG were normal. Baby was on artificial feeding option chosen by his mother as her preferred option due to her HIV seropositivity. He had normal developmental milestones.

Patient had monthly βhCG monitoring, which remained undetectable from 8 weeks till 6 months before discharge from follow-up care.

Patient's Perspective

I have never been so scared and near death when I had the torrential bleeding from my vagina after I went for a repeat evacuation following my miscarriage. I could feel the helplessness in the private hospital doctor before he referred me to the Teaching Hospital under the care of Dr Ago. It was like a miracle. The difference in care was clear but with a huge financial burden doing the serial hCG testing and imaging. When I was taken to theatre because of another episode of bleeding, I overheard some consultants saying that in their opinion my womb should be removed. It was distressing, as I had wanted to have another child. It was a huge relief when I was told later that bleeding was controlled without removing the womb.

When I became pregnant again after the successful treatment, I was so scared. The fear of another bleeding, miscarriage and even death. I called Dr Ago who told me to do an Ultrasound scan. The subsequent care and successful delivery is really worth celebrating.

III. Discussion

There have been several cases of successful pregnancies after complete treatment of choriocarcinoma, but none has been reported from our centre.

Initially, this patient was referred to us from a peripheral centre with uncontrollable vaginal bleeding following excision of a metastatic suburethral nodule. It is often not advisable to remove such nodules because of major haemorrhage.[6] Her positive HIV status also impeded frantic effort to control the bleeding at the peripheral centre. The diagnosis of choriocarcinoma was also not suspected.

We made the diagnosis of choriocarcinoma through the clinical history and examination, βhCG titres and chest X-ray. She responded well to EMA-CO regimen with complete remission without hysterectomy. This case supports the efficacy of the EMA-CO regimen.[9] It was even more exciting that she did not suffer premature menopause following the multi-agent chemotherapy, which has an increased risk.[6]

Follow up requires a minimum of one year.[6] It is important that an ultrasound scan be done early in pregnancy to ensure that pregnancy is not abnormal. Our patient's first trimester scan (Figure 1) revealed no abnormalities. This was in keeping with recommendations by Lurain.[9] Patients with past obstetric histories suggestive of cervical insufficiency may have cervical cerclage placed prophylactically.[10] This was the case in our patient and cervical cerclage was placed at 16 weeks of pregnancy. Anomaly scan (Figure 2) done at 18 weeks did not show any fetal anomalies.

Although the pregnancy appeared normal till term, the presence of abnormal lie, spontaneous rupture of fetal membranes necessitating emergency Caesarean section, a type 2b placental praevia and a healthy baby with bilateral talipes equinovarus, are thought provoking. The presence of this congenital anomaly may not have been due to her previous disease,[9] neither could it be explained by oligohydramnios because emergency Caesarean Section was done within 24 hours of membranes rupture. The ultrasound diagnosis of 'fundoposterior placenta' a day prior to delivery may have been an observer error using a transabdominal probe.

The placenta was histologically normal. However, βhCG surveillance was done and the values were normal for 6 months before discharge from follow-up.

We have reported a case of successful pregnancy and delivery in a 40 year-old woman who had EMA-CO regimen without hysterectomy for the treatment of high-risk metastatic choriocarcinoma two years previously.

IV. Conclusion

EMA-CO regimen successfully treated metastatic choriocarcinoma with no need for hysterectomy. Successful pregnancy and delivery was achieved after EMA-CO regimen in a 40 year old woman. Although the baby had bilateral talipes equinovarus deformity at birth, we are uncertain of any associations between this deformity with previous maternal exposures (HIV, antiretroviral drugs, choriocarcinoma, chemotherapy), and the obstetric complications (premature rupture of membranes and type 2b placenta praevia) in our patient.

ACKNOWLEDGEMENT
Not applicable
CONFLICT OF INTEREST
The authors declare no Conflicts of interest and no funding.
AUTHOR CONTRIBUTIONS
BUA: wrote the manuscript, did literature search and review, got patient's consent and approved the final draft.
EEE: reviewed the manuscript with professional grammar and linguistic revision, and approved the final draft.
ETHICAL APPROVAL
No ethical issue of conflict declared. The patient gave an informed written consent for the publication.
DATA AVAILABILITY STATEMENT
The data used in this manuscript are available online and easily accessible

References

[1]. Lurain, JR. 2019. "Hydatidiform mole: Recognition and management." *Contemporary OB/GYN Journal* 64(3).
[2]. Savage P, Monk D, Mora J, Westhuizen N, Rauw J, Tinker A, Robinson W, Song Q, Seckl M, Fisher R. 2019. "A case of intraplacental gestational choriocarcinoma;characterized by the methylation pattern of the early placenta and an absence of driver mutations." *BMC Cancer* 19:744.
[3]. Lurain JR. 2010. "Gestational trophoblastic disease 1: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole." *American Journal of Obstetrics & Gynecology* 531-539.
[4]. Stockton L, Green E, Kaur B, De Winton E,. 2018. "Non gestational choriocarcinoma with widespread metastasespresenting with type1 respiratory failure in a 39 year old female: case report and review of literature." *Case Rep Oncol* 11(1):151-158.
[5]. Maasoumeh M, Maasoumeh S, Kimiaee P. 2016. "A case study of choriocarcinoma following a term pregnancy." *Acta Medica Mediterranea* 32:1025-1028.
[6]. Tidy J, Seckl M, Hancock BW on behalf of the Royal College of Obstetricians and Gynaecologists. 2020. "Management of Gestational Trophoblastic Disease." *BJOG* https://doi.org/10.1111/1471-0528.16266.
[7]. Ganapathi KA, Paczos T, George MD, Goodloe S, Balos LL, Chen F. 2010. "Incidental finding of placental choriocarcinoma after an uncomplicated term pregnancy: a case report with review of the literature." *Int J Gynecol Pathol* 29(5):476-478.
[8]. Garcia MT, Lin LH, Fushida K, Francisco RP, Zugaib M. 2016. "Pregnancy outcomes after Chemotherapy for Trophoblastic Neoplasia." *Rev Assoc Med Bras* 62 (9):837-842.
[9]. Lurain JR. 2011. "Gestational trophoblastic diseases II: Classification and management of gestational tropholastic neoplasia." *American Journal of Obstetrics and Gynecology* 11-18.
[10]. Brown R, Gagnon R, Delisle M-F. 2013. "Cervical Insufficiency and Cervical Cerclage." *J Obstet Gynaecol Can* 35(12):1115-1127.