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Contents lists available at Sjournals

Scientific Journal of Medical Science

Journal homepage: www.sjournals.com

Review article

Critical illness in pregnancy

Siniša Franjić*

Independent Researcher, Croatia.

*Corresponding author: sinisa.franjic@gmail.com

ARTICLE INFO

Article history,

Received 12 February 2020

Accepted 13 March 2020

Available online 20 March 2020

iThenticate screening 14 February 2020

English editing 11 March 2020

Quality control 18 March 2020

Keywords,

Cancer

Shock

Hypertension

ABSTRACT

Diseases in pregnancy are rare, and in most cases the growth and development of the baby does not in the least impair the health of the mother. However, during this dynamic period, numerous and rapid changes occur in the body of the pregnant woman, which inevitably affect her life, daily activities and indirectly affect her loved ones. This paper discusses some illnesses and conditions that can occur in pregnancy.

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1. Introduction

The successful epidemiologic evaluation of any particular disease or condition has several prerequisites (Ananth and Smulian, 2010). Two of the most important prerequisites are that the condition should be accurately defined and that there should be measurable outcomes of interest. Another requirement is that there must be some systematic way of data collection or surveillance that will allow the measurement of the outcomes of interest and associated risk factors. The epidemiologic evaluation of critical illness associated with pregnancy has met with mixed success on all of these counts.

There are many common conditions in pregnancy such as the hypertensive diseases, intrapartum hemorrhage, diabetes, thyroid disease, asthma, seizure disorders, and infection that occur frequently and require special medical care, but do not actually become critical illnesses. Most women with these complications have relatively uneventful pregnancies that result in good outcomes for both mother and infant. Nevertheless, each of

these conditions can be associated with significant complications that have the potential for serious morbidity, disability and mortality. The stage at which any condition becomes severe enough to be classified as a critical illness has not been clearly defined. However, it may be helpful to consider critical illness as impending, developing, or established significant organ dysfunction, which may lead to long-term morbidity or death. This allows some flexibility in the characterization of disease severity since it recognizes conditions that can deteriorate rather quickly in pregnancy.

2. Cancer

Very small early cancers may be treated by surgical removal of the lining of the cervix only, especially in women who wish to have more babies (Stephens and Aigner, 2009). Larger invasive cancers are best treated by removal of the uterus (total hysterectomy). Cancers that have begun to spread from the cervix onto the adjacent vagina present more of a problem. They often respond well when initially treated with a combination of chemotherapy/radiotherapy given together as concomitant treatment and sometimes followed by hysterectomy.

If cancer of the cervix has not been diagnosed until it is quite advanced, there is a risk of metastatic spread to lymph nodes, especially lymph nodes in the pelvis. This situation is more likely in women of more than 40 years of age who have not had regular Pap tests. These women often complain of some bleeding and discharge between menstrual periods or after intercourse. If an advanced, ulcerating or fungating cancer is present it should be obvious on examination of the cervix. Surrounding tissues such as the ureters or the rectum may become involved as well as the local draining lymph nodes in the pelvis. CT scans will help detect the extent of the cancer. Such advanced cancers are usually treated by radical surgery or by radiotherapy or both or by radiotherapy and chemotherapy concomitantly followed by radical surgery.

Diagnosis is often delayed because bleeding is erroneously attributed to pregnancy-related complications (Eifel et al., 2001). All pregnant patients should have a careful pelvic examination and Pap smear at their first antenatal visit. Any suspicious lesion should be biopsied. If the Pap smear result is positive for malignant cells and the diagnosis of invasive cancer cannot be made with colposcopy and biopsy, a diagnostic conization may be necessary. Because conization subjects the mother and fetus to complications, it should be performed only in the second trimester and only in patients with inadequate colposcopy and strong cytologic evidence of invasive cancer. Conization in the first trimester of pregnancy is associated with an abortion rate of up to 33%. Conservative conization under colposcopic guidance may reduce the risk.

Traditionally, gynecologic cancers are approached in a multimodal fashion, employing surgery, chemotherapy, and radiation (Brown and Chu, 2016). These important therapies, while often very effective at treating malignancy, often result in difficult multisystem toxicities for patients. Identification of genomic and molecular differences between normal and cancer cells has allowed development of targeted therapies that focus on inhibition of pathways involved in cancer proliferation and metastasis. These therapies ideally provide a more directed approach by selectively acting on targets that are expressed on or in close proximity to tumor cells, thereby limiting toxicity and allowing administration at minimum effective dose rather than maximum tolerated dose, as is standard for traditional cytotoxics. Pathways involving DNA damage repair, angiogenesis, signal transduction, cell proliferation, survival, and metabolism are under active investigation in gynecologic malignancies. Immune therapies involving vaccination and adoptive T-cell infusion are also under evaluation to augment innate tumor-specific immunity.

Cancer is the second leading cause of death in women between the ages of 20 and 39, following closely behind accidents (Singh and Silverman, 2006). The most frequent cancer deaths in this age group are cancers of the breast, lung, colon, and rectum, leukemia, and nervous system cancers. Because of differences between incidence and mortality, the malignancies seen most often in conjunction with pregnancy are lymphoma, leukemia, melanoma, and cancers of the breast, cervix, ovary, thyroid, and colon. Evidence does not support an increased incidence of cancer during pregnancy. The coincidence of pregnancy and cancer does not influence the biology of cancer, nor does it worsen the prognosis of cancer, except when it delays diagnosis or alters therapy. No firm data exist supporting a greater likelihood of a previously treated cancer relapsing during pregnancy. Cancer itself rarely affects the fetus, with only rare reports of placental metastases or fetal malignancy. The impact on mother and fetus may, however, be profound. Diagnostic and therapeutic interventions that are selected may affect the fetus and may even include terminating the pregnancy. Delays in diagnosis or alterations in treatment based on the coincidence of cancer and pregnancy may affect maternal outcome.

The optimal management of a cancer associated with pregnancy requires cooperation and collaboration with a multidisciplinary team that may include obstetricians, gynecologists, medical and radiation oncologists, surgeons, neonatologists, psychologists, nurses, and social workers. It demands intensive interaction between the patient and her care team, and increases the burden of education of the patient and her family members. Ideally, a desired pregnancy will continue without fetal injury or interruption, with delivery of a normal infant at term. Ideally, the mother will receive optimal cancer treatment without delay. Balancing these ideals and making reasonable compromises constitute the crux of medical decision making when cancer is diagnosed during pregnancy.

3. Shock

The overall principles of management of shock in the obstetric population should not differ much from the general population; however, it should take into consideration the physiology of pregnancy (Zouein and Bourjeily, 2015). Identifying pregnant patients in shock may be challenging as early signs of shock such as tachycardia and reduced blood pressure may also be observed in normal pregnancies. Changes in these measurements over time may be more helpful clues. One of the mainstays of the management of critically ill gravidas is maintaining adequate tissue perfusion and oxygenation of both the mother and the fetus. Placental blood flow is proportional to uterine blood flow. The latter is dependent on uterine perfusion pressure which is directly proportional to the maternal systemic blood pressure and cardiac output. Moreover, as uterine blood flow is at its maximal capacity under normal conditions, it is unable to adapt to low perfusion states.

4. Heart and vessels

Pregnancy causes changes in the appearance and function of the heart and great vessels (Beall and Jelks, 2008). Elevation of the hemidiaphragms, which accompanies advancing pregnancy, causes the heart to assume a more horizontal position in the chest, and this results in lateral deviation of the cardiac apex, with a larger cardiac silhouette on chest x-ray and a shift in the electrical axis. The heart does increase in size in pregnancy, but only by about 12%. Cardiac output increases by 30-50%, with most of the increase occurring in the first trimester. Both stroke volume and heart rate increase. The heart rate increases by about 17%, with the maximum reached by the middle of the third trimester (32 weeks). Stroke volume increases by 32%, with the maximum reached by midgestation. After 20 weeks, cardiac output may decrease significantly (25-30%) when the patient lies in the supine position as compared with the left lateral position. This is apparently due to compression of the inferior vena cava by the pregnant uterus with resulting decreased venous return. The distribution of cardiac output is altered as well. At term, 17% of the cardiac output is directed to the uterus and its contents, and an additional 2% goes to the breasts. The skin and kidneys also receive additional blood flow compared with the nonpregnant state. Blood flow to the brain and liver may increase. Perfusion of other organs such as the skeletal muscle and gut is unchanged.

5. Oxygen

Total body oxygen uptake at rest increases by about 30-40 mL/min in pregnancy, or about 12-20% (Beall and Jelks, 2008). Most of the oxygen is needed to meet maternal metabolic alterations. The increased oxygen need is met by increased tidal volume alone because the pulmonary diffusing capacity appears to be decreased in pregnancy, and the respiratory rate does not significantly increase. There is a total increase in minute ventilation of 48% at term, which exceeds the need for increased oxygen delivery. This "hyperventilation of pregnancy" appears to be hormonally mediated and results in a decrease in PaCO₂ to below 30 mm Hg in normal women. Maternal pH does not change because there is a reciprocal decline in bicarbonate concentration. The net result of these acid-base alterations is facilitation of fetal/maternal CO₂ exchange.

6. Blood

Both the volume and the composition of the blood change during pregnancy (Beall and Jelks, 2008). Plasma volume increases by 40-60%, the bulk of the increase occurring before the beginning of the third trimester. The red

blood cell mass also expands, with a total increase of 25% at term. This percentage can be maximized (to about 30%) by iron supplementation. An increase in red blood cell mass occurs throughout pregnancy, but the early-and in some patients disproportionate-increase in plasma volume leads to a dilutional anemia. Normal pregnant women who are not iron-supplemented have hemoglobin concentrations of approximately 11 g/dL at 24 weeks of gestation, with little change until term. Those supplemented with iron have similar hemoglobin concentrations at 24 weeks but manifest an increase in hemoglobin to near-normal at term.

The white blood cell count increases to about 10,000/ μ L at term. The platelet count may decrease slightly to a mean value of 260,000/ μ L at 35 weeks of gestation. Platelet levels above 120,000/ μ L generally are regarded as normal in pregnancy.

7. Immunity

Pregnant women appear to be at increased risk of certain infections, probably owing to the same immune alterations that allow tolerance of the antigenically foreign placenta (Beall and Jelks, 2008). For this reason, reactivation of viral diseases and tuberculosis are more common during pregnancy. Severe complications of common disorders such as varicella and pyelonephritis are also more frequent. Measurable indices of immune function such as white blood cell counts and immunoglobulin levels do not explain the maternal immune dysfunction. Various theories have been offered to explain these observations, but none has achieved general acceptance.

8. Hypertension

Hypertensive disorders of pregnancy affect 1 in 10 pregnancies overall and 1 in 50 severely (Medforth et al., 2011).

Midwives play a critical role in screening and identification of women who are developing pregnancy induced hypertension. During each antenatal care appointment the midwife measures the blood pressure, tests the woman's urine for protein, and observes for signs of excessive oedema.

If the midwife detects mild hypertension without proteinuria an increased level of surveillance will be required and the woman asked to attend more frequently to have her blood pressure and urine monitored. Collaborative care provides the most effective management and after referral to the consultant for investigation the woman can often resume her care in the community provided her condition does not deteriorate.

Once protein appears in the urine the woman should be referred to consultant led antenatal care and this may take place on an outpatient basis, in a day care setting or the woman may be referred to triage with a view to further management. Admission to hospital is required when the mother and fetus require more monitoring and evaluation than can be provided in a day care setting.

The midwife's role is to provide whatever emotional and supportive care is appropriate for the practice setting. Once admitted to hospital the woman will have a daily antenatal examination including urinalysis and the condition of the fetus is monitored by daily cardiotocograph. Blood pressure recording will be undertaken at least every 4h during the day and if the mother wakes during the night.

FBC (full blood count), renal and hepatic chemistry, plasma proteins, and clotting factors will be monitored closely and any deterioration in the maternal or fetal condition will lead to the decision to deliver the baby either by induction of labour or caesarean section.

9. Monitoring

When caring for a critically ill pregnant patient, the question of how to monitor the fetus arises frequently (Beall and Jelks, 2008). Monitoring by auscultation of fetal heart tones is considered one of the vital signs in any hospitalized pregnant women. However, continuous fetal heart rate monitoring with an electronic monitor may be indicated in the viable or near-viable fetus (23 weeks and beyond), especially if the maternal condition affects pulmonary or hemodynamic function. Use of the continuous fetal monitor requires personnel skilled in its interpretation.

Fetal monitoring may be especially helpful during special procedures or surgery when maternal position, hypotension, or anesthesia can lead to fetal compromise that could be reversed with changes in position or fluid

resuscitation. Fetal heart rate monitoring according to a predetermined schedule (nonstress testing) also may be useful in gauging fetal response to the mother's illness and in determining when fetal compromise may necessitate early delivery. This strategy (as opposed to continuous fetal heart rate monitoring) should be reserved for the stable patient whose underlying condition might result in decreased uteroplacental perfusion or altered placental function.

Assessing and monitoring the critically ill pregnant woman is a challenge, notably because of the physiological changes that occur during pregnancy (Jevon and Ewans, 2012). The ABCDE approach to assessing the acutely unwell patient is recommended in assessment but requires the practitioner to possess essential knowledge of these physiological changes to ensure that its application meets the needs of the patient. The onus is on the individual practitioner to ensure that this process occurs.

As with any acutely unwell patient, a multidisciplinary approach and senior assistance are required at the earliest opportunity. This approach is extended in treating the pregnant patient to include groups of staff not frequently called upon in other situations, e.g. obstetricians/neonatologists and midwifery staff. Collaborative working among these professional groups/staff is the key to optimising maternal and fetal outcome. There is an urgent need for the routine use of a national obstetric early warning chart, similar to that in use in other areas of clinical practice, which can be used for all obstetric women, helping the more timely recognition, treatment and referral of women who have, or are developing, a critical illness.

10. Withdraw or Withhold

The decision to withdraw or withhold life-sustaining treatment is most difficult for patients, families, and health professionals (Burke et al., 2009). The ethical aspect of foregoing treatment resides in the legal and ethical right of the patient to self-determination. Unfortunately, the majority of critically ill patients are unable to speak for themselves when decisions to limit treatment are considered. Therefore, careful attention must be paid to previously expressed wishes and the input of surrogate decision makers. If a medical power of attorney is not in place, some states stipulate who the surrogate will be by a legal hierarchy. The ethical basis for identification of an appropriate surrogate is primary if none of the preceding legal bases apply. In this situation, the physician and other health care providers have the responsibility to help identify the person or persons who have knowledge of the patient's values and preferences in order to assist with medical decisions on the patient's behalf. This process can become difficult in circumstances when family members or others close to the patient are in disagreement as to who should be the surrogate or what the patient would prefer. In these cases, health care providers should be knowledgeable of applicable legal directives and their ethical responsibility to act in their patient's best interest. Consultation with the institution's ethics committee may be helpful in trying to reach consensus. Although not responsible for the patient's death, those close to the patient often are left with feelings of guilt and anxiety in addition to their bereavement. It is important that the health care providers support the family both before and after the decision to withhold or withdraw life-sustaining treatment has been made.

End of life care of patients in the ICU (intensive care unit) requires a dramatic paradigm shift in attitude and interventions from intensive rescue-type care to intensive palliative care. When considering the array of interventions that may be discontinued or held, physicians and surrogates should focus on clearly articulating the goals of care. For example, a goal for survival until the patient's important loved ones can gather to say their goodbyes may justify short-term continuation of ventilator support. If the only goal is patient comfort, then such treatment should be stopped. The withdrawal of life-sustaining treatment is a clinical procedure that deserves the same preparation and expectation of quality as other medical procedures. Honest, caring, and culturally sensitive communication with the patient's loved ones and the patient, if competent, should include explanations of how therapies will be withdrawn, what symptoms are expected, strategies to assess and ensure the patient's comfort, and information about the expected survival after interventions are withdrawn.

11. Molecular research

Molecular investigation, carried out in detail by the researcher, will permit the identification of subgroups of patients to be treated more or less conservatively, taking into consideration the "state of health" of the genes and the proteins (Bovicelli et al., 2007). From this "state of health," it should be understood precisely, which neoplasias will respond efficaciously to chemotherapy or surgery and which, will not respond. The clinical management of

patients should therefore understandably be influenced by this knowledge. The biological distinctiveness of the pathology must modify the attitude of the clinician. It is therefore necessary that medical updating take place at many levels, expanding the horizons of one's speciality beyond those considered insurmountable until a few years back. In order to completely take advantage of the theoretical results obtained, it is essential that the updating of the clinician is continuous, and completely well rounded with special attention being paid to the achievements of the pathologist and researcher.

In particular, in daily practice, the jobs of the clinician, the pathologist, and the researcher have to be united as much as possible through the creation of mixed units with the same objectives. It is no longer the various specialities, which condition the creation of work groups, but instead the common fields of interest, which bring together professional figures coming from different fields of interest. Wherever these research units have been constituted, the results are tangible both in terms of clinical care and research. The creation of work groups made up of gynecologists, pathologists, molecular biologists, oncologists, and radiotherapists has profoundly modified the treatment protocols of gynecological neoplasias. Meetings are held weekly during which clinical cases are discussed, problems linked to research under way are addressed, updating takes place in a continuous and reciprocal manner by comparisons with the international literature. Other than the increase in clinical care, this has led to a notable improvement of the quality of teaching offered to residents. Only in this way, through close collaboration, clinical and basic research, and patient care can offer better results.

The way of curing cancer has therefore changed because today research is part of the cure. Because through analysis of the genetic profile of a cancer cell, molecular medicine is capable of reading the cell's capacity of growth and diffusion, and simultaneously, its possible response to medical therapy. Therapy is also research. In addition to personalized and less toxic therapy, innovative therapies have also been introduced because the transfer of research data to the clinic is more rapid.

12. Conclusion

Pregnancy is a normal physiological process, a state of health and joy. Pregnancy complications are a relatively rare. Pregnant women, as well as women who are not pregnant, can be fall ill of various diseases. They are susceptible to, and easily susceptible to, diseases caused by all types of microorganisms. Diseases manifest as acute or chronic. When they occur in pregnancy, they have a more heavier shape than outside of pregnancy, and are often accompanied by severe complications.

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How to cite this article: Franjić, S., 2020. Critical illness in pregnancy. Scientific Journal of Medical Science, 9(2), 443-449.

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