MOLAR PREGNANCY: A SYSTEMATIC REVIEW

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ABSTRACT

Molar pregnancies represent a significant burden of disease on the spectrum of gestational trophoblastic diseases. The incidence appears to be higher in women from South Asia. This higher trend in some populations has been attributed to nutritional and socioeconomic status. Most cases of molar pregnancy are diagnosed in the first trimester by ultrasound or as early pregnancy losses. The cure rate for molar pregnancies, including for those women requiring chemotherapy, is 99%. The purpose of this review article is to determine the incidence, presentation, and outcomes of all molar pregnancies. The specific aims in this review literature are to determine the incidence, the associated morbidity, presentation, risk factors, and complications noted throughout UK countries. This would really be helpful in the context of the cities which serves as the tertiary referral center for all the cases from the largest province of the countries of UK.

KEYWORDS: molar pregnancy, trophoblast, chemotherapy, choriocarcinoma, hydatidiform moles.

INTRODUCTION

A molar pregnancy — also known as hydatidiform mole — is a noncancerous (benign) tumor that develops in the uterus. A molar pregnancy starts when an egg is fertilized, but instead of a normal, viable pregnancy resulting, the placenta develops into an abnormal mass of cysts. In a complete molar pregnancy, there's no embryo or normal placental tissue.[1] In a partial molar pregnancy, there's an abnormal embryo and possibly some normal placental tissue. The embryo begins to develop but is malformed and can't survive. A molar pregnancy can have serious complications — including a rare form of cancer.[2]
In a normal pregnancy the fertilized egg is made up of 23 of the mother’s chromosomes and 23 of the father’s chromosomes. The placenta provides nourishment to the developing baby and removes waste products. The placenta is made up of millions of cells known as trophoblastic cells.\(^3\) This can be depicted by the following diagram(figure 1).

The diagram in Fig 1 is a reminder of normally how an egg develops, is fertilized and then implants in the wall of the uterus.\(^3\)

In a complete molar pregnancy the egg contains no maternal chromosomes and only the 23 paternal chromosomes, meaning there is no fetus or amniotic sac present. Trophoblastic cells behave abnormally as soon as the egg has been fertilized by the sperm. This results in a mass of abnormal cells that can grow as fluid-filled sacs (cysts) with the appearance of white grapes.\(^4\) These cells grow rapidly within the womb, instead of developing into a baby. The abnormal cells are referred to as a "mole", which is from the Latin for mass or lump. These cysts grow in clusters like grapes and are visible by ultrasound.\(^5\)

**Molar pregnancy (figure 2)**
During a molar pregnancy, the placenta develops into an abnormal mass of cysts. The embryo either doesn't form or is malformed and can't survive.\textsuperscript{[5]}

**Grape-like cysts from a hydatidiform mole (figure 3)**\textsuperscript{[5]}

A partial molar pregnancy occurs when there are 23 chromosomes from the mother and double from the father, making 69 chromosomes in total rather than the normal 46. This can occur because two sperm enter the egg and fertilise it, or because the sperm replicates itself once inside the egg.\textsuperscript{[6]} In a partial molar pregnancy there will be some normal placental tissue amongst the abnormal cells, and an embryo does develop. This may be a foetus or foetal cells but is genetically abnormal and not compatible with life, and will not survive longer than three months.

**Diagram of Partial Mole (figure 4)**\textsuperscript{[6]}

Types of molar pregnancy
There are two main types of molar pregnancy, depending on the balance of chromosomes in the egg. These are:

- **complete moles** – when no normal placental tissue forms and no foetus develops; instead, a mass of abnormal cells grow.\textsuperscript{[7]}

- **partial moles** – when some abnormal placental tissue forms along with some abnormal foetus; the foetus cannot develop into a baby.

In very rare cases, a twin pregnancy can include a normal foetus and a mole.\textsuperscript{[7]}
How common is molar pregnancy

Molar pregnancies are rare. About one to three in every 1,000 pregnancies turns out to be molar. With only 1600 cases registered in the UK each year, most individual obstetric or gynecology teams are only likely to see a case every few years. The incidence is higher amongst women of Asian origin, but the reasons for this are still unknown.

Etio-pathogenesis

Molar gestations are increased in older and very young females of reproductive age and in those with a history of prior molar pregnancy. Advanced paternal age may be a risk factor for a complete molar pregnancy.

1. A complete molar pregnancy occurs when a sperm fertilizes an empty ovum, resulting in the development of only placental parts. A complete mole is completely paternal in origin, with a karyotype of usually 46 XX.

2. A partial mole results when two sperms fertilize a single ovum and results in development of certain or all fetal parts. A partial mole predominantly has a triploid karyotype of 69XXX or 69 XXY or 69 XYY; however, a diploid karyotype may also exist.

Genetics

Molar pregnancies are the premalignant forms of gestational trophoblastic neoplasia, a group of illnesses that also includes the rare but aggressive malignancies of choriocarcinoma and placental site trophoblastic tumours. Fortunately, in the absence of any indication for additional treatment, women with simple molar pregnancies should be reassured that they have not had cancer but will just need close monitoring. The genetic events occurring in normal conception and in complete and partial molar pregnancies are shown in Figure 5.

Genetic status in normal conception and molar pregnancy

Genetic events occurring in normal conceptions and complete and partial molar pregnancies (figure 5)
In a normal conception, 23 chromosomes are derived from the mother and 23 from the father, but in complete molar pregnancies the genetic material of the trophoblast cells is entirely of male origin following the loss of the maternal chromosomes from the oocyte. Usually the chromosome count is 46XX, which results from a single sperm duplicating within an empty oocyte. Less often, a 46XY genotype can occur when an empty ovum is fertilized by two sperm. In partial molar pregnancies, the trophoblast cells have three sets of chromosomes: two from the father and one from the mother. Partial molar pregnancy is believed to occur as a result of two sperm entering the oocyte at the same time: this leads to fertilization but with twice the normal complement of genetic material from the father.

**Risk factors**

Whilst the diagnosis of molar pregnancy is rare, there are two groups of women who have significantly elevated risks of developing a molar pregnancy. At the extremes of the reproductive age, girls under the age of 15 years have a risk approximately 20 times higher than women aged 20–40, whilst women aged over 45 have a several hundred-fold higher risk than those aged 20–40. The increased risk for these groups is mainly for complete molar pregnancy, with the incidence of partial molar pregnancy changing less across the age groups. The second group of women with an increased risk of molar pregnancy is those who have had a molar pregnancy previously. In this group, the risk appears to be approximately 1 in 55 for those with one previous molar pregnancy and 1 in 10 for those with two.

A molar pregnancy is thought to be caused by a problem with the genetic information from either the sperm or the egg. Factors that may increase your risk of having a molar pregnancy are:

- **Age** – complete molar pregnancies are more common in teenage women and women over 45 years old. Age has little or no effect on the risk of partial molar pregnancy.

- **Previous molar pregnancy** – if you have had one molar pregnancy before, your chance of having another one is around one to two in 100, compared with one in 600 for women who haven't had a molar pregnancy. If you have had two or more molar pregnancies, your risk of having another is around 15-20 in 100.

- **Ethnicity** – molar pregnancies are most common in Asian countries, such as Taiwan, the Philippines and Japan, and also among Native Americans. However, in recent years, the differences in the incidence of molar pregnancy between these communities and the general population have become less marked.

- **A low intake of carotene** (a form of vitamin A).
- Ovulatory disorders, such as Polycystic Ovary Syndrome (PCOS).
- Living in, or coming from certain geographic areas (as mentioned before women from Southeast Asia).\(^{[19]}\)

**Signs & Symptoms**

A molar pregnancy may seem like a normal pregnancy at first, but most molar pregnancies cause specific signs and symptoms, including:

- Dark brown to bright red vaginal bleeding during the first trimester
- Severe nausea and vomiting
- Sometimes vaginal passage of grape-like cysts
- Rarely pelvic pressure or pain\(^{[20]}\)

In many cases there may be no signs that patient is having a molar pregnancy and it may go undetected until routine early pregnancy scan at 10-12 weeks. If patient experience any signs or symptoms of a molar pregnancy, she should consult physician or pregnancy care provider.\(^{[21]}\) He or she may detect other signs of a molar pregnancy, such as:

- Rapid uterine growth — the uterus is too large for the stage of pregnancy
- High blood pressure
- Preeclampsia — a condition that causes high blood pressure and protein in the urine after 20 weeks of pregnancy\(^{[22]}\)
- Ovarian cysts
- Anemia
- Overactive thyroid (hyperthyroidism)\(^{[22]}\)

**How molar pregnancies diagnosed**

- The diagnosis of a molar pregnancy might be suspected based on a number of clinical features: abnormal vaginal bleeding in early pregnancy is the most common presentation;\(^{[23]}\) uterus large for dates (25%); pain from large benign theca-lutein cysts (20%); vaginal passage of grape-like vesicles (10%); exaggerated pregnancy symptoms including hyperemesis (10%), hyperthyroidism (5%), early preeclampsia (5%).
- Nowadays ultrasound scan often permits to diagnose molar pregnancy before 12 weeks, showing a fine vascular or honeycomb appearance. Later a complete mole is characteristically described as snowstorm appearance of mixed echogenicity, representing hydroptic villi and intrauterine hemorrhage. The ovaries often contain multiple large theca-lutein cysts as a result of increased ovarian stimulation by excessive beta-hCG\(^{[24]}\).
Ultrasound diagnosis of partial mole is more difficult: the fetus may be still viable, but may show signs consistent of triploidy, such as unusually early growth restriction or developmental abnormalities. There may be only scattered cystic spaces within the placenta, and ovarian cystic changes usually much less pronounced. In case of doubt, the scan should be repeated in 1 to 2 weeks.

In women with a complete mole, the quantitative serum beta-hCG level is higher than expected, often exceeding 100,000 IU/L. In case of a partial mole, the level of beta-hCG is often within the wide range associated with normal pregnancy and the symptoms are usually less pronounced. For these reasons the diagnosis of a partial mole is often missed clinically and made from subsequent histologic assessment of the abortive material.\cite{25}

**Imaging**

- The diagnosis of molar pregnancy can nearly always be made by ultrasound, because the chorionic villi of a typical complete mole proliferate with vacuolar swelling and produce a characteristic vesicular sonographic pattern.\cite{26}
- Previously when the diagnosis was made at a later stage, the classical ‘snowstorm’ pattern of the uterus was described; however this is not commonly seen now.
- The majority of first trimester complete moles demonstrated a typical sonographic appearance of a complex and echogenic intrauterine mass containing many small cystic spaces (which correspond to the hydropic villi on gross pathology).
- One may see a large, central fluid collection that mimics an anembryonic gestation or abortion.\cite{27}
- Occasionally, there is merely a central mass of variable echogenicity, presumably because the villi are too small to be seen with sonography at that time.

**Scan of the uterus(figure 6)**\cite{28}

The classical bunch-of-grapes appearance or snow-storm appearance in the uterine cavity is noted. This is the typical appearance of a gestational trophoblastic disease.
Transverse sonogram of the uterus(figure 7)\textsuperscript{[28]}

Transverse sonogram of the uterus demonstrates the heterogeneous mass within the endometrial cavity. The visualized anterior and posterior myometrium appear to be normal and uninvolved.

Sagittal scan of the uterus(figure 8)\textsuperscript{[29]}

This is the sagittal view of the uterus demonstrating that the endometrial cavity is filled with an echogenic mass containing cystic spaces.

Non-invasive GTD may appear avascular and contain many cystic spaces within, which correspond to the swollen chorionic villi. Invasive GTD including choriocarcinomas however show increased intratumoral blood flow, and focal areas of increased flow in the myometrium as well, if there is local invasion.\textsuperscript{[30,31]} Presence of extrauterine gestational disease confirms the aggressive nature of the GTD. In borderline cases, the final diagnosis of invasion versus
non-invasion is confirmed only by histopathology and hence all the evacuated moles need to undergo a complete pathological workup.

Ovarian enlargement with bilateral theca – lutein cysts is a common association.

Studies have concluded that it is not always possible to make a diagnosis of early molar pregnancy by ultrasonography and therefore, histological examination of the aborted or evacuated specimens remains important and DNA analysis should be carried out for the final diagnosis, if histology is inconclusive. Genetic marker analysis using polymerase chain reaction is rapid and accurate in identifying and classifying complete and partial moles. A complete mole has about a 15% chance of recurrence, while a partial mole has about a 3% chance.

Serum quantitative beta HCG levels provide important information for deciding on the likelihood of a molar pregnancy. These levels are usually very high for the given gestational period, although early stages may have normal levels. Failure of these levels to return to a normal value, post treatment, is a prognostic indicator of retained molar tissue. The present data indicates that ultrasound can correctly identify molar changes in early pregnancy and together with HCG levels and uterine Doppler measurements may establish the differential diagnosis in utero of the various forms of placental molar transformations. Patients are often counseled to avoid pregnancy for at least one year to minimize the risk of missing persistent trophoblastic neoplasia.

With a standard ultrasound, high-frequency sound waves are directed at the tissues in the abdominal and pelvic area. During early pregnancy, however, the uterus and fallopian tubes are closer to the vagina than to the abdominal surface, so the ultrasound may be done through a wand like device placed in patient’s vagina.

**Transvaginal ultrasound (figure 9)**
An ultrasound of a complete molar pregnancy — which can be detected as early as eight or nine weeks of pregnancy — may show:[35]

- No embryo or fetus
- No amniotic fluid
- A thick cystic placenta nearly filling the uterus
- Ovarian cysts

An ultrasound of a partial molar pregnancy may show:

- A growth-restricted fetus
- Low amniotic fluid
- A thick cystic placenta

If health care provider detects a molar pregnancy, he or she may check for other medical problems, including:

- Preeclampsia
- Hyperthyroidism
- Anemia

**Treatment & Drugs**

A molar pregnancy can't continue as a normal viable pregnancy. To prevent complications, the molar tissue must be removed. Treatment usually consists of one or more of the following:

- **Dilation and curettage (D&C).** To treat a molar pregnancy, doctor removes the molar tissue from patient’s uterus during a procedure called dilation and curettage (D&C). A D&C is usually done as an outpatient procedure in a hospital.

During the procedure, patient receives a local or general anesthetic and lie on her back with legs in stirrups. Doctor inserts a speculum into patient’s vagina, as in a pelvic exam, to see his/her cervix. Doctor then dilates his/her cervix and removes uterine tissue with a vacuum device. A D&C usually takes about 15 to 30 minutes.

- **Hysterectomy.** If the molar tissue is extensive and there's no desire for future pregnancies, patient might have surgery to remove her uterus (hysterectomy).

- **HCG monitoring.** After the molar tissue is removed, doctor repeats measurements of your HCG level until it returns to normal. If patient continue to have HCG in her blood, she may need additional treatment.[37] Once treatment for the molar pregnancy is
complete, doctor may continue to monitor her HCG levels for six months to one year to make sure there's no remaining molar tissue. Because pregnancy makes it difficult to monitor HCG levels, doctor may recommend waiting until after follow-up before trying to become pregnant again.[37]

After treatment
Following the mole's removal, some cells will be left in the womb. These cells usually die off over time in around 90% of women. To check the cells have died, all women who have had a molar pregnancy in the UK undergo monitoring of the hormone hCG (human chorionic gonadotrophin) via the National Trophoblastic Screening Centre's surveillance programme.[38,39] hCG is the pregnancy test hormone produced by a normal placenta, but also by the mole cells, and is the hormone detected in a pregnancy test. It can also be detected in blood and urine tests.

Women on the surveillance programme send in blood or urine samples every two weeks. This is so they can be monitored for signs of persistent trophoblastic disease, which is a risk after all molar pregnancies.[39] Persistent trophoblastic disease needs further treatment with chemotherapy.

Management
In case of a suspected mole, further investigations include a complete blood count, measurement of creatinine and electrolytes, liver - kidney - thyroid function tests, and a baseline quantitative beta-hCG measurement. A careful pelvic and abdominal ultrasound scan should be done to look for evidence of an invasive mole, exclude a coexisting pregnancy, and look for possible metastatic disease. Computed tomography or magnetic resonance imaging may provide further information. Chest radiography or computed tomography should be considered if there are symptoms that suggest pulmonary metastases.[40]

Suction curettage is the preferred method of evacuation regardless of uterine size in patients who desire to preserve fertility.[41] It is best to avoid prior cervical preparation, oxytocic drugs and sharp curettage or medical evacuation, to minimize the risk of dissemination of tissue leading to metastatic disease.[42] Oxytocic agents and prostaglandin analogues are best used only after uterine evacuations when there is significant hemorrhage.
Total abdominal hysterectomy is a reasonable option for patients who do not wish to preserve their fertility. Hysterectomy is particularly advisable for patients >40 years whose risk of developing GTD is significantly increased. Though hysterectomy eliminates the risk of locally invasive disease, it does not prevent metastases and reduces the subsequent risk of persistent trophoblastic disease by up to 50%. [43]

**Histopathology**

The evacuation specimen from women with suspected molar pregnancy should always be sent for histological analysis. In the UK, all specimens from cases of suspected molar pregnancy are also sent for central review. The final diagnosis is frequently altered between the types of molar pregnancy and sometimes to or from non-molar diagnoses. Typically, in a complete molar pregnancy the pathology shows hydropic villi with trophoblastic hyperplasia, while in partial molar pregnancy it frequently shows only focal changes and it is usually far less florid than a complete mole. Newer diagnostic tests, such as immunostaining with p57KIP2, are available at specialist centres and help confirm the diagnosis of complete moles.

Guidelines from the Royal College of Obstetricians and Gynecologists and the British Blood Transfusion Society recommend that all Rhesus-negative women who have a molar pregnancy should be given 250 IU anti-D immunoglobulin after surgical evacuation. [44]

**Follow-Up**

The aims of follow-up are to confirm successful treatment and to identify women with persistent or malignant GTD who may require adjuvant chemotherapy or surgery at an early stage. Persistent vaginal bleeding and above all elevation of serum beta-hCG levels are the main indicators of residual disease.

The outcome of a partial hydatidiform mole after uterine evacuation is almost always benign. Persistent disease occurs in 1.2% to 4% of cases; metastasis occurs only in 0.1% of cases. [45]

In complete moles, these risks are approximately 5 times greater after treatment with uterine evacuation and 2-3 times greater after hysterectomy. [46] The risk of persistent or recurrent GTD is greatest in the first 12 months after evacuation, with most cases presenting within 6 months.
A variety of hCG criteria have been used to diagnose postmolar gestational trophoblastic disease. Recently, the International Federation of Gynecologists and Obstetricians (FIGO) standardized the following hCG criteria for the diagnosis of postmolar gestational trophoblastic disease:

- An hCG level plateau of four values ±10% recorded over a 3-week duration (days 1, 7, 14, and 21).
- An hCG level increase of more than 10% of three values recorded over a 2-week duration (days 1, 7, and 14).
- Persistence of detectable hCG for more than 6 months after molar evacuation.

Use of reliable hormonal contraception is recommended while hCG values are being monitored. Oral contraceptives do not increase the incidence of postmolar gestational trophoblastic disease or alter the pattern of regression of hCG values. Frequent pelvic examinations are performed while hCG values are elevated to monitor the involution of pelvic structures and to aid in the early identification of vaginal metastases. Although pregnancies after molar evacuation usually are normal gestations, pregnancy obscures the value of monitoring hCG levels during this interval and may result in a delayed diagnosis of postmolar malignant gestational trophoblastic disease. A new intrauterine pregnancy should be ruled out on the basis of hCG levels and ultrasonography, especially when there has been a long delay in follow-up of serial hCG levels and noncompliance with contraception. After completion of documented remission for 6-12 months, women who desire pregnancy may discontinue contraception, and hCG monitoring may be discontinued. Patients with prior partial or complete moles have a 10-fold increased risk (1-2% incidence) of a second hydatidiform mole in a subsequent pregnancy. Therefore, all future pregnancies should be evaluated by early obstetric ultrasonography.

**Chemotherapy**

Complete molar pregnancy is well recognized to have the potential for local invasion and distant spread. After evacuation, local uterine invasion occurs in about 15% and metastases in 4%. Complete molar pregnancy is usually divided into low and high risk for persistence based on signs and symptoms of marked trophoblastic proliferation at the time of evacuation, i.e. hCG >100,000 mIU/mL; excessive uterine enlargement; theca-lutein ovarian cyst >6 cm in diameter; older maternal age; a previous molar pregnancy. The risk of postmolar GTD is significant less with partial molar pregnancy and is seen in approximately 1-6%.
Unfortunately there are no distinguishing clinical or pathologic features for predicting persistence after complete molar pregnancy.

Although controversial, the use of chemoprophylaxis at the time of evacuation of high-risk complete molar pregnancy has been shown to significantly decrease the development of GTD from approximately 50% to 10-15%. A number of chemotherapy regimens are used for treating the disease, but the best seems to be the association between methotrexate, actinomycin D and cyclophosphamide.[49]

Subsequent fertility after chemotherapy treatment

Despite exposure to cytotoxic drugs, the fertility of most women is maintained after low- or high-risk chemotherapy treatment and menstruation resumes within 6 months of completing chemotherapy. Chemotherapy does cause some damage to ovarian function, as indicated by the menopause being brought forward by approximately 1 year for low-risk methotrexate and 5 years for high-risk EMA/CO.15After completion of chemotherapy, we recommend that pregnancy is avoided for 12 months to minimise any damaging effects on developing oocytes and to minimise the confusion over disease relapse from hCG produced in pregnancy.[50] Despite the exposure to cytotoxic chemotherapy, particularly in the high-risk group, there does not appear to be any significant increase in fetal abnormalities and most women wishing to conceive are successful. With the increasing number of long-term survivors after chemotherapy for gestational trophoblast tumours, it has become clear that intensive chemotherapy treatment with the EMA/CO and EP/EMA regimens results in an increased risk of second malignancies. An analysis of the gestational trophoblast tumours patient database indicates that the lifetime risk of further malignancy is increased approximately 1.5-fold, with the largest increase being found for myeloid leukaemia.[50] In contrast, single-agent methotrexate does not appear to produce any increased risk of future malignancy or other serious health issues.

Complications

In some cases, the molar disease left after the evacuation of the uterus regrows rather than dies out, and is then known as a persistent disease. This is one of the malignant forms of gestational trophoblastic disease and includes invasive mole and choriocarcinoma. A further suction evacuation may help in a few patients, but chemotherapy is usually necessary to cure the problem.[51]

The risk of needing further treatment is:
1 in 10 after a complete molar pregnancy
1 in 100 after a partial molar pregnancy

Invasive molar pregnancy is usually treated with chemotherapy in the form of methotrexate and folinic acid. Methotrexate is given as an intramuscular (into the muscle) injection, and folinic acid as a tablet. The injection and tablet are given on alternate days for eight days, followed by a six-day rest period. The eight-day cycle of injections and tablets then begins again.[51]

This continues until six weeks after the hCG levels return to normal. Between one and three in every 100 women may see the condition flare up again, so all women are put into a follow-up programme to monitor their hCG after treatment.[52]

Persistent trophoblastic disease is different from normal types of cancer, and the cure rate for women developing it after a molar pregnancy is about 100%. This means that around 100 in 100 women who develop persistent trophoblastic disease after molar pregnancy are cured.

Prevention
If patient had a molar pregnancy, she has to talk to her doctor or pregnancy care provider before conceiving again. He or she may recommend waiting for six months to one year before trying to become pregnant.[53] During any subsequent pregnancies, care provider may do early ultrasounds to monitor her condition and offer reassurance of normal development.

Prognosis
With appropriate treatment, all hydatidiform moles are curable, and nearly all cases of more aggressive molar tumors can be cured. Even with tumors whose features categorize them as having a poor prognosis, 80% to 90% are cured with a combination of surgery and, if needed, chemotherapy.[54]

It is important for women with molar pregnancies to be evaluated periodically after the problem has been treated. Women are advised not to attempt pregnancy for some time in order to be sure that levels of HCG remain at zero and that no further treatment is needed. There is a risk that a molar pregnancy can come back after treatment. Recommendations are changing and vary by hospital.
It is usually possible for women to have a normal, healthy pregnancy after treatment for a molar pregnancy.\textsuperscript{[54]}

**Getting pregnant again**

It is recommended that patient does not get pregnant again until she completes her hCG hormone monitoring, following a molar pregnancy. This normally happens within a few months, but in some cases can take up to a year. Most women who have chemotherapy treatment for persistent trophoblastic disease will have started their periods again six months after treatment.\textsuperscript{[55]}

The Charing Cross Hospital trophoblastic disease treatment team suggest that patient does not try to get pregnant again for 12 months after finishing chemotherapy. She can use any method of contraception, including the pill.\textsuperscript{[56]}

**Emotional effects**

While physical recovery is often relatively quick, it can take longer to recover emotionally from a molar pregnancy. Not only does molar pregnancy involve the loss of a foetus, it also carries the slight risk of a cancerous growth. This can create an enormous emotional strain.\textsuperscript{[57]}

Communicating patient’s feelings with her partner, a doctor, a counsellor, or someone else who has gone through a similar experience can be beneficial. There are support groups and forums that can help people handle the stress of a molar pregnancy, such as the Molar Pregnancy Support Group and the Hydatidiform Mole UK Information and Support Service.\textsuperscript{[57]}

**CONCLUSION**

The general understanding of the natural history and management of molar pregnancy has advanced considerably in recent years. The key-role in obtaining a high cure rate becomes an early diagnosis and the subsequent strictly follow-up. Efforts are still necessary to develop effective new second-line therapies for patients with drug-resistant disease.

**REFERENCES**


