

Preoperative pregnancy testing in surgical patients: How useful is policy of routine testing

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Received: 11th April, 2019

Revision: 28th May, 2019

Accepted: 11th June, 2019

Publication: 10th October,
2019

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ABSTRACT

Surgery in a patient with unrecognised pregnancy has serious ethical and medicolegal implications. There are no guidelines in India for preoperative pregnancy testing (POPT) in surgical patients. This review was undertaken to ascertain utility of routine POPT and whether any specific indication for POPT could be suggested. We performed a literature search to identify publications pertaining to POPT in surgical patients. Searches included PubMed, Google Scholar and internet search for national guidelines. Studies pertaining to incidence of unrecognised pregnancy, cost-effectiveness of POPT, effect of surgery and anaesthesia on pregnancy are included. We excluded articles which were available in languages other than English and those whose full texts were unavailable. Most of the literature about reproductive outcomes after anaesthesia exposure is based on old data. The evidence for teratogenic effect of anaesthetic drugs on human foetus is still inconclusive. Apart from anaesthesia and surgery, the outcome after surgery in unrecognised pregnant patient depends on other factors such as indication for surgery, high incidence of foetal loss in early pregnancy, stress and lifestyle of patient. As it is difficult to unsnarl the effect of these factors, POPT should be offered to all patients who based on history could be possibly pregnant. The cost-effectiveness of POPT appears doubtful, but considering costs associated with miscarriages and medicolegal litigations due to unclear association with anaesthesia, it may indeed be cost-effective.

Key words: Anaesthesia, preoperative pregnancy testing, surgery

Access this article online
Website: www.ijaweb.org
DOI: 10.4103/ija.IJA_293_19
Quick response code


INTRODUCTION

The utility of routine preoperative pregnancy testing (POPT) in surgical patients is nebulous. Despite decades of arguments, this remains a controversial issue. Those favouring routine POPT in surgical patients cite lack of reliability of patient's history in detecting pregnancy, potential of anaesthesia in causing foetal loss or harm and fear of medicolegal issues if maternal and/or foetal injury occurred during or after surgery. Cost-effectiveness, low positive yield in this population, ethical concerns of POPT without explicit informed consent and unclear association between single anaesthesia exposure and foetal or maternal harm are arguments against the routine testing.^[1]

Currently, there is no national guideline in India regarding whether women presenting for surgeries should routinely undergo pregnancy testing or not. The

updated American Society of Anaesthesiologists (ASA) practice advisory recommends that pregnancy testing may be offered to female patients of childbearing age and for whom the result would alter the patient's management.^[2] The National institute for Health and Care Excellence guideline recommend enquiring sensitively on day of surgery to all surgical women of child-bearing potential regarding any possibility of them being pregnant. The women who *could* be pregnant should made aware of risk of anaesthesia and surgery to the foetus and with their consent pregnancy

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How to cite this article: Kerai S, Saxena KN, Wadhwa B. Preoperative pregnancy testing in surgical patients: How useful is policy of routine testing. *Indian J Anaesth* 2019;63:786-90.

testing should be carried out. All discussion with women *whether to carry* out a pregnancy testing should be documented.^[3] A retrospective analysis of universal POPT implementation demonstrated positive results in only 0.06% patients. In view of low yield, the authors recommended *considering* the characteristics of the surgical population with regard to pretest probability of *unrecognised* pregnancy when planning the indications for preoperative pregnancy screening.^[4]

METHODS

This review was conducted with objectives to assess the recent developments in evidence for utility of routine POPT. Studies for reliability of POPT and patient's history in assessing pregnancy status, *cost-effectiveness* and yield of POPT, relationship between anaesthesia exposure and maternal and foetal outcomes were evaluated.

We performed an extensive literature search to identify publications pertaining to POPT in surgical patients. Searches included PubMed, Google Scholar and internet search for national guidelines. A PubMed search using MeSH terms 'preoperative pregnancy testing', 'anaesthesia', 'first trimester anaesthesia' was conducted. Result mostly yields retrospective studies and systematic reviews and editorials. We excluded articles which were available in languages other than English and those whose full texts were unavailable. As anaesthesia drugs and surgical techniques have changed significantly, we limited search to articles between 1/1/2000 and 11/04/2019.

Reliability of POPT

Pregnancy is established by qualitative or quantitative detection of hormone human chorionic gonadotropin (hCG) in urine or serum samples. The serum hCG detection has advantages of appearing 5 days earlier than urine sample and more sensitive, whereas urine hCG is noninvasive, cheaper and can be done on point of care. The trophoblastic cells after implantation of fertilised egg in uterus produce hCG, usually occurring 6–12 days after ovulation. The amount of hCG increases exponentially following implantation, doubling every 1–1.5 days in the first 8–10 weeks of pregnancy.^[5]

There are many factors affecting performance of pregnancy testing kits. The detection limit of most of the commercial kit is between 25 and 50 mIU/ml.

The low levels of hCG in early pregnancy can give false-negative (FN) report. There is variation in the timing of implantation in relation to expected day of period. Many patients test positive a week before or more before *first day of expected period* and 10% of clinical pregnancies occurred only week afterward.^[6] Other factors such as urinary dilution, bacterial contamination or prolonged storage of sample may give FN report. Another reason for FN result is measurement of only intact hCG by some kits, whereas others measure intact plus variants hCG core fragment (hCG β cf). Seven weeks of gestation concentration of hCG β cf is 10-folds higher than intact hCG in urine giving FN result.^[7] False-positive results may be obtained after delivery, abortion, gestational and non-gestational trophoblastic disease and malignancy and in perimenopausal women.^[8] Therefore, interpretation of urine POPT should be done carefully in light of other clinical information. For any result if there is disagreement with patient's history confirmation by serum assay should be considered.

Reliance on patient's history

There is traditional teaching of mistrust in patient's history in assessment of pregnancy status. Ramoska *et al.* reported a 7% pregnancy rate in patients reporting normal and on time menstrual period as well as suggesting that there was no chance of pregnancy.^[9] They recommended liberal use of pregnancy testing in emergency department. However, this study was undertaken in populations where the overall pregnancy rate was very high. Contrary to this, many recent investigators found that self-assessment of pregnancy is more reliable than previously reported. The difference in hospital populations and pretest probability criteria, change in attitudes in discussion of reproductive issues and increase accessibility of home pregnancy testing have been suggested for this discrepancy in studies. Strote *et al.* reported that sexual history and self-assessment are more reliable than a normal menstrual history or use of birth control in determining pregnancy status of patients.^[10] There is 99.7% negative prediction value for answering 'no' to both 'Do you think you might be pregnant?' and 'Is there a chance you could be pregnant?' Stengel *et al.* similarly found only one of 128 patients who denied any possibility of pregnancy being incorrect.^[11]

Cost-effectiveness and yield of POPT

In surgical patients, the incidence of detecting a previously *unrecognised* pregnancy ranges from 0.06% to 5%. Gong *et al.* recently reported extremely low

incidence of undetected pregnancies found on day of surgery urine testing. The surgical patient population studied by authors had relatively high proportion of patient's age >35 and patients who suspected possibility of pregnancy were given opportunity to self-test before scheduling for surgery.^[4] Authors reporting relatively higher incidence of positive pregnancy test had either small sample size or included exclusively those who are undergoing laparoscopic sterilisation or infertility treatment [Table 1].^[4,12-16]

As the levels of β hCG rise exponentially during early pregnancy, most of the studies had policy of POPT done on the morning of scheduled surgery. The positive result of POPT done on morning of surgery contributes to delay in operative schedule, extra workload and cost. The cost per true-positive pregnancy is found to vary from \$1005.29 to \$49,000 in different studies. Another measure for *cost-effectiveness* of POPT is number needed to treat (NNTT), defined as the number of patients who must undergo a preoperative pregnancy test in order to detect one pregnancy. Kahn *et al.* found that the NNTT was 647 to detect one true-positive result, with a cost of \$3273 per true positive.^[14]

Effects of single anaesthesia exposure on foetal and maternal outcomes

Since many decades, surgical procedure under anaesthesia in a pregnant *patient* is believed to increase risk of abortion, stillbirth and preterm labour. They have never been quantified and there is a lack of evidence-based data while counselling these patients.

The estimation of effect of surgery and anaesthesia during first trimester on foetal outcome is extremely difficult to perform for various reasons. There is high

incidence of natural spontaneous abortion of human pregnancy. About 70–80% of conceptions are lost prior to live birth. Data from published studies suggested that 30% of conceptus is lost before implantation; a further 30% is lost following implantation but before missed period and 10% as clinical miscarriage. More than half of early abortions are due to chromosomal abnormalities.^[17] A number of studies done 20–30 years back have concluded increased incidence of spontaneous abortion after surgery.^[18,19] The interpretation of these studies is complex given the background of high incidence of early pregnancy loss. In all these studies, it is difficult to untangle the composite effects of anaesthesia, surgical procedure, indication for surgery and assess independent contribution of each. Other factors such as anxiety and life stress in patient have also been associated with adverse pregnancy outcomes.^[20] Therefore, any documented effects of anaesthesia and surgery on reproductive outcomes should be interpreted as multifactorial origin.

The ASA practice advisory committee has classified surgeries involving the uterus and uterine cavity and those potentially compromising uterine blood flow as high risk for foetal viability.^[2] These include uterine surgeries such as dilatation and curettage, myomectomy, hysteroscopy and cardiac, major vascular surgeries. The risk of abortion in females undergoing these procedures appears to be higher compared to other surgeries at anatomically remote from site of conception and those having minor effect on uterine blood flow.

Recently, Balinskaite *et al.* retrospectively evaluated 47,628 pregnant patients undergoing non-obstetric

Table 1: Incidence of unrecognised pregnancy in surgical patients

Study	Type of study	Study population (n)	Time of test	Type of test	Positive pregnancy test	Cost
Gong <i>et al.</i> (2018)	Retrospective	Elective surgical (8245)	On day of surgery	Urine followed by serum quantitative testing for positives	True positive -0.06%	49,000
Douglas <i>et al.</i> (2015)	Retrospective	Elective gynaecological patients (5477)	On day of surgery	Urine followed by serum quantitative testing for positives	Total positives - 0.6% True positives - 0.6%	3568
Herr <i>et al.</i> (2013)	Retrospective	Infertility evaluation (410)	On day of surgery	Urine followed by serum quantitative testing for positives	Total positive - 0.5% True positive - 0.24%	-
Kahn <i>et al.</i> (2010)	Retrospective	Elective orthopaedics (2588)	On day of surgery	Urine followed by serum quantitative testing for positives	Total positives - 0.3% True positives - 0.15	3273
Hutzler <i>et al.</i> (2014)	Retrospective	Elective ambulatory acute orthopaedics (4723)	On day of surgery	Urine followed by serum quantitative testing for positives	0.19% True positive - 0.15%	1005.39
Manely <i>et al.</i> (1995)	Prospective	Ambulatory surgery (2056)	Within 6 days of scheduled surgery	Urine or serum	0.3%	2879

surgeries.^[21] Although they included data from patients belonging to different gestational ages, they reported increased risk of stillbirths, preterm delivery, low birth weight and caesarean section in pregnant patients undergoing non-obstetric surgeries. The risk is increased in successive trimesters. The most common surgical procedures were abdominal. In first trimester, the laparoscopic procedures were 5 times more common compared to open. They found laparoscopic procedures to have increased risk of miscarriage (RR 3.82, 95% CI 3.29–4.41). They found overall attributable risk of 0.4% for stillbirth and 2.6% for low birth weight. The relatively low risk demonstrated showed that with advances in surgical and modern anaesthesia techniques, risk associated with non-obstetric surgery is low.

Risk of teratogenicity of anaesthetic agents

Anaesthesia exposure during pregnancy does not result in congenital anomalies at birth as suggested by literature review.^[22] However, various studies have demonstrated first-trimester anaesthesia to increase rate of spontaneous abortion and low birth weight. As discussed above, a wide range of factors are attributable for this causation. Classically, anaesthetic gases including nitrous oxide and halogenated volatile agents are suspected to be responsible. In experimental animal models, nitrous oxide has been shown to be teratogenic. The threshold concentration for induction of teratogenicity in these studies is about 50%, the threshold exposure time is still not determined. The mechanisms contributing are N₂O induced methionine synthase inhibition which impairs DNA synthesis and sympathomimetic effects leading to maternal decrease uterine blood flow. The teratogenic potential of N₂O in humans has not been established. Exposure to N₂O during anaesthesia in women during early pregnancy has not demonstrated to induce teratogenicity.^[23]

Halothane, enflurane and isoflurane exposure to pregnant mice showed increased incidences of congenital malformations. Despite common use, these teratogenic effects are not observed in humans. No teratogenic effects of sevoflurane and desflurane are reported in animal models. Experimental animal studies of propofol, etomidate, ketamine, thiopentone and opioids revealed no teratogenic effects in foetus. Neuromuscular blocking agents and local anaesthetics do not reach foetus circulation in significant amounts. Few studies have reported association between maternal diazepam use and oral clefts.^[22] Erickson *et al.* reported first-trimester NSAIDS use to be associated with mild

cardiac defects.^[24] More recent studies however have refuted these findings.^[25] There is emerging evidence from animal studies about foetal brain vulnerability to both inhalational and intravenous anaesthetic prolonged exposure.^[26] However, no such impact of anaesthesia during first-trimester exposure has been reported.

AUTHOR'S RECOMMENDATIONS

1. Recent literature indicates low risk of anaesthesia and surgery to foetus in female surgical patient with undiagnosed pregnancy. The reproductive outcome is composite effect of anaesthesia exposure, surgery and underlying condition for which surgery is undertaken. As these variables are difficult to disentangle, pregnancy status should be determined in all surgical patients
2. During pre-anaesthetic evaluation in all female surgical patients of reproductive age, pregnancy status should be determined by asking sexual history and patient's self-assessment which are more reliable than a normal menstrual history
3. If pregnancy status is unclear, point-of-care urinary pregnancy testing should be considered. In case patient refuses testing, it should be documented
4. Institutional local policy for POPT should be developed depending on surgical characteristics of patient. The surgeries involving the uterus and uterine cavity and those potentially compromising uterine blood flow pose high risk for foetal viability. In these patients, conservatively universal POPT may be considered.

SUMMARY

The usefulness of routine POPT in female surgical patients remains unclear. With advances in surgical techniques and anaesthesia, recent literature indicates low risk of either to foetal outcomes. As there is no mean to disentangle composite effects anaesthesia exposure, surgery and underlying condition for which surgery is undertaken, it is imperative to offer POPT to all women surgical patients. The surgical population of patient and intended surgical procedure is important consideration while formulating policy of universal POPT. Contrary to previous literature, patient's sexual history and possibility of being pregnant provides important clue for carrying out POPT. After initial

clinical evaluation, the patient should be informed regarding possibility of pregnancy and its implications with regard to surgery and anaesthesia. Based on conjecture from clinical history, POPT should be offered to patients and indications or refusal for testing should be clearly documented.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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