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Enlightening the Path for Next Generation of Gynaecologists

Dedicated Issue:

Recent Advances in Obstetrics and Gynecology

AOGD SECRETARIAT

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From the President's Pen

Dear AOGD colleagues,

This is the last issue of AOGD Bulletin from team AIIMS. The offices of AOGD are now shifted to Ganga Ram Hospital. In this issue you find interesting articles on Recent Advances. I will like to thank Dr JB Sharma and his team of editors for this wonderful job of bringing out monthly bulletin.

Dr Sunesh Kumar
President, AOGD

From the Secretary's Desk

Dear Friends

It is time to bid adieu, AIIMS secretariat completed its tenure on 31st March 2020. We congratulate Dr Mala Srivastava and her team and wish them all the best as they take over the AOGD secretariat.

Our last flower in the bouquet, this issue of AOGD Bulletin covers some important topics, which could not be covered in theme based previous issues. Hope this bulletin is as useful as the previous ones. We are humbled at your appreciation of each and every issue of AOGD bulletin.

Unfortunately, these are bad times, so we could not conduct the March Monthly Clinical Meeting in LHMC. With social distancing becoming the norm, we would be seeing more of Webinars and meetings on online platforms.

On behalf of Dr Sunesh, President, and all team members I thank each one of you for your constant support throughout the year. We are grateful to you for making the Annual Conference a grand success.

Stay safe and take care.

Dr Vatsla Dadhwal
Hon. Secretary

From the Editor's Desk

Dr J B Sharma
Editor

Dr Reeta Mahey

Dr P Vanamail

Dr Vidushi Kulshreshtha

Co-Editors

We are delighted to bring the last issue of AOGD Bulletin, "Recent Advances in Obstetrics & Gynecology" with the satisfaction that all the previous issues of the bulletin were well appreciated by the esteemed readers. In this issue we have various miscellaneous recent topics and advances in Obstetrics and Gynecology.

We have an interesting article on "Robotic Surgery in Gynecology" by Dr Anupama Bahadur from AIIMS, Rishikesh, as robotic surgery has a special place especially in oncology and other gynecological surgeries. We have another useful article on "Health related statistics", by Dr P. Vanamail from AIIMS, Delhi.

A clinically useful article on "Caesarean Scar Pregnancy" by Dr Ritu and Dr Monica has been included in the bulletin for benefit of esteemed readers as caesarean scar pregnancy is becoming more common in current practice and is associated with significant morbidity. Similarly placenta accreta is becoming more common and is associated with significant morbidity and mortality. It is partly due to caesarean section epidemic all over the world. We have an interesting article on this topic by Dr Jyotsna Suri and Dr Pratima Mittal from Safdarjung Hospital considering their vast experience in this clinical condition.

Enhanced recovery after surgery (ERAS) is a newer concept in Obstetrics & Gynecology and is associated with better outcomes after surgery. Dr Anju Singh and co-authors enlighten us with an interesting article on this topic. Polycystic ovary syndrome: recent updates is another suitable article and recent topic with lot of new research and advances. Dr Reeta Mahey and co-authors have beautifully outlined the recent advances on this subject. Non invasive Prenatal testing (NIPT) is becoming a commonly used screening modality for chromosomal aberrations and in comparison to invasive testing (amniocentesis and CVS) there is no risk of miscarriage or other complications with this testing method. Dr Vatsla and Dr Anubhuti with special expertise in Fetal Medicine from AIIMS have clearly outlined the various prenatal screening tests.

Besides, as always we have the "Journal Scan", Maze of knowledge and Pictorial Quiz to rock your brains.

We wish our esteemed readers a happy reading. We thank all esteemed AOGD colleagues for the cooperation they offered us during last one year and best wishes for the new team of AOGD at SGRH led by Dr Mala Srivastava. Special thanks to Dr Sunesh Kumar, President AOGD and Dr Vatsla Dadhwal, Secretary AOGD for guiding and supporting us in this journey.

The Editorial Team

Robotic Surgery in Gynaecology

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Introduction

The da Vinci Robotic surgical system was approved for use in gynaecologic surgery in 2005 by the U.S. Food and Drug Administration[1]. Since then, its use in gynaecologic procedures have seen an exponential growth owing to both surgeon's comfort and easy completion of complex surgeries. Today, its use is not only limited to benign gynaecologic procedures but also in staging of certain gynaecologic malignancies.

Robotic Machine and Instruments

There are five models of da Vinci surgical system (Standard, S, Si, X and Xi), da Vinci Xi model being the latest one. The da Vinci Surgical system has three main components- surgeons console, the patient cart and the vision cart.

Surgeons console- is the part wherein the surgeon sits and performs the surgeries. It consists of- stereo viewer, master controllers, foot switch panel, touchpad and arm rest bar. (Figure 1). With the availability of dual console system, the surgeon can train and mentor the trainee in a better way. Touch pad further allows easy give and take of instruments between the surgeon and mentee allowing better collaboration between the two. With the stereo viewer, the surgeon gets a 3D real-time high-resolution image of the surgical field, magnified almost 10 times. In fact, the adjustable Velcro strips at the master controllers allow the surgeon to easily control the camera and instruments by putting in index finger and thumb. A stable camera further helps the surgeon in precise surgical dissection. The surgical system converts the surgeon's hand, wrist and finger movements into real-time, precise movements of surgical instruments.

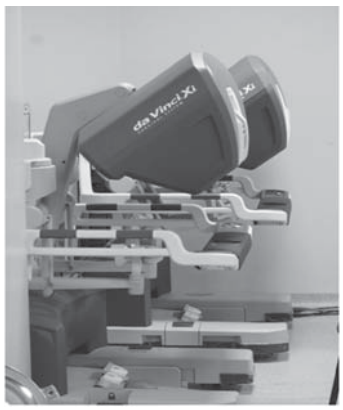

Figure 1: Surgeon Console

Patient cart- is the part where the patient gets positioned during surgery. (Figure 2) It consists of boom, universal arms and a helm touchpad. The arms follow the surgeons command based on his hand, wrist and finger movements. The arms move around fixed pivot points.

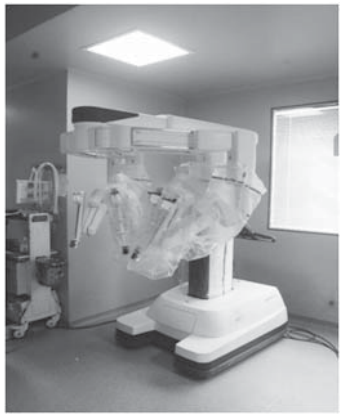

Figure 2: Patient cart

Vision cart

The vision cart has a high definition 3D endoscope and an image processing device that results in real high definition images of the patient's anatomy. (Figure 3) The images are seen on a large monitor placed at the top of the vison cart.

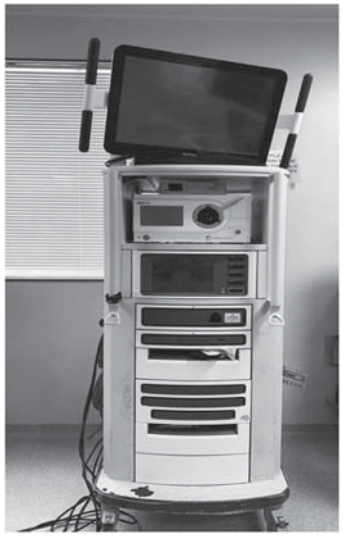

Figure 3: Vision cart

EndoWrist instruments- have seven degrees of motion - a range of motion even greater than the human wrist. (Figure 5)

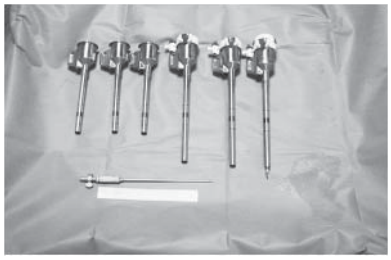

Figure 4: Robotic Trocar

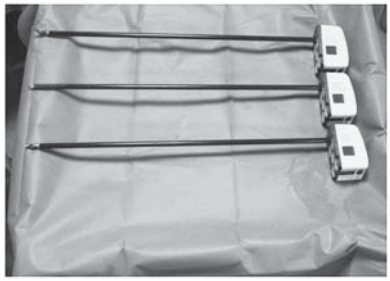

Figure 5: Robotic Instruments

Benefits of Robotic Surgery Over Conventional Laparoscopy

Robotic surgery has all the benefits of minimally invasive surgery in terms of decreased blood loss, faster recovery, better cosmetics, less postoperative pain and shorter hospital stay.

As compared to conventional laparoscopic surgery-

- Robotic camera control lies with the surgeon itself thereby providing a fixed and stable surgical field view as compared to laparoscopic surgery wherein the vision changes based on assistant's hand-eye coordination, patient breathing and pneumoperitoneum[2].
- With the addition of Endo Wrist technology, complex and prolonged surgeries can be performed with ease making them same as open surgical manoeuvres.
- Self-control of camera with an ergonomic console designed to reduce fatigue contributes to shorter learning curve for robotic surgery[3].
- Suturing is less tiring.
- Faster learning curve as compared to laparoscopic surgery. In laparoscopy, the learning curve is long, hand movements are counterintuitive and usage of long instruments through a fixed entry point results in increased tremors leading to fatigue and irritation among surgeons during lengthy surgeries.

Disadvantages of Robotic Surgery

- Lack of tactile sensation during surgery results in increased tissue damage, less secured knots with weakening of sutures[3].
- Robotic surgeon needs assistance for change or removal of instruments as compared to laparoscopic surgery.
- Cost of the Robot is the most prohibitive factor regarding its uptake[4]. Each instrument has a fixed number of life (10 usage only) thereby making the surgical cost go higher as compared to conventional laparoscopy.

Patient Positioning and Trocar Placement During Robotic Surgery

The patient is placed in dorsal lithotomy position. Arms need to be secured at her sides padded shoulder blocks must be put. Correct placement of trocar ensures that the robotic arms will not collide during the surgical procedure. Robotic surgery needs Trendelenburg position and prolonged such positioning have been associated with corneal abrasion, cerebral oedema, laryngeal oedema and posterior ischaemic optic neuropathy[5]. The da Vinci Xi has four identical flexible arms (8mm each) which needs to be put in 8 mm ports. This facilitates camera and working trocars to be exchanged as and when needed.

The endoscope port is placed almost 20 cm above the pubic symphysis (almost 8-10 cms above the fundus, i.e., slightly above the umbilicus in the midline). The remaining three ports for instruments must be 8 cms from the initial endoscope port marking. All these four points are more or less in a straight line or a slightly curved line. (Figure 6) A minimum of 2 cm gap must be there between any port and bony prominence.

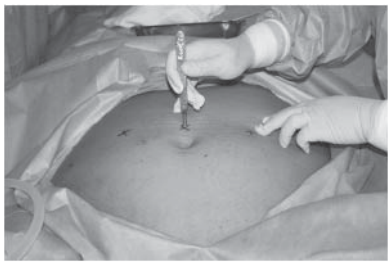

Figure 6: Port Markings

Additional assistant ports can be created depending on the surgical need. Robotic trocar is inserted in a way that the thick black band of the canula (remote centre) is seen at the abdominal wall. When all the trocars are in their proper position, the patient cart is brought in from one of the patient's side showing the laser beam at the centre of the endoscope port. (Figure 7 & 8)) Finally, the endoscope arm is docked in to the canula. (Figure 9) The endoscope is then inserted inside and targeting is completed. Then all the remaining working ports are docked followed by insertion of required instruments.

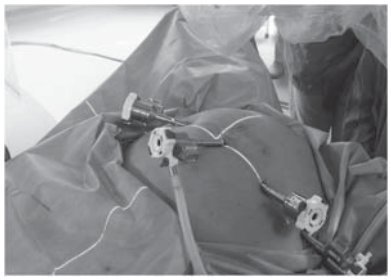

Figure 7: laser beam at endoscope port

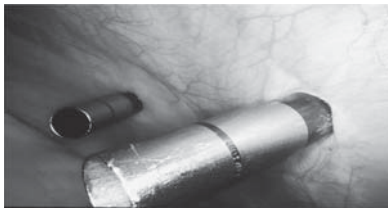

Figure 8: correct placement of trocar- remote centre at abdominal wall

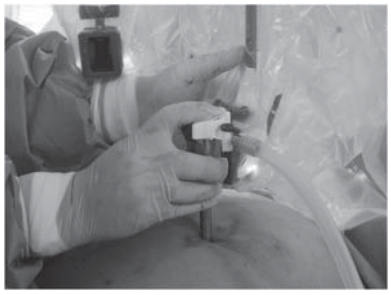

Figure 9: Endoscope port docked into cannula

Indications for Robotic Gynaecologic Surgery

Clinical considerations in Benign surgery

Hysterectomy--The first hysterectomy done robotically was published in 2001[6]. Wright JD et al[7] in their cohort of 264,758 women undergoing hysterectomy for benign gynaecologic disorders at 441 hospitals across United States from 2007 to 2010 concluded that robot-assisted hysterectomy had significantly lower risk of hospitalization longer than 2 days compared to conventional laparoscopy (24.9% versus 19.6%,) but with a significantly higher total cost ($2,189 more per case).

Chiu et al reported that compared with the laparoscopic approach, robotic surgery seems to be a feasible alternative for doing hysterectomy in cases with severe adhesions[8].

Risk of vaginal cuff dehiscence is higher in robotic approach (1.64%) as compared to 0.66% in laparoscopic group[9].

Myomectomy--Minimally invasive management of fibroids pose a real challenge to surgeons, considering the difficulties encountered while doing hysterotomy, enucleation, multilayer closure, and myoma extraction[10]. Barakat et al in their retrospective review of 575 myomectomy cases analysed the outcomes between robotic-assisted, conventional laparoscopic, and open abdominal approaches. Robotic-assisted laparoscopic myomectomy had decreased blood loss and shorter hospital length of stay when compared with both conventional laparoscopic myomectomy and open abdominal myomectomy. In terms of operative time (181 vs 155 minutes) there was no statistically significant difference between robotic-assisted and conventional laparoscopic myomectomy despite the fact that a significantly higher tumour load was removed in the robotic-assisted group (223 [85.25, 391.50] g) compared with the laparoscopic group (96.65 [49.50, 227.25] g; p, .001)[11].

Endometriosis- Robotic assisted surgery seems to be a suitable surgical option in endometriotic surgeries wherein extensive & precise dissections are needed. In a retrospective study conducted by Nezhat et al. among 86 conventional laparoscopic and 32 robotically assisted cases for advanced stage endometriosis, it was seen that despite a longer operating time, robotic surgery seems safe approach in obese patients, with clinical outcomes comparable with those in nonobese patients undergoing conventional laparoscopy[12].

Tubal re- anastomosis- Robotic surgery can lead to better visualisation and delicate handling of tubes. Robotic-assisted tubal anastomosis was associated with increased operative time but shorter length of hospital stays, recovery time, and time to return to normal activities compared to minilaparotomy group[13].

Sacrocolpopexy-

At present, literature is too less to precisely indicate which minimally invasive approach should be recommended. Anger JT et al conducted an RCT of 78 women with symptomatic stage POP II or greater, they concluded that costs of robotic Sacro colpopexy are higher than laparoscopic, with short-term outcomes and complications being similar[14].

Clinical implications in gynaecologic oncology-

Robot assisted surgeries are increasingly being used for staging endometrial cancer. Wang et al in their meta-analysis using 27 articles, including one randomised controlled trial and 26 observational studies using 6568 patients concluded that robotic surgery is safe approach when compared to laparoscopic and open approach in staging of endometrial cancer with less blood loss, blood transfusion and same number of lymph nodes harvested[15].

There exists limited data regarding the use of minimally invasive surgery for ovarian cancer cases necessitating the need for systematic reviews and meta - analysis to determine the oncological safety with robotic surgery.

With the results of LACC trial, currently open approach remains the standard of care for cervical cancer[16].

Conclusion

Greater precision due to better visualisation and self-camera control, robotic surgery finds its way in both benign and malignant gynaecologic surgeries. The only concern lies in its cost and maintenance. Further randomised trial is needed to establish its long-term safety and efficacy. Till then, judicious patient selection should be done for robotic approach.

Key Learning Points

- FDA approved the robot assisted surgery gynaecologic surgery in 2005.
- Da Vinci Xi model is the latest robot.
- Self-control of camera with an ergonomic console designed to reduce fatigue contributes to shorter learning curve for robotic surgery.
- Each instrument has fixed life, thereby making the surgery cost go higher as compared to conventional laparoscopy.
- Today robotic surgery finds its way not only in benign gynaecologic procedures but also in surgical staging of gynaecologic malignancies.

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Author Contribution- Dr AB instigated the article, wrote the first draft and revised the manuscript. Dr RM contributed to the first draft and revised the manuscript.

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Heath Related Questionnaire Design and Testing Process

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Introduction

Questionnaires constitute the basis of every survey-based statistical measurement. They are the most important measurement instruments to grasp the phenomena to be measured. Errors due to an insufficient questionnaire can hardly be compensated at later stages of the data collection process. Therefore, having systematic questionnaire design and testing procedures in place is vital for data quality, particularly for a minimization of the measurement error. The process of questionnaire design includes various successive steps: the development of a conceptual framework, writing and sequencing the questions, making proper use of visual design elements as well as implementing electronic questionnaires technically. To achieve cross-national comparability to international surveys, two further tasks are necessary. The translations of the questions or questionnaires have to be functionally equivalent, i.e. the respondents in different countries must have the same understanding of the questions. The demographic as well as socio-economic variables have to be harmonized through commonly accepted instruments. Therefore, possible approaches towards the translation of questions and a number of tested and accepted measurement instruments for demographic and socioeconomic variables are briefly outlined in this paper.

Recommended Practices for Questionnaire Design

The questionnaire in the first instance is a measurement instrument. Its main purpose is to operationalize the user's information demand into a format which allows a statistical measurement. The concepts of "reality" must be operationalized in a way that enables the subject-matter specialists and users to carry out the necessary analyses, that the questionnaire designer can implement into the questionnaire, and that the respondents can understand and answer properly. Hence, the design of questionnaires must primarily take into account the statistical requirements of data users. To provide a valid and reliable measurement, the wording, structure, and layout must make allowance for the nature and characteristics of the respondent population. The questionnaire should ask relevant questions and permit data to be collected efficiently and with minimum error, while facilitating the coding and capture of data and minimizing the amount of editing and imputation that is required.

The following recommendations support an efficient implementation of the questionnaire design process.

Literature Review

Every questionnaire design should start with a review of the existing literature as well as other data sources (including available registers and non-official statistics) or surveys with similar research topics.

Specification of the Survey Objectives

Before starting to draft the questionnaire, the survey objectives should be specified in co-operation with important users and stakeholders. At the same time, decisions should be made on basic concepts such as the target population, on sampling design, and also on the available resources and possibly the data collection mode to be preferred. Especially in the case of new surveys or major redesigns of surveys, an intensive user-focused consultation should be conducted to identify the concepts required. Besides informal communication with experts and users, expert group meetings involving key users should be held to identify the concrete information demand to be satisfied. These user requirements should be documented, and reconciled (in case of trade-offs).

Exploring concepts: focus groups and in-depth interviews

Especially in new surveys it should be explored whether the concepts and indicators the users are seeking are compatible with those the respondents have in mind. A number of qualitative methods are available in order to get an idea of how respondents think about what survey designers have conceived. Such methods include for instance focus groups and in-depth interviewing. *Focus groups* are composed of a small number of target population members guided by a moderator. The objective is to learn how potential respondents use the terms related to the topic, how they understand general concepts or specific terminology,

and how they perceive the questions in terms of sensitivity or difficulty. Additionally, focus groups could also be a useful method for pre-field testing of questionnaires. *In-depth or qualitative interviews* in a similar way focus on the respondents' understanding of the concepts, on how the respondents interpret certain questions and on how they arrive at their answers. In contrast to focus groups, in-depth interviews are not based on a group discussion.

Conceptualization and Operationalization

Once the survey concepts have been established, they need to be translated into observable variables. The complexity of the theoretical concepts – even in apparently simple cases – requires a strict selection of empirical traits (often referred to as measurable indicators), which can be observed in a survey. These indicators are deemed to be a suitable (though never direct or perfect) representation of the concept. When specifying the survey concepts and variables, standard definitions of concepts, variables, classifications, statistical units and populations should be used (if available).

Definition of a list of Variables and a Tabulation Plan

Once the objectives and concepts are defined, a concrete tabulation plan and a list of variables should be laid down specifying the expected output of the survey. The variable and value list is to be seen as a simple list of variable names and values as well as of the corresponding definitions. With regard to the variable list, it is recommended to draw a distinction between background variables (e.g. demographic variables), variables used to measure the survey concepts, and technical variables (e.g. required for weighting).

Decision on the Data Collection Mode

The selection of an appropriate data collection mode must take into account the number, the contents and the scope of the survey variables. Also, aspects like the sensitivity of the questions or possible problems of information retrieval should be considered. Additionally, possible preferences of the target population should be taken into consideration. It is important to note that the questionnaire should not be designed without a previous decision on the data collection mode. Standard data collection modes are listed in table below.

Data Collection Modes

Technology	**Type of administration**	
	Interviewer administration	**Self-administration**
Computer-assisted data collection	CAPI, CATI	CASI: WBS (or CAWI), DBM, EMS and TDE
Paper and Pencil (PAPI)	PAPI face-to-face interview	PAPI (mail surveys)

CAPI: Computer-Assisted Personal Interviewing, CATI: Computer-Assisted Telephone Interviewing, CASI: Computer-Assisted Self-Interviewing, WBS: Web Based Survey, EMS: E-Mail Survey, TDE: Touch-tone Data Entry, PAPI: Paper-and-Pencil Interviewing, DBM: Disk by Mail, CAWI: Computer-Assisted Web-Interviewing.

Writing and Sequencing the Questions

Questionnaires must translate the variables to be measured into a language that respondents understand. It is essential that the words used in questionnaires have the same meaning for all the respondents and at the same time correspond to the concepts to be measured. Additionally, one should only ask questions on which the respondents can actually retrieve the necessary information. To understand correctly, questions should be worded using *simple* and *unequivocal* terms, which have the same meaning for all members of the target population. Notions which respondents might not be familiar with should be defined. *Long* or *complex questions* as well as *hypothetical questions*, *loaded questions*, and questions with *double negations* should be avoided. The questionnaire designer has to be particularly careful when choosing the *stimuli* of the questions. The stimuli should measure the variables of interest appropriately. Never more than one stimulus should be used in a question. Every question should be explicit about the *reference period*, which is best placed before the stimulus of the question as such.

The answer categories must cover all possible responses and correspond as closely as possible to the variation in the population. Furthermore they must be disjoint, i.e. there should be no overlaps leading to ambiguous results. The respondents and/or interviewers should be provided with clear *instructions*. Instructions should however only be used if necessary and should be kept reasonably short and they have to be placed close to the question to which they refer.

Also, the *questionnaire structure* should encourage respondents to answer the questions as accurately as possible. To this end, the questionnaire must focus on the topic of the survey, be as brief as possible,

flow smoothly from one question to the next, facilitate respondents' recall and direct them to the appropriate information source. Respondents should have the feeling that filling in the questionnaire is an interesting and diverting task. In the introduction to the questionnaire, the title or subject of the survey should be provided, the purpose of the survey should be explained, and the respondent should be asked for his or her cooperation. The respondents should be assured that their responses will be kept secretly and the survey findings will be shared to interested respondents.

The *sequence* of the questions should be self-evident to the respondents, so that the questionnaire follows a logical stream. Questions should be arranged into logical groups and the questions on the same topic should be grouped in the same section. With regard to section ordering, one should proceed from less to more complex topics. The use of checks should be carefully evaluated against the increase of difficulties in controlling the interview. The opening questions should be applicable to all respondents, be easy and interesting to complete, and establish that the respondent is a member of the survey population. More importantly sensitive questions such as name of religion/caste, income and their life-style characteristics/activities should be placed at the last. At the end of the questionnaire, space for additional comments by respondents should be provided and an expression of appreciation to the respondent should be included.

Apart from creating a smooth logical flow of the questions, one should be aware of the fact that the *order of questions* could have a strong impact on the results. Therefore, the questions must be scrutinized with respect to their context. The respondent's interpretation of a certain question may be influenced by earlier questions. To facilitate the measurement of sensitive questions, the topic should be reached gradually and in a way that makes the respondent feel at ease, and the wording should be as neutral as possible. In general, sensitive questions should not be placed at the beginning of the questionnaire. In order to avoid context effects, bias due to the sequence of questions should be addressed during the questionnaire testing.

Visual Design Elements

Besides the wording and structure of the questionnaire, visual design elements require some consideration. Not only verbal, but also non-verbal stimuli guide the respondents and interviewers when filling in the questionnaire. Using the right non-verbal stimuli (like VAS and pictorial layout) is vital to achieve valid and reliable estimates and to enhance the usability for both respondents and interviewers. When looking at visual design elements, the emotional, functional and reflective levels have to be distinguished.

At the *emotional level* (determined by the connection of the brain with the visceral nervous system), the respondent and the interviewer produce positive or negative reactions (emotions) without reasoning. To understand correctly it is important that a questionnaire produces immediate positive reactions. It is therefore much more than just a cosmetic detail that questionnaires should be visually pleasing and look easy to complete. For the same reason, it is vital to give a positive first impression in the cover letter and on the front cover, and to make the questionnaire appear professional.

The *functional level* determines the usability of the questionnaire, i.e. whether the information is cognitively processed by the respondent as intended by the survey designer: The structure of tasks as well as the cognitive processes required of the respondent and the interviewer should be designed in a way as to enable them to give the correct answer. Therefore, questionnaire designers have to be aware of how non-verbal information is processed. There are a number of general findings which should be taken into account when constructing a questionnaire. (1) The structure of tasks should not be too complex (e.g. one question should be asked at a time, the number of items per question should be reduced, and complex matrices should be avoided etc.). (2) The questionnaire should make use of the "natural" mappings of the respondents, so that it is self-evident how to navigate through the questionnaire. For example, the questions should start where the respondent and interviewer expect them to start, i.e. in the upper left corner of the page or the screen. Elements that belong together in the questionnaire should be grouped together (like the question, the respective answer space and response options, as well as the instructions on that question). The visual design should also make clear where the respondents and interviewers are expected to enter their responses (e.g. by the use of a figure/ground contrast). Skip instructions should always use strong visual symbols (like arrows). (3) Where the questionnaire cannot make reference to a pre-established conceptual model (mapping) in the mind of the respondent or interviewer, one should standardize the verbal as well as the design elements for similar questions throughout the questionnaire.

Finally, the respondents take a conscious and reflected decision when participating in a survey or answering survey questions. This level is referred to as the *reflective level*. At the reflective level, respondents and interviewers attribute meaning also to non-verbal features of the questionnaire and to their activity of providing answers. Those involved in questionnaire design should be aware that this can influence the readiness to participate in a survey as well as the responses to the questions.

Electronic Questionnaire Design

A number of special considerations apply regarding the design of electronic questionnaires, as used for CATI and CAPI surveys. Electronic questionnaires of course have the same main objectives as PAPI questionnaires, namely to collect information according to the survey information needs. Given the special opportunities due to the electronic implementation, however, the design of the screen layout, the management of the various types of errors and the wording have to be tailored to the needs of both the respondent and the interviewer. The screen layout setting must enable the interviewer immediately to understand what to read and where to find it. At the same time, electronic questionnaires enable us to detect and reconcile inconsistencies already during the interview. The electronic questionnaire must be designed in such a way as to solve the greatest number of inconsistencies while paying attention to the fluency of the interview and not frustrating the respondent. The error management should make the interviewer understand sooner what kind of error happened and which questions were involved in it. The customization of texts is to help the operator in reminding the respondent of the information previously collected.

An electronic questionnaire should allow the possibility of modifying responses previously given, without missing any relevant information (i.e. to allow a change of route when backing up). If the questionnaire contains ad hoc modules and some of them are "stand alone", it should allow the possibility of completing them in any order. In the case of CATI surveys, the call scheduler must be planned in such a way as to give the sample units the same probability of being contacted without changing their inclusion probability.

From a technical point of view, an electronic questionnaire must measure what it is intended to measure (*effective),* be easy to modify when changes occur and easy to correct in case of errors (*flexible*), be structured in modules which may be used for other studies or survey waves, be easily adaptable to different hardware or software platforms (*portable*) and be *efficient* in terms of response time for screen replacement.

Two testing methods are particularly useful when the data collection mode is computer-assisted, hence implying the implementation of a software for the interview management: the functionality and the usability tests. The former consists in the assessment that the electronic questionnaire performs according to the given specifications and is robust with respect to unexpected events. In the latter, the interest shifts towards the users of the system, thus testing if they use the system in a correct and efficient way.

Cross-national Harmonization of Questions

To achieve cross-national comparability in international surveys, the questionnaires used in different countries have to be functionally equivalent, i.e. must actually measure the same concepts in different cultures and languages. Therefore, in cross-national research, the translation of questionnaires plays an important role. Secondly, the harmonization of demographic and socio-economic variables is a further prerequisite to cross-national comparability.

Functionally equivalent translations require quite sophisticated techniques for translation, taking into account the syntactic, semantic and pragmatic levels of the source language questionnaire. Normally, cross-national research starts with the agreement that one language (mostly English) is used as reference language. A drafting group formulates the questions of the questionnaire. Native speakers of the reference language (English) in this drafting group will be not only language experts, but also experts for the cultural background of the concepts and questions. During the actual translation process ideally a bilingual but "unicultural" member translates the questionnaire. It is important to note that cultural differences are ignored if an item is only translated from one language into another without analyzing the cultural background of the national question wording in the (English) master copy. Normally, two independent draft translations should be made per language. A pretest should be an integral part of the translation process.

Besides appropriate translation techniques, it is important to use harmonized demographic and socioeconomic variables. Context variables or background variables are variables that contain information necessary to define homogeneous subgroups, to establish causal

relations between attitudes and societal facts, and to define differences between scores on scales. In cross-national research, standardized instruments or indices exist only for a very small group of variables including "occupation", "education", and "status". For the variables "income", "family", and "ethnicity", there is preparatory work in progress.

Recommended Practices for Questionnaire Testing

Questionnaire testing is critical for identifying problems for both respondents and interviewers with regard to, e.g. question wording and content, order/context effects, and visual design. Problems with question wording include, for example, confusion with the overall meaning of the question as well as misinterpretation of individual terms or concepts. Problems with skip instructions may result in missing data and frustration of the interviewers and/or respondents. Visual design especially concerns self-administered questionnaires; however, poor visual design can easily lead to confusion and inappropriate measurements also in interviewer-administered surveys.

Questionnaire testing is a broad term that incorporates many different methods or combinations of methods. This section summarizes and briefly describes those methods that should be used to test and evaluate questionnaires. These methods have specific strengths and weaknesses that make them valuable for different types of problems. Consequently, they are useful at different stages of questionnaire development. In order to get a sound understanding of the response process, to identify problem questions and to suggest adequate improvements, the use of a combination of questionnaire testing methods is indispensable. In most cases, the use of one single method will not be sufficient. The appropriate combination of these methods determines their suitability to meeting the objectives of questionnaire testing.

In the Recommended Practices, we distinguish two major categories of questionnaire testing methods – pre-field and field methods. This distinction is an analytical one, but nevertheless reflects some principal and operational differences.

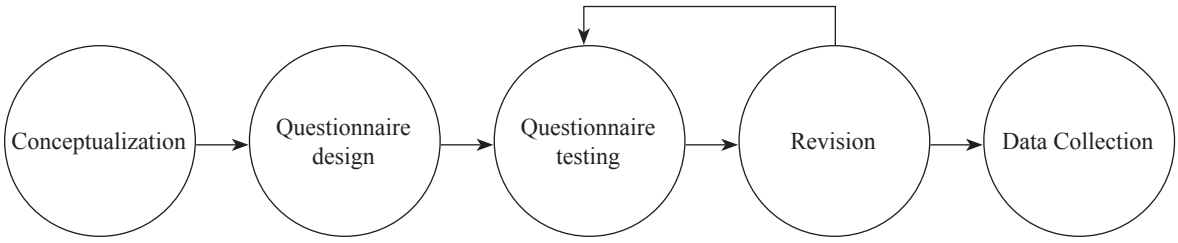
Pre-field methods are normally applied under laboratory conditions. This means that the interviews are not carried out in exactly the same way as later on in the field. "Laboratory conditions" refer to an observational environment which may totally or partially differ from the actual field conditions. The interviews may not be carried out in the same environment as in the field (e.g. in a cognitive laboratory). Only small parts of the questionnaire might be included. Additional questions might be added with regard to how the respondents perceive the questions. Consequently, the interview flow might deviate from the later fieldwork quite substantially. They are generally used in a preliminary stage of the questionnaire testing process and mostly qualitative in nature. Pre-field methods are particularly suitable to collect information on how respondents proceed when answering the questions. Often, the focus is on single questions rather than the whole questionnaire. They include expert group (composed of survey methodologists or questionnaire design experts, but also subject-matter experts) reviews and cognitive interviews such as think aloud interviews, probing, respondent debriefings, confidence ratings, paraphrasing, sorting, vignette techniques, and analyses of response latencies. One method sometimes described in the literature as a pre-field method is the use of focus groups that we treated in the design of the questionnaire, since it is more closely related to a preliminary analysis and the development of concepts than to the actual testing of a draft questionnaire. Nevertheless, focus groups might also play a role in pre-field testing.

Field methods are those used to evaluate questionnaires tested under field conditions. This means that the interview is carried out in a way very similar to the subsequent fieldwork (regarding setting, lengths, choice and order of questions, etc.), and the majority of the conditions mirror the real survey situations. The test might be conducted during the data collection phase, e.g. in the context of a pilot study, in conjunction with the actual data collection, or in parallel to ongoing or recurring surveys. Therefore, field testing often includes bigger sample sizes and allows quantitative analyses. The focus is more on the complete questionnaire instead of individual questions. Field methods include behavior coding, interviewer debriefings, respondent debriefings, follow-up interviews, experiments.

It is important to note that, in practice, some of the methods could be used either under laboratory or under field conditions. In our classification we refer to what can be seen as the major area of application.

Other techniques, based on the analysis of item non-response, editing and imputation rates, or response distributions, are commonly performed on the data coming from the testing methods as well as on data from the real data collection phase. In the last case, these analyses result particularly useful especially for ongoing surveys.

The five stages of questionnaire design and testing



Rating scales. There is a type of ordered closed question that is commonly used when the researcher seeks to locate a respondent's opinion - the favourability of an item, the frequency of behaviour etc. - on a rating scale with a limited number of points. There is a wide variety of response scales and they could be characterised by type of labelling used (verbal or numeric), number of scale points (even or odd), dimensionality (bipolar or unipolar) and direction (ascending or descending). Some examples of scales are reported below.

Verbal scales:

Strongly Disagree Disagree Agree Strongly Agree
|_| |_| |_| |_|

Numeric (endpoint-labelled) **scales:**

Strongly disagree |_| |_| |_| |_| |_| |_| |_| |_| Strongly agree

Even Scales:

Unimportant |_| |_| |_| |_| |_| |_| Very important

Odd Scales:

Unimportant |_| |_| |_| |_| |_| |_| |_| Very important

Ideally, a good response scale should: be easy to interpret by respondents, have a discrimination that fits the respondents' perceptions, and cause minimal response bias. In practice, determining a scale with a "certified" minimal respondent bias is a difficult task because each of those above-mentioned varieties produces specific effects on the responses. Therefore it is important to state that scales – even neutral looking ones, like the numerical scales – are not at all "neutral". Research findings proved that scales which are formerly equivalent but differ in, for example, their numeric labelling, are often answered very differently.

In general, from the scale respondents get "information" about:

- The distribution of "real" situations, or behaviors and,
- Their own position in this distribution.

Thus, as already mentioned, respondent knowledge of the subject matter is important to consider. It is worth considering how familiar the potential respondents are with the issues that are addressed in the survey.

Although much research has been devoted to scales, its results show a great deal of disagreements, so it would be unwise to give hard-and-fast recommendations on how to define scales. There is, however a set of important issues that should be taken into consideration when constructing one:

1) Category Labels.

   The words used as labels in a rating scale require some caution. For creating interval scales (scales in which the respondent perceive equal-sized gradations between the points on the scale) category descriptors that are truly equal-interval should be carefully chosen. For verbal scales, it is helpful to look for possibly existing lists providing the scale value means of selected adjectives and descriptors that might be used to create rating scales.

   If the rating scales contain numbers, then these numeric values can change the meanings of the scale descriptors. For example, research has shown some evidence that respondents perceive the negative-evaluation side of the scale as being more negative when there are negative numbers on that side rather than positive numbers. Therefore, it is advisable that the points of scale should not be associated with negative digits.

2) Balanced/unbalanced rating scales.

   Rating scales can be structured either balanced, with an equal number of favorable and unfavorable response choices, or unbalanced. Generally, rating scales should be balanced, with an equal number of favorable and unfavorable response choices. This means that there should be an equal number of positive and negative options to choose from. Using more opinions for one side (usually positive) biases the responses towards that side for several reasons. One of them is social desirability, where the lack of sufficient negative options leads the respondent to believe a negative response is undesirable (Tourangeou and Smith, 1996). Using the categories as information the respondent might incorrectly assume the range represents the true distribution of the population (Schwarz and Hippler, 1991 & 1992).

Friedman and Amoot (1999) say that "the only justification for using an unbalanced rating scale is in a situation where it is known *a priori* that virtually all respondents are leaning in one direction (if you know that one side of the scale will not really be used.)".

As part of balancing the options it is important to test whether the descriptors chosen for negative and positive options, e.g. "Difficult" and "Easy", are actually considered to be opposite by respondents. The negative and positive options should also be equivalent in intensity, e.g. "Very difficult" versus "Very easy" rather than "Extremely difficult" versus "Fairly easy".

To prevent that the question itself does not bias the respondent's answer, it is important to word the rating question in a balanced way, e.g. "Do you favor or oppose …" to imply that responses in either direction are acceptable (Schuman and Presser, 1981).

3) Neutral option.

When a rating scale has odd numbers of points, the scale has a midpoint at which there is a transition. This midpoint can indicate either indifference (e.g. neither unimportant nor important) or ambivalence (e.g. unimportant in some ways and important in others), so that the definition of the midpoint potentially affects the meaning of other points as well.

"Don't Know", "Don't Remember", "Not Applicable" categories. "Don't know" and "Not applicable" are response categories directly related to the relevance issue: sometimes it is appropriate to include those categories, for example, when the researcher has previous sufficient awareness that a fairly good amount of respondents might have "no opinion" or when he/she knows that a particular question does not apply to a subset of the target population.

For factual questions, these categories are kinds of item nonresponse. For opinion questions "Don't know" or "Don't remember" might be used by the respondent as a neutral answer, if this is not present among the responses' options. The decision about whether to include or exclude these categories depends to a large extent on the subject matter. Excluding these options may not be a good idea.

In CATI/CAPI surveys it is recommended to include these options among the response categories, but to instruct the interviewer not to read them aloud.

Summary

A good questionnaire is imperative for good survey results. A questionnaire can be judged based on its relevance and accuracy. The first step in questionnaire designing is arriving at preliminary decisions regarding the issues of required information, the target respondents and the interview techniques to be adopted. This is necessary as the content, format, wording and sequencing of the questionnaire will depend on these basic factors. The next step is to determine the questionnaire content, so that it deals with identifying the need for data, the question's ability to yield data, the participant's ability to answer without generalizations and estimates and willingness to answer sensitive questions.

Knowing how each question should be phrased requires familiarity with the different types of questions. This leads to the next step of the questionnaire designing that is questionnaire response format. Experiences from previous researches would be general guidelines regarding questionnaire wording and sequence. It should be ensured that questions resort to shared vocabulary and adequate alternatives for better understanding and response rates. The questions should be free of implicit assumptions, biased and loaded words. It should also be free of questions that are double-barrelled and that would provoke the respondent to provide generalizations and estimated answers. Questionnaire sequencing is very important to elicit required information from the participant. The opening questions should arouse the respondent's interest in the survey. The specific and general questions should be followed in order. Last, the questionnaire should be pre-tested before administration for detecting flaws and revised with necessary corrections and deletions.

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Caesarean Scar Pregnancy: Diagnosis and Management

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Introduction

Caesarean scar pregnancy (CSP) is a type of ectopic pregnancy where the embryo is fully or partially implanted in the muscle or fibrous tissue at previous caesarean scar site. The incidence of CSP ranges from 1/1800 to 1/2500 of all pregnancies, which constitutes approximately 6.1% of all ectopic pregnancies, in patients with at least one previous caesarean section (CS).[1,2] The increase in incidence of CSP is primarily due to increase in incidence of CS and advanced imaging modalities which provide accurate diagnosis.

Pathophysiology

Endometrial and myometrial disruption or scarring is a predisposing factor for abnormal pregnancy implantation. The implanting blastocyst invades through a microscopic tract formed by previous CS trauma. The risk of scar implantation might be proportional to the size of the anterior uterine wall defect.[3] Future risk of CSP is more frequently seen after CS for breech presentation due to higher and larger scar defect in poorly formed lower uterine segment.[4]

Diagnosis

After a period of amenorrhoea and positive pregnancy test women may present with slight vaginal bleeding and abdominal discomfort or acute pain and profuse vaginal bleeding. Sometimes it is diagnosed during surgical evacuation for missed abortion. Ultrasonography (USG) based criteria used to diagnose CSP are as follows (Figure 1):

- Empty uterine cavity along with closed and empty cervical canal
- Gestational sac embedded at CS scar site
- Thin or absent myometrial layer between gestational sac and bladder
- Yolk sac, embryo and cardiac activity may or may not be present
- Functional trophoblastic/placental circulation on colour flow Doppler characterised by high velocity and low impedance blood flow
- Negative 'sliding organ' sign

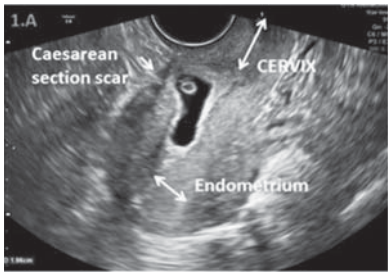

Figure 1. USG features of CSP

CSP can be classified into two types based on imaging findings and pregnancy progression as shown in table 1.

Table 1. Types of CSP

Type 1 (Endogenic CSP)	Type 2 (Exogenic CSP)
• Gestational sac grows towards the cervico-isthmic or uterine cavity • Less risk of early rupture • Medical treatment and dilatation and curettage with or without uterine artery embolization (UAE) can be used as primary treatment	• Gestational sac is deeply embedded in the scar and surrounding myometrium and grows towards the bladder • More risk of early rupture • Primarily managed by surgery

Differential Diagnosis

Up to 13.6% of CSP are misdiagnosed as either inevitable miscarriages with a low-lying sac or cervical pregnancies[5]. The differentiating USG features are as described in table 2.

Table 2. Differential diagnosis of CSP

USG feature	CSP	Cervical pregnancy	Inevitable abortion
Location of gestational sac	Low in the uterine cavity or in the cervico-isthmic area	Below the internal os inside the cervical canal with ballooning of cervix	Irregular and crumpled located within the uterine cavity
Colour flow	Normal and good flow	Normal and good flow	Minimal and absent
Sliding organ sign	Absent	Absent	Present

Three-dimensional USG, colour doppler and magnetic resonance imaging (MRI) are useful in making a reliable diagnosis when clinical and two-dimensional ultrasound features are unreliable.

Recurrence of CSP

The risk of recurrence is 3.2–5.0% in women with one previous CSP treated by dilatation and curettage with or without UAE.[3]

Factors Associated with Increased Risk of Recurrence

- A lower uterine segment thickness <5 mm
- Gestational sac bulging into the utero-vesical fold
- Caesarean delivery in a rural community hospital
- History of irregular vaginal bleeding and abdominal pain during previous CSP.[4]

Surgical management with closure of defect restores normal anatomy and reduces the risk of recurrence.[6]

Management options for CSP

1. **Expectant management -** Expectant management is recommended in asymptomatic patients with nonviable CSP and declining beta hCG levels.
2. **Medical management**
   - Systemic methotrexate is used in haemodynamically stable patients with unruptured CSP. It is successful when beta hCG is < 5000 IU/ml and gestational age is < 8 weeks.
3. **Local injection and embolization procedure**
   - Local injection of methotrexate with sac aspiration. This method when combined with systemic methotrexate has better success rate and fewer additional interventions are needed.
   - Local injection of other embryocidal agents like potassium chloride (KCl), etoposide and hyperosmolar glucose.
4. **Surgical management**
   - Surgical evacuation – It is suitable for endogenic CSP with at least 2 mm myometrial thickness. Risks associated with this procedure are bleeding and incomplete removal of pregnancy tissue. USG guidance may aid in complete removal. UAE if used prior to procedure significantly reduces the risk of acute bleeding during suction evacuation.
   - Abdominal/laparoscopic resection – Resection and closure of defect is suitable for exogenic CSP with thin overlying myometrium. Minimally invasive route should be employed if appropriate and expertise available. Advantages of this treatment modality are possibility of complete removal of pregnancy tissue and repair of myometrial defect, quick return of beta hCG to normal and early discharge from hospital.
   - Hysteroscopic resection - As primary treatment for endogenic CSP or sequential treatment after methotrexate or UAE. Also used to remove persistent or remnant CSP after medical management or incomplete surgical evacuation.
   - Vaginal excision and re-suturing of defect.
   - Combined laparoscopic and hysteroscopic procedure.
   - Combined laparoscopic and vaginal procedure.
   - Hysterectomy.
5. **Uterine artery embolization (UAE)** – It can be combined with systemic or local methotrexate to improve success rate of medical management. UAE when performed during or before surgical removal of CSP prevents excessive bleeding.

Heterotopic pregnancy with CSP – It is a condition with one sac in the CS scar and the other in uterine cavity. It is challenging both in diagnosis and management. They can be successfully managed with local injection of KCl into the CSP sac and continuation of the normal intrauterine pregnancy to term.[7] Exogenous CSP can also be excised either by laparoscopy or open surgery with added advantage of closure of defect which maintains lower segment integrity. However, there is risk of haemorrhage and complete loss of intra uterine pregnancy.

Follow-up and future pregnancies

Time taken for beta hCG to reduce to nonpregnant level and for the CSP mass to resolve completely, varies, and depends on multiple factors such as the gestational age at time of diagnosis, beta hCG value, size of CSP and treatment modality used. Medical management takes longer time for complete resolution compared to surgical treatment. Follow up should be done until complete resolution of the CSP mass and normalization of beta hCG levels.

Future pregnancy management involves:

- Early USG to rule out recurrence.
- Since there is increased risk of morbidly adherent placenta, any suspicion should prompt further measures for correct diagnosis and management.
- Delivery should be performed by CS in surgically managed CSP to reduce the risk of rupture uterus and allow adequate closure of lower segment.

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Answer: March Issue

Crossword

Across

1. Indocyanine green
2. Neuroendocrine
3. ls3
6. Portec
7. Breast
8. Lymph node
9. Two
10. p53

Down

4. Neuroepithelium
5. Dextrose

Pictorial Quiz

Case 1

1. Type 2 transformation zone
2. Swede score:7, Plan Biopsy

Case 2

1. Cervical intraepithelial neoplasia 2
2. Excisional procedure. Patient was offered LEEP. Follow up with co-test/ HPV/cytology at 6 months, 1year & 2 years and if test is negative, return to routine screening.[1]
3. Since the second follow up was during her pregnancy Pap smear was done. There is no indication of repeat colposcopy.

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Current Diagnosis and Treatment of Placenta Accreta Spectrum

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Introduction

Placenta accreta spectrum (PAS) is a general term used to describe abnormal trophoblast invasion into the myometrium of the uterine wall and includes placenta accreta, increta and percreta. It is clinically important because the placenta does not spontaneously separate as the plane of cleavage is absent (Fig 1); and any attempt of manual removal results in hemorrhage, which can be ***life-threatening*** and usually necessitates hysterectomy. The pathogenesis of most cases of PAS is thought to be placental implantation at an area of defective decidualization caused by preexisting damage to the endometrial-myometrial interface. The most important risk factor for PAS is placenta previa after a prior cesarean delivery, the risk of which increases exponentially with number of previous cesareans. Other risk factors associated are placenta previa, advanced maternal age, grand multiparity, previous curettage, scar pregnancy, uterine surgeries like myomectomy, hysteroscopic adhesiolysis, endometrial ablation, submucous myoma, post-partum endometritis, infertility procedures and previous adherent placental disorders.

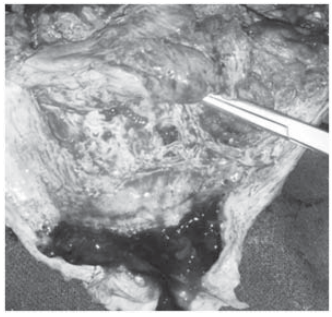

Fig 1: Hysterectomy specimen of PAS showing invasion of placenta into the myometrium

PAS has taken epidemic proportions of late which parallel's the rise in cesarean deliveries[1]. It was reported as 1:30,000 deliveries in 1950 and has dramatically increased to 1:700 in recent years[2–4]. A recent study conducted by the authors at Safdarjung Hospital, Delhi reported the incidence as 1:1101 deliveries (0.09%)[5].

Prenatal Diagnosis

Ultrasonography: Women with a placenta previa or a low anterior placenta and prior uterine surgery, should have thorough transabdominal and transvaginal sonographic evaluation of the interface between the placenta and myometrium, approximately between 18 and 24 weeks of gestation. At this gestational age, the prenatal diagnosis of PAS can be made or ruled out with close to 90 percent accuracy. The ultrasonographic findings which are associated with PAS are[6]:

1. Loss of 'clear zone' i.e the hypoechoeic area in the retroplacental region (Fig 2).
2. Presence of multiple lacunae in the placenta (Fig2,3).
3. Absence of 'bladder line'- Loss or disruption of the normally continuous white line representing the bladder wall-uterine serosa interface can be caused by placenta percreta.
4. Myometrial thinning in the areas where placental invasion has taken place.

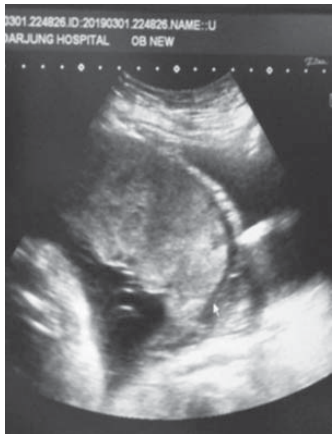

Fig 2: Sonography film showing normal retroplacental clear space

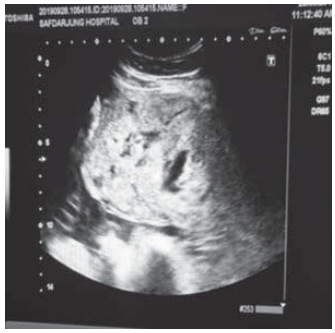

Fig 3: Sonographic film in PAS showing loss of retroplacental clear space and multiple irregular lacunae

Colour Doppler: Colour Doppler is very useful to confirm diagnosis of PAS. The salient features which are seen in PAS[7,8]:

1. Turbulent lacunar blood flow.
2. Diffuse or focal intraparenchymal flow.
3. Hypervascularity of serosa-bladder interface.
4. Prominent subplacental venous complex.
5. Bridging vessels- they are color Doppler signals that arise in the myometrium and appear to travel into the bladder and then disappear. They are an ultrasound artifact rather than a true bridge into the bladder. They are seen in cross-sectional images of peritoneal neovascularity caused by dilation of large and deep subplacental myometrial vessels (Fig 4).

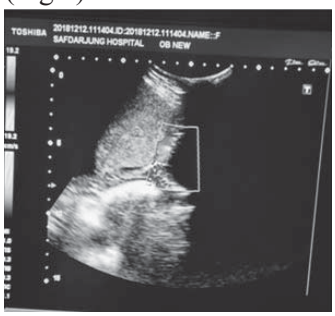

Fig 4: : Sonographic film in PAS showing bridging vessels from placenta going into the bladder

Three-dimensional power Doppler ultrasound: Three-dimensional ultrasound has been used successfully for evaluation of PAS. Diagnostic criteria include[9]:

1. Irregular intraplacental vascularization with tortuous confluent vessels crossing placental width
2. Hypervascularity of uterine serosa-bladder wall interface

MRI: MRI may be more useful than ultrasound in two clinical scenarios: (1) evaluation of a possible posterior PAS because the bladder cannot be used to help clarify the placental-myometrial interface, and (2) assessment of the depth of myometrial and parametrial involvement, and, if the placenta is anterior, bladder involvement. 24 to 30 weeks is considered as the ideal gestational age for imaging invasive placentation with MRI as false positives and negatives are more likely earlier and later in gestation. MRI findings in placenta accreta include[10]:

1. Uterine bulging into the bladder
2. Heterogeneous signal intensity within the placenta
3. Presence of intraplacental bands on the T2-W imaging
4. Abnormal placental vascularity
5. Focal interruption of the myometrium

Placenta Accreta Index: A scoring system called the 'Placenta Accreta Index' has been proposed recently for prediction of PAS in women with placenta previa and previous cesarean section. This incorporates history, location of placenta, thickness of myometrium, absence of retro placental clear zone, presence of bridging vessels and size and number of lacunae to determine the score [11] (Table 1). A score of 9 means 96% chance of PAS with sensitivity of 17% & specificity of 100%, PPV 100%, NPV 72%. A score of 1 means 5% chance PAS with sensitivity of 100% & specificity of 19% PPV 38%, NPV 100%.

Table 1: Placenta Accreta Index Score

Value of each Parameter is added together to generate placenta accreta index score	
Parameter [a]	*Value*
≥ 2 caesarean deliveries	3.0
Lacunae	
Grade 3	3.5
Garde 2	1.0
Sagittal smallest myometrial thickness [b]	
≤1mm	1.0
< 1 but ≥ 3 mm	0.5
>3 but ≤ 5 mm	0.25
Anterior placenta previa [c]	1.0
Bridging vessels	0.5

[a] - if parameter is not present, then value is 0

[b] - measured in sagittal plane.

[c] – if any potion of placenta is anterior

First trimester ultrasound: PAS should be suspected if first-trimester ultrasound examination reveals a gestational sac in the lower uterine segment (rather than the fundus) next to or lower than the hysterotomy scar or a cesarean scar pregnancy [12]. The characteristic second-trimester findings of placental lacunae (which appear as intraplacental sonolucent spaces) and disruption of the interface between the bladder wall-uterine serosa (bladder line) also may be observed in the first trimester

Management of PAS

Antenatal diagnosis of placenta accreta spectrum is crucial in planning its management and has been shown to reduce maternal morbidity and mortality (RCOG 2018 Level D)[13]. The same has been observed by the authors in a retrospective case control study of 74 cases of PAS [5]. Hence all high risk women should be screened by ultrasonography. **Patients who have been diagnosed in the antenatal period should be referred to** a **tertiary care Level 3 or 4 center for delivery.**

Women presenting with PAS disorders with or without placenta previa should have their delivery

scheduled in a Center of Excellence with a dedicated multidisciplinary team and care plan. (FIGO 2018, strength of recommendation strong)[14]. The multidisciplinary team should consist of senior anesthesiologist, senior obstetrician (who is expert in retroperitoneal dissection), neonatologist, intervention radiologist, urologist, hematologist & blood bank officer and maternal-fetal critical medicine specialist.

The important components of prenatal care are as follows:

1. Prevention and treatment of anemia
2. Anti-D immune globulin if vaginal bleeding occurs and the patient is Rh(D)-negative
3. Avoidance of pelvic examination and rigorous activity
4. Avoidance of sexual activity though not of proven benefit
5. In diagnosed cases repeat scan at 32-34 weeks to assess likelihood of bladder invasion
6. Bed rest and/or hospitalization in the third trimester if vaginal bleeding, contractions occur or if residence of patient is at a remote distance from a center of excellence for PAS.
7. Asymptomatic women can be followed as outpatients with counseling about the danger signs.
8. A single course of antenatal corticosteroid therapy is recommended between 34^{+0} and 35^{+6} weeks of gestation for pregnant women with a low□lying placenta or placenta previa and is appropriate prior to 34^{+0} weeks of gestation in women at higher risk of preterm birth (RCOG 2018)[13].

Planning of delivery

Timing of delivery: A planned preterm delivery is recommended in PAS

In the absence of risk factors for preterm delivery in women with placenta accreta spectrum, planned delivery at 35^{+0} to 36^{+6} weeks of gestation provides the best balance between fetal maturity and the risk of unscheduled delivery (RCOG Sept. 2018)[13].

However ACOG recommends even earlier intervention between *34^{+0}* to 35^{+6} weeks of *gestation* (ACOG Dec 2018)[15].

Preoperative and Intra-operative Steps:

The standard treatment consists of planned preterm cesarean hysterectomy with placenta in situ[13-15]. The important preoperative and operative steps are as follows:

1. **Pre op counseling & consent of the patient and her relatives** should include discussion regarding the need for hysterectomy, bladder and ureteric injury, bowel injury, massive blood loss and massive blood transfusion and its consequences, liberal longitudinal skin incision, internal iliac artery ligation, sepsis, need for postoperative ventilation and ICU care and risk of mortality.
2. Prophylactic antibiotics should be administered according to the hospital policy.
3. Packed RBCs, FFP and PRP (2-3 units of PCV in OT) kept cross matched in blood bank (1:1:1).
4. Pre-op ureteric stenting, 3 way Foleys in selected cases with bladder involvement.
5. Pre-op placements of catheters/balloons in pelvic arteries by interventional radiology is controversial-routine use not recommended (ACOG 2018).
6. Pneumatic compression stockings to be instituted pre-op and continued per operatively
7. Anesthesia may be GA/Regional.
8. Patient to be placed preferably in lithotomy position (helps in monitoring blood loss)
9. Midline vertical incision should be used for opening abdomen.
10. Intra-operative USG for localizing the placenta is advisable to plan uterine incision.
11. Classical uterine incision is given to avoid placenta and allow delivery of infant
12. Incision should be given up to 2 finger breath above the placental margin.
13. Should wait for 15-20 minutes for spontaneous placental separation, if patient is hemodynamically stable and not bleeding. In case patient starts bleeding, proceed for hysterectomy straightaway. **Never attempt manual removal of placenta in patients suspected of PAS**.
14. If hysterectomy necessary, leave placenta in situ, close hysterotomy incision by 'whip stitch'→ and proceed for hysterectomy (Fig 5).

Fig 5: Hysterectomy specimen of PAS. Note the classical cesarean and placenta in situ

Challenges During Surgery for PAS

The surgery for PAS has serious complications as shown in Table 2. The chief amongst them are massive blood loss and bladder injury. The various challenges which are faced by the surgeon include dense pelvic adhesions; thin and hyper-vascular lower uterine segment; bulky in- situ placenta; deep pelvis neovascularization; and invasion to bladder, bowel, cervix, and parametrium in cases of placenta percreta.

Table 2: Complications of Surgery in PAS

Complications	
Median estimation of blood loss	2-3 L
Median units of packed red blood cells transfused	3.5-5.4 L
Large- volume blood transfusions(>10L)	5%-40%
Injury to bladder	7%-48%
Injury to ureter	0-18%
Admission to intensive care unit	15%-66%
Bowel injury/obstruction	2%-4%
Venous thromboembolism	4%
Surgical site infection	18%-32%
Reoperation	4%-18%
Maternal mortality	1%-7%

(Source – FIGO consensus guidelines on PAS Disorders, 2018)

Retrograde Hysterectomy

This technique has been recently described as an alternative to conventional hysterectomy especially in cases of placenta percreta involving the bladder. It has been seen to decrease blood loss in patients with invasive placenta and facilitate bladder dissection. The baby is delivered through classical section and placenta is left in situ. The round ligaments are divided and retroperitoneal space developed. Bilateral internal iliac arteries are ligated. Following this the vaginal vault is opened posteriorly followed by division of utero-sacrals and Mackenrodts ligaments and plane developed through lateral dissection to separate bladder; if there is invasion into bladder, a deliberate cystostomy is performed and hysterectomy completed.

Endovascular Intervention

Prophylactic endovascular intervention with a balloon catheter, arterial embolization, or a combination of the two may be used to decrease hemorrhage during or after delivery. Preoperatively under fluoroscopic guidance, a catheter is inserted into each femoral artery and guided to the desired target vessel. For embolization, Gelfoam is used after delivery of the infant and for balloon occlusion, the balloon-tipped catheters are introduced into the target artery. After delivery the balloons can be inflated intermittently for up to 20 minutes to reduce bleeding in the operative field, which facilitates placement of clamps and sutures and decreases total blood loss. Use of a pressure manometer-endoflator allows inflation and deflation of the balloons to pressure without the use of fluoroscopy [16]. The catheters may be left in situ for several hours postoperatively, and used for selective embolization of small pelvic vessels if postoperative bleeding occurs. They are removed under fluoroscopic guidance.

Larger studies are necessary to determine the safety and efficacy of interventional radiology before this technique can be advised in the routine management of placenta accreta spectrum. (Grade of recommendation: D, *RCOG 2018*).

Conservative Management

Conservative management implies preserving the uterus and managing the patient without performing hysterectomy. It is considered in women desirous of preserving their reproductive function and sometimes in cases where surgeon deems it appropriate (eg in percreta with extensive invasion into bladder and surrounding tissues). Conservative management should be considered only for carefully selected case of PAS after detailed counseling about risks, uncertain benefits and efficacy and should be considered investigational *(ACOG 2018, 2C)*

There are 2 types of scenarios which merit this treatment. In the first instance the entire placenta is left in situ after delivery of the baby through classical cesarean; extensive preoperative counseling is required regarding its risks. The prerequisite is that the patient should not be bleeding and should be hemo-dynamically stable. The placenta is left in situ after clamping & cutting the cord close to it. These patients are followed closely by regular ultrasound to look for spontaneous resolution of placenta. Beta hcg monitoring is helpful only in initial follow up period. Methotrexate adjuvant therapy should not be used for expectant management as it is of unproven benefit and has significant adverse effects. (*RCOG 2018* Grade of recommendation: C). In some cases, a planned secondary hysterectomy may be performed, after the vascularity of the uterus and placenta has significantly diminished, making the surgery much safer.

The second situation is when there is a focal accreta, wherein the conservative surgery like **Triple P Procedure** may be performed [17]. Triple P Procedure has been described as a conservative surgery for focal placenta accreta; the steps include; 1. Preoperative

localization of placenta using TAS and delivery of fetus by transverse incision 2 finger breath above it; 2. Pelvic devascularization by inflating pre placed occlusion balloons in both internal iliac arteries and 3. Area of placental non separation is dealt by en bloc myometrial excision and reconstruction of the uterine wall.

Outcome of Conservative Management

When the placenta is left in situ, local arrangements need to be made to ensure regular review, ultrasound examination and access to emergency care should the woman experience complications, such as bleeding or infection. *(RCOG 2018, Grade of recommendation D)*

In a large series of patients managed conservatively it was seen that the treatment was successful in 78% of the cases. Severe maternal morbidity was seen in 6.0%, whereas infection was observed in 28%. Secondary PPH occurred in 11% and sepsis in 4%. The median interval from delivery to delayed hysterectomy was 22 days (9-45) and mortality rate was 0.6% [18].

Conclusion

PAS is a potentially life threatening condition which is associated with placenta previa in a previously scarred uterus. All high risk women should be screened for PAS in the antenatal period as prenatal diagnosis is associated with better outcomes. Planned preterm classical cesarean followed by hysterectomy with placenta in situ at a center with a dedicated multidisciplinary team is considered as the standard treatment for PAS disorders although conservative management can be instituted in selected patients after extensive counseling.

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ERAS and its Application in OBGYN

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What is ERAS?

Enhanced Recovery After Surgery (ERAS), also known as "fast-track surgery" is a multidisciplinary, multimodal evidence-based perioperative care that aims to hasten patient's recovery and improve surgical outcomes. This paradigm shift from traditional aspects of perioperative care to a more active approach was first introduced by Kehlet in 1997. Since then it is enriched with new protocols over the years and being adopted by various surgical specialities including gynaecological procedures. The ultimate goal of ERAS is to mitigate the physiological stress of surgery and optimize functional rehabilitation of patients after surgery.

How does it work?

The key mechanism for all the ERAS programs is to prevent surgical stress response (SSR). Surgical stress disrupts the normal physiological balance and triggers a catabolic state resulting in increased cardiac demand & relative tissue hypoxia. It also leads to increased insulin resistance, impaired coagulation pathways and altered pulmonary, immunological, neurological, gastrointestinal function, etc. This disruption of normal physiological balance results in delayed postoperative recovery and increased morbidity. ERAS implementation reduce this catabolic insult & maintain normal physiology in the perioperative period, thus optimizing patient outcomes without increasing the complication and readmission rates.

Traditional components of perioperative care include bowel preparation, cessation of oral intake after midnight, liberal use of narcotics, patient-controlled analgesia use, prolonged bowel and bed rest, use of nasogastric tubes and drains, and gradual introduction of feeding. However, all of these are not evidence-based and hamper early recovery. Keeping this in mind, ERAS pathways are developed based on interventions which are data supported. These pathways primarily focus on reducing perioperative stress, achieving satisfactory pain control, resumption of normal gastrointestinal function and early mobilisation.

The basic principles of ERAS focus on

1. **Preoperative-** counselling and nutrition strategies.
2. **Intraoperative-** focus on regional anaesthesia and non-opioid analgesic approach, fluid balance, and maintenance of euthermia.
3. **Postoperative-** early mobilization, appropriate thromboprophylaxis etc.

Why to adopt ERAS in Gynaecological Surgeries?

There is enough evidence in the literature highlighting the implementation of ERAS protocols and their benefits in various elective and emergency procedures of surgical specialities like colorectal surgeries, spine surgery, urological procedures, etc. Studies comparing ERAS protocols to conventional patient care in gynaecological procedures have shown that such programs significantly reduce the length of hospital stay (LOS), fasten patient recovery without an increase in readmission and postop complication rates. These benefits have been replicated for caesarean sections and all spectrum of gynaecological procedures including open & minimally invasive approaches, benign and oncological surgeries. Yoong et al (2014) have shown that by implementing ERAS to patients undergoing benign vaginal hysterectomies, there was a 51.6% reduction in LOS and early discharge within 24 hours without an increase in readmission rates. For patients with gynaecological cancers, early recovery has an additional advantage of the accomplishment of planned adjuvant therapies without delay, resulting in better oncologic outcomes. ERAS adoption also helps in improving patient satisfaction, quality of life, reducing in-patient load on overburdened hospitals by reducing LOS. It ultimately reduces overall healthcare costs and leads to positive economic benefits.

Applicability of ERAS to cesarean deliveries?

As the rate of cesarean deliveries (CD) is on the rise, there is a substantial increase in patient load and postoperative morbidity. ERAS implementation in CD can facilitate earlier discharge without an increase in complication rates, earlier return to normal activities, and a reduction in postop care load.

Hedderson M et al (2019) conducted a pre-post study of ERAS implementation (n= 4689 vs 4624) in planned/ unplanned CD. This study showed a significant decrease in mean inpatient opioid exposure (10.7 equivalents to 5.4 equivalents), decrease in time to first postsurgical ambulation (by 2.7 hrs),

and decrease in time to first postsurgical solid intake (by 11.1 hrs) after ERAS implementation. However, there were no significant changes in the length of stay in the hospital, surgical site infections, hospital readmissions, or breastfeeding rates.

Similarly, Emily E Fay (2019) also concluded that implementation of the ERAS CD pathway resulted in a significant decrease in postoperative length of stay (by 7.8% or 4.86 hours), an 8.4% decrease in total postoperative direct costs for both planned and unplanned CD. There were no significant differences in readmission rates. As supported by literature evidence, ERAS pathways can be safely applied for CD at both government and private institutions. The guidelines on ERAS CD pathways (Part 1-3) have provided a detailed preoperative, intraoperative and postoperative recommendation on this. These guidelines can be used as a prototype tool to formulate institution-specific ERAS protocol for clinical practice.

Barriers to Implementation of ERAS?

1. It is a new concept against deep-rooted traditional perioperative care
2. Require major changes in daily clinical practices.
3. It requires participation and commitment of the entire team members
4. Significant variations in protocols amongst different institutions
5. Lack of confidence of surgeons in ERAS protocols

How to implement ERAS successfully?

Institutions considering the adoption of such programs should carefully examine their infrastructure and patient flow through the preoperative and postoperative phases of care.

Implementation of successful ERAS program can be achieved through the following three elements:

1. **An ERAS protocol** - The entire team should develop speciality specific, standardized set of guidelines before implementation. It is needed as some of the protocol recommendations by ERAS society have more than one option, so the team can decide the best-suited option by mutual discussion. A defined protocol will also help in maintaining a uniform standard of care and the auditing process.
2. **An ERAS team** – A crucial component of any ERAS program is the formation of a multidisciplinary team consisting of an ERAS coordinator, surgeons, anaesthetists, residents, nurses, dietician, physiotherapist and data manager. This team will be actively involved in the implementation of defined protocol into clinical practice, reviewing compliance through auditing and troubleshooting with inputs from all experts.
3. **An Audit system**- A continuous auditing system is a necessary component of any ERAS program to ensure adherence and success of the program. It can be done either by use of ERAS Interactive Audit System (EIAS) or with a tailored database. The database should record each of the compliance elements and also the components of perioperative outcomes like length of stay, readmissions, complication rate, etc.

The recommendations for implementation of ERAS involve pre-, intra- and post-operative stage and are summarized in Table 1. It must be emphasized that multiple components of the ERAS should be implemented together and no single element by itself will serve the goal of improved patient outcome. A holistic approach should be used to resolve any issue or complication hampering the early recovery.

Table 1: Main recommendations for ERAS pathway for Gynaecological Surgeries

Preoperative Stage	
Area	**Intervention**
1. Prehabilitation	• Patient Education & counselling, psychological preparation • Alcohol & Tobacco cessation (ideally at least 4 weeks before surgery) • Optimization of the co-morbid condition like anaemia, diabetes & BP control
2. Fasting guidelines	• Light meal allowed up to 6 hrs and clear liquid up to 2 hrs before the procedure, fasting only for 2 hrs • Carbohydrate loading drink 2 hrs before procedure
3. Bowel preparation	• Elimination of oral mechanical bowel preparation and rectal enemas for most of the procedures
4. Premedications	• Avoid long or short–term sedative agents like pregabalin, acetaminophen i.v
Intraoperative Stage	
1. Nausea and vomiting prophylaxis	• Transdermal scopolamine 1.5 mg patch 2 hrs preoperatively for patients at high risk of postoperative nausea and vomiting. • Dexamethasone 8 mg i.v once at induction, ondansetron 4 mg i.v before emergence • Alternative regimens at the discretion of anaesthesiologist and surgeons
2. Fluid therapy	• Goal-directed fluid therapy with a net-zero balance at the end of surgery • Prefer ringer lactate over normal saline for electrolyte balance Decrease crystalloid & increase colloid administration if needed

3. Analgesia	• Before OT entry: consideration of celecoxib 400 mg orally, acetaminophen 1000 mg P.O and gabapentin 600 mg P.O • Regional anaesthesia • IV Opioids at the discretion of the surgical team, supplemented with ketamine/ketorolac or both • Consideration of transversus abdominis plane block vs local infiltration vs local wound infiltration depending on surgical consideration • For pelvic organ prolapse surgery: spinal block containing bupivacaine plus hydromorphone (40-100 micrograms); sedation versus light general anesthetic at the discretion of surgical team
4. Antimicrobial therapy	• Injectable antibiotic (first-generation cephalosporin or amoxicillin–clavulanic acid) within 60 minutes before skin incision • Increase prophylactic antibiotic dosage in obese patients • Additional intraoperative doses if heavy blood loss (>1.5 l) or lengthy procedure • Use of an alcohol-based agent for skin cleansing • Use either 4%chlorhexidine gluconate or povidone-iodine for vaginal cleansing • Hair clipping rather than shaving
5. Drains and packs	Avoidance of drains and vaginal packs.
6. Temperature	Maintenance of euthermia
Postoperative stage	
1. Fluid optimization	• Operation room fluids discontinued on floor arrival • Fluids 40ml/hr until 8 am day after surgery, then discontinue • Stop IV fluids when oral intake is 600 mL or at 8 am day after surgery (whichever is first)
2. Diet	• No NG tube (remove at extubation if placed) • Start a regular diet and chewing gum 4 hrs after the procedure • Day of surgery: oral intake at least 800 mL fluid but no more than 2000 mL by midnight • Day after surgery until discharge: encourage daily oral intake of 1500- 2000 ml fluids • Maintain blood glucose levels (180-200 mg/dL)
3. Analgesia	• Opioid-sparing analgesia • Scheduled ketorolac / NSAID'S / Acetominophen / Gabapentin
4. Mobilization	• Evening of surgery: out of bed for > 2 hrs • Day after surgery till discharge: out of bed for > 8 hrs • Up in chairs for all meals
5. Catheters	• Removal of urinary catheters within 24 hrs • Consider early removal of drains and vaginal packs
6. Discharge	• Defined discharge pathways (eg. full mobilization, oral analgesia, able to tolerate solids without nausea and vomiting)

Conclusion

ERAS pathways represent a comprehensive bundle of interventions and successful implementation depends on the adaption of multiple ERAS principles. The use of ERAS has resulted in more rapid surgical recovery, shorter length of stay, greater patient satisfaction and decreased costs when compared with traditional approaches. However, to make ERAS sustainable, it should be adopted as a standard model of care in the healthcare delivery system.

Scope of Further Research

There is currently a paucity of data on the impact of an ERAS program specifically targeting patients undergoing high complexity procedures, such as pelvic exenteration and HIPEC surgery. Further research is needed from high-volume referral centers to document the outcomes of ERAS programs in this patient population.

Suggested Reading

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Polycystic Ovary Syndrome: Recent Update

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Introduction

Polycystic ovarian syndrome (PCOS) is the most common endocrinological disorder among females with reproductive, metabolic and psychological consequences. The prevalence varies from 8-13% depending upon diagnostic criteria used and population studied [(1)]. In India there is paucity of epidemiological studies, however prevalence among adolescent and young girls (15-24yrs) as 22.5% by Rotterdam criteria and 10.7% by the Androgen excess society criteria has been reported[(2)].

Main clincial features include oligomenorrhea, excessive hair growth, acne, weight gain, infertility, depresssion and long term complications include like type II diabetes, hypertension and increased risk of cardiovascular disease.

Exact etiopathogeneis of PCOS is not clear as multiple factors including genetic, metabolic and environemental factors have been involved. Figure 1 shows the pathophysiology of disease and various outcomes.

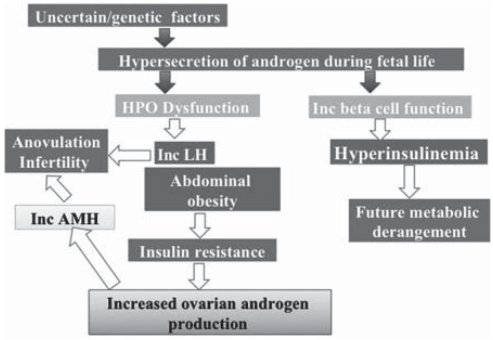

Figure 1: Pathophysiology of PCOS

Diagnosis

To diagnose PCOS, different diagnostic criteria have been given by NIH (1990), ESHRE/ASRM (2003), AE-PCOS (2006) and NIH 2012. Latest PCOS guideline in 2018 recommends Rottterdam criteria to be used for diagnosis of PCOS. In addition it is recommneded to specify phenotype depending upon presence or absence of diagnsotic criteria present[(3)]. Table 1 shows the evolution PCOS definition and Table 2 shows the classification of different PCOS phenotypes.

Rotterdam criteria: PCOS is diagnosed if 2 of 3 criteria are present. (1) - Clinical and/or biochemical hyperandrogenism; (2) Oligo/amenorrhea, anovulation; (3)- Polycystic ovaries appearance on ultrasound (PCOM)

Ovulatory dysfunction- Ovulatory dysfunction is reflected by presence of oligomenorrhea/ amenorrhea or rarely polymenorrhea[(4)]

- In intial 1-2 years post menarche, irregular cycles should be considerd as normal and should not be labelled as ovulatory dysfunction
- Between >1- <3 yrs post menarche, irregular menstrual cycle is defined as <21 days or >45 days
- After 3yrs post menrache, oligomenorrhea is defined as menstrual cycles >35 days; less than 8 menstrual cycles per years or polymenorrhea as cycles <21 days interval
- In women with evidence of clinical/biochemical hyperandrogenism, even if menstrual cycles are regular, ovulation should be documented by serum progesterone (P4) on day 20-24 of cycle on one or two consecutive cycles.

Table 2: PCOS phenotypes

Phenotypes	PCOS Features	Prevalence
A (Frank PCOS)	HA+OD+PCOM	55.8%
B (Non PCO PCOS)	HA+OD	15.2%
C (ovulatory PCOS)	HA+PCOM	11.4%
D (Non-hypernadrogenic PCOS)	OD+PCOM	17.5%

HA=Hyperandrogenism; PCOM= Polycystic ovarian morphology; OA= Ovulatory dysfunction

Table 1: Evolution of PCOS diagnostic criteria

NIH* consensus 1990 (all required)	ESHRE**/ASRM***/Rotterdam Consensus 2003 (two out of three required)	AEPCOS**** 2006 (Androgen excess and one other criterion)	NIH 2012 extension ESRM/ASRM/ Rotterdam 2003 (two out of three required)
HA	HA	HA	HA
OD	OD	OD	OD
	PCOM	PCOM	PCOM Identification of different Phenotypes (Table 2)

NIH* National Institute of Child Health; ESHRE ** European Society for Human Reproduction and Embryology; ASRM***American Society of Reproductive Medicine; AEPCOS****Androgen Excess and PCOS Society.

Clinical/biochemical hyperandrogenism

- Clinical hyperandrogenism (HA) is diagnosed according to modified Ferriman Gallwey score (mFG). Score more than 4-6 is considered as evidence of clinical HA.
- Although acne and female pattern hair loss (FPHL) are also seen in PCOS, they are not considered as markers of HA
- Biocehmical HA is diagnosed with raised free Testosterone (fT) as most sensitive marker. Dehydroepiandrosterone (DHEA-S) and androstenedione (A4) may also be used to diagnose biocehmical HA.
- Biocehmical HA should be assessed only when evidence of clinical HA is not present in women with 2 other Rotterdam criteria.

*TSH, Prolactin and 17 (OH) Progesterone should be done in all cases of PCOS to exclude other causes.

Polycystic ovarian morphology- There is wide subjective variation in diagnosing follicular number and volume. In the initial Rotterdam criteria, PCO was diagnosed if follicular count was >12 or follicular volume >10cc. but with advanced technology and availability of better USG machines, following cut-off are taken:

- Cut-off for AFC is □20 per ovary when modern technology USG machine (8MHz)is used
- When old technology or abdominal scan is used then ovarian volume >10cc should be taken as cut-off to diagnose polycystic ovary.
- Ovarian USG is not recommneded in intial 8 years post menarche for diagnosis of PCOS[4]

The exact prevalence of different phenotypes is also different in different ethinic groups but phenotype A has been reported to be highest in most of the studies[5]. The clinical, biochemical and metabolic characteristics, of phenotypes A and B, are similar, but phenotype A has higher hirsutism score and androgen level. Phenotype C has intermediate metabolic characteristics between A and controls whereas phenotype D has the mildest metabolic abnormalities among the four phenotypes. Significant predictors for metabolic syndrome within the PCOS cohort are waist circumference >35inches, hypertension, fasting glucose >100 mg/dL, HDL-cholesterol <50 mg/dL and triglyceride >150 mg/dL [6].

Serum Antimullerian hormone levels (AMH) and PCOS-

Serum AMH is secreted by pre and small antral follicles and inhibit the follicular growth. PCOS is associated with high levels of AMH which causes anovulation and its associated features [7]. Levels more than 5ng/ml are associated with more severity of PCOS although different studies have given different cut-offs and exact value has not been defined. Also AMH is still not considered as diagnostic criterion for PCOS.

Assessment of clinical symptoms and signs of PCOS should be done to diagnose PCOS and to specify clinical phenotype. Figure 2 shows the algorithm to screen and diagnose different phenotypes according to Rotterdam criteria.

Associated Metabolic features

- Although not included in diagnostic criteria, hyperinsulinemia and insulin resistance (IR) occurs in approximately 80% of women with PCOS and central obesity, as well as in 30–40% of lean PCOS women[8].
- IR is considered as the key to pathophysiology of PCOS and it determines hyperandrogenism by acting synergically with LH on ovarian steroidogenic enzymes and SHBG production by the liver[9].
- There is reduced production of SHBG (Sex hormone binding globulin) and IGFBP-1 (Insulin growth factor binding proteinin liver).

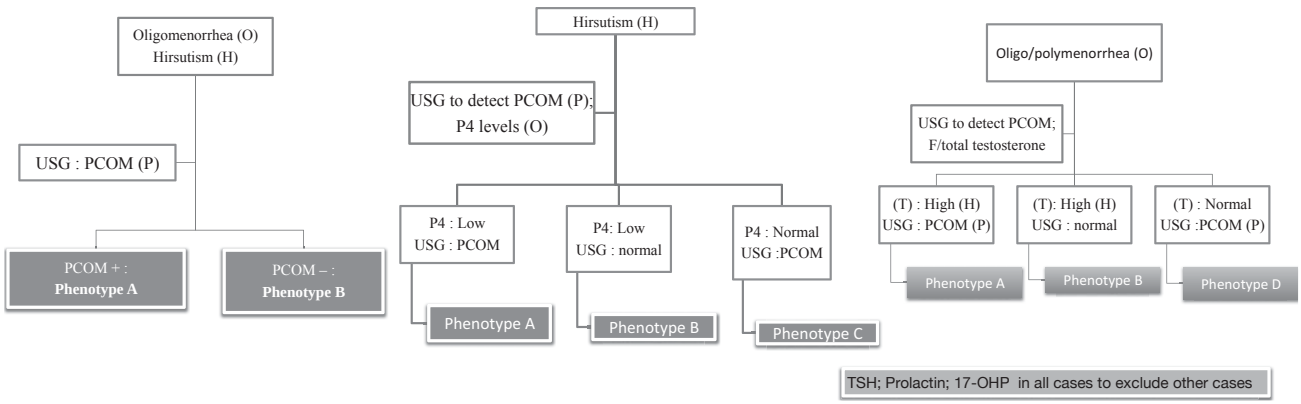

Figure 2: Algorithm to screen and diagnose different PCOS phenotypes

- There is altered production of inositols and production of DCI is increased as compared to Myo-inositol[10].

Additional work up[6]

- Blood pressure; BMI (Kg/m^2); waist hip ratio
- Look for acne, hirsutism, alopecia, acanthosis nigricans
- Investigations as given in algorithm (figure 2)
- Glucose tolerence test (2hr GTT)
- Fasting lipid profile
- Optional tests
  - o Fasting insulin levels in younger women, those with severe stigmata of insulin resistance, hyperandrogenism, or those undergoing ovulation induction
  - o HOMA-IR- fasting glucose (mg/dL) x fasting insulin (uU/mL) /405 (OR) fasting glucose (mMol/L) x fasting insulin (uU/L) /22.5 (>2.5 considered abnormal)
  - o FSH/LH to know cause of ammenorhea
  - o AMH – infertile women planned for ovulation induction

Management of PCOS

Treatment

- *Weight reduction* -Main stay of the treatment is life style modification which includes exercise and dietary modification. Achievable goals such as 5% to 10% weight loss yields significant clinical improvements and is considered successful weight reduction within six months. This can be achieved with an energy deficit of 30% or 500-750 kcal/day (1,200 to 1,500 kcal/day)
- *Exercise intervention*- In adult PCOS women, a minimum of 150min/week of moderate intensity exercise or 75 min/week of vigorous intensities or combination of both, including muscle strengthening activities on 2 non-consecutive days/week. In adolescents, at least 60 minutes of moderate to vigorous intensity physical activity/day, including muscle strengthening exercises at least 3 times per week.
- *Behavioural Strategies and psychological intervention* -Behavioural strategies such as goal-setting, self-monitoring, stimulus control, problem solving, assertiveness training, slower eating, reinforcing changes and relapse prevention, to optimise weight management, healthy lifestyle, yoga, meditation to relieve stress and emotional wellbeing should be incorporated.

Rest of the management depends upon the need of the women like menstrual regularization, clinical and biochemical hyperandrogenism, hyperinsulinemia, anovulation and infertility management.

Menstrual Regularization

Combined oral contraceptive pills (COCPs) are the first line for treatment of irregular periods. COCPs with 20-30mcg of ethinyl oestradiol or equivalent should be used. COCPs with anti-androgen like drosperinone can be considered in women with hirsutism. COCPs with cyproterone acetate should not be considered first line in PCOS as per general population guidelines, due to adverse effects including venous thromboembolic risks.

Insulin Sensitizing Agents

Improvement in insulin resistance in PCOS decreases androgen levels and improves glucose tolerance and ovulation rates[11]. Among insulin sensitizers, metformin has been studied most extensively and there is evidence that it may have metabolic and reproductive benefits[11]. Dose of 500-1500 mg/ day is given in divided doses. Treatment should be for a period of minimum 3-6 months and maximum 2 years. It is generally safe with few gastrointestinal side-effects like nausea, bloating, which are generally dose dependent and self-limiting and alleviates if starting with the low dose and with 500mg increments in 1-2 weeks.

Inositol

Myoinositol (MI), a nutrient belonging to vitamin B complex, is being studied since last decade As a mediator of insulin action, evidence has shown that MI, may decrease the hormonal profile, decrease hypernadrogenism, oxidative abnormalities, as well as the metabolic factors in patients with PCOS, probably due to amelioration of insulin resistance (HOMA-IR) in these patients[10]. Various studies are showing favourable results with inositols and Myo-inositol in dose of 4g per day alone has shown favourable results in terms of improvement in metabolic and endocrine and reproductive functions.

Inositols especially MI can be given in PCOS women with BMI >25Kg/m^2 and in women with persistant anovulation and poor response to ovulation induction drugs.

Anovulation and Infertility

Ovulation inducing drugs are the first line agents where anovulation is the cause of infertility.

Letrozole

Letrozole is considered the first line for ovulation induction with half-life approximately 45 hrs resulting in mono follicular growth. As compared to Clomiphene citrate, letrozole causes mon-ovulation, no effect on endometrium, less chances of multiple pregnancies and OHSS. Dose of 2.5-5 mg for 5 days from Day 3- 7 of menstrual cycle is given[12].

Gonadotropins

Gonadotrophins (Gn) can be added if there is inadequate response to letrozole/clomiphene.

Strict USG monitoring is must while adding Gn for ovulation induction. Ovulation trigger with hCG should be avoided if there are 3 or more mature follicles.

Laparoscopic Ovarian Drilling (LOD)

Obesity, hyperandrogenism, insulin resistance, excessive ovarian volume and chronic anovulation are considered predictors of failure of ovulation induction. In these women LOD can be considered as second line management option.

Indications: (1) no ovulation/conception after multiple (4-6) OVI cycles; (2) when laparoscopy is performed for some other indication; (3) when patient is unable to follow up for regular ultrasound scans while on gonadotropin injections; (4) previous history of ovarian hyperstimulation syndrome

Risks need to be explained to all women with PCOS considering laparoscopic ovarian surgery. Armar's rule is used of 4:4 punctures /ovary with 40 watts, 4 sec and 4mm depth with effective thermal dosage 60 J/cm^3.

In vitro fertilization (IVF)

In the absence of an absolute indication for IVF women with PCOS and anovulatory infertility could be offered IVF as third line therapy where first/ second-line OVI therapies have failed. Antagonist protocol is preferred in women with PCOS to reduce the incidence of ovarian hyperstimulation syndrome (OHSS). In order to prevent OHSS, GnRH agonist trigger (Inj. Leuprolide 1-2mg subcutaneous injection) is preferred in antagonist cycles.

If there are >15 oocytes recovered or features of OHSS, elective freezing and embryo transfer in next cycle should be planned.

Summary

- Phenotypic classification of PCOS helps to define the severity of PCOS and to individualise treatment.
- Life style modification is the first line of management in PCOS
- Ovulation induction with letrozole is the first line of ovulation induction.
- Insulin sensitizers (metfromin and myoinositol) can be added to improve endocrine, metabolic and reproductive functions.
- Laparoscopic ovarian drilling should be reserved as second line option of treatment
- IVF with antagonist protocol, GnRh analouge trigger, elective freezing and frozen embryo transfer should be considered to reduce chances of OHSS during IVF.

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Non Invasive Prenatal Test (NIPT): Current status

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Introduction

Fetal genetic and chromosomal aberrations are quite common and approximately 1 in 150 live births is afflicted with some form of chromosomal abnormality which can cause abnormal phenotypes in the fetus. 60% of occult spontaneous abortions are secondary to chromosomal aberrations; also, cytogenetic abnormalities are responsible for approximately half of the recognized first trimester abortions and approximately 5 % of still births. These chromosomal abnormalities include alterations in number or function, with aneuploidy being the most common abnormality in number of chromosomes secondary to either an extra or a missing chromosome. Among aneuploidies, trisomy 21 (T 21) accounts for >50% of cases, trisomy 18 (T 18) for about 15% cases, and trisomy 13 (T 13) for about 5% cases. Early detection of aneuploidies during pregnancy can have an overwhelming social as well as economic impact on the family. Thus, screening for aneuploidies has become an integral part of obstetric care. Screening identifies high risk population who will benefit from prenatal invasive procedures which are required for diagnosis.

Non-invasive prenatal screening that uses cell-free DNA from the plasma of pregnant women offers incredible possibility as a screening method for fetal aneuploidy.

Goals of NIPT

The goals of performing NIPT include:

- Offer a non-invasive test which is easily available to all pregnant women
- Reduce the risk of miscarriage associated with invasive procedures
- Enable a high detection rate
- Reduce the number of false positive results, hence invasive procedures

Technical Basis of NIPT

NIPT is a relatively new method of prenatal screening to detect aneuploidy using cell free fetal DNA (cff DNA) in maternal blood. Cff DNA originates from the placenta resulting from the apoptosis of the syncytiotrophoblasts and is released as small DNA fragments of 150-200 bp. It can be detected as early as 7 weeks of gestation and increases in conditions of abnormal placentation. It is not detectable within hours postpartum.

Types of Methodology used for NIPT

Next generation sequencing is used with bioinformatic algorithms to determine the probability of certain fetal chromosomal conditions in pregnancy. There are three commonly used methods for performing the tests and each tests has its own advantages and disadvantages. The methods for performing the tests are and describe below:

1. Whole Genome Sequencing
2. Targeted Sequencing
3. Single Nucleotide Pleomorphism (SNP) based tests

Whole Genome Sequencing (Massive parallel sequencing):

In this test, the whole fetal DNA is sequenced in short reads and referenced in comparison to a standard human genomic database such that every sequence can be matched to a specific chromosome. It is important to know that it detects the amount of fetal DNA of a particular sequence which is less or more in a particular fetus and not the change in sequencing. Also, this method of massive parallel sequencing essentially sequences the total amount of DNA in the plasma and does not differentiate maternal DNA from the fetal DNA. Inconsistent amplification is another limitation of this method. The methodology is depicted in Figure 1.

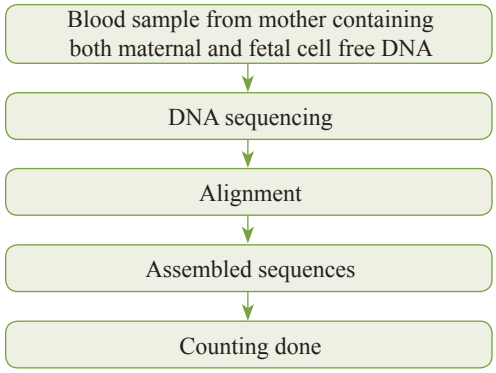

Figure 1: Methodology for massive parallel sequencing.

Targeted sequencing:

With the advancement in technology, the method of targeted sequencing was evolved. In this method, rather than total amount of DNA, the sequences are localized to chromosome of origin, and counted to detect extra sequences.This method is more cost effective. The methodology of targeted sequencing is depicted in Figure 2.

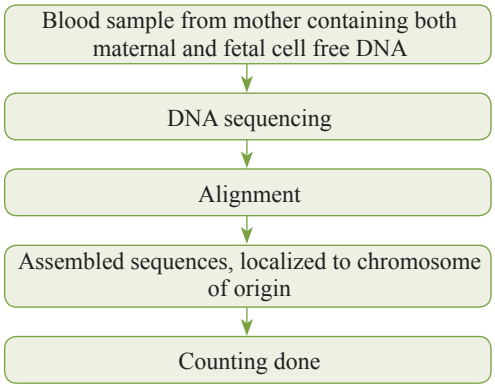

Figure 2: Methodology of Targeted Sequencing

Single Nucleotide Pleomorphism (SNP) based tests:

SNPs occur in 1/300 base pairs and are very specific parts of DNA which are unique to each individual. Using SNP sequencing, the maternal genotype can be determined and the fetal genotype can be deduced by comparing with the combination of maternal and fetalcfDNA sequences.This method is not possible in egg-donation, surrogacy, consanguinity, maternal transplant samples. However, it can be used as the method of choice in cases of vanishing twins. The methodology of SNP based test is depicted in Figure 3.

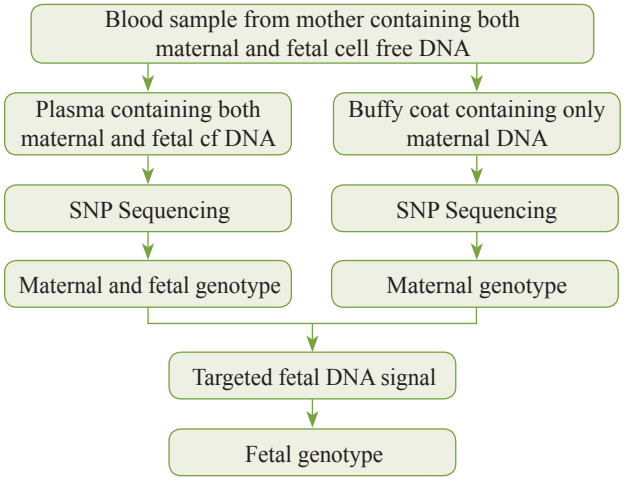

Figure 3: Methodology of SNP based test

Performance of NIPT:

NIPT has been globally adopted in clinical practice due to it improved accuracy and detection rates. The performance of the test for detection of various aneuploidies, comparison with other screening protocol and comparison with diagnostic tests are depicted below in Table 1, 2 and 3 respectively.

Table 1: Performance of NIPT for detection of aneuploidy

	Detection Rate (DR) (%)	False positive rate (FPR) (%)
T 21	**99.2**	**0.09**
T 18	**96.3**	**0.13**
T 13	**91.0**	**0.13**
Monosomy X	**90.3**	**0.23**

Table 2: Comparison of Performance of NIPT for aneuploidy with other screening protocol of first trimester

Test	DR for T 21 (%)	DR for all aneuploidies (%)
First trimester screen	80	69
NIPT	99	72

Table 3: Comparison of Performance of NIPT for aneuploidy with diagnostic tests

Test	DR for T 21 (%)	DR for all aneuploidies (%)
NIPT	99	72
Invasive procedure (CVS/ Amniocentesis)	>99	>99

Counselling before using NIPT:

As for any screening test, patients should be appropriately counselled before offering NIPT. The following points should be explained in detail to the patients:

- This test does not screen for all aneuploidies and genetic syndrome
- This test cannot distinguish full trisomy from that from unbalanced translocation.
- The test also has false positives and false negatives results like any other screening test.
- This test should not be done with any structural anomaly or raised NT, as various chromosomal aberrations such as unbalanced translocations, deletions, and duplications may not be identified by NIPT.
- As it is a screening test only, no obstetrical decision should be based alone on NIPT results without confirmatory results from invasive tests.
- After a normal report, a routine anomaly ultrasound is still a must
- Performing NIPT does not preclude the requirement to perform a detailed 11-13+6 week ultrasound as a lot of additional information such as about dating, nuchal translucency and structural anomalies can be gathered by the ultrasound.

Clinical Implementation of NIPT and Current Status:

The current position of NIPT in screening algorithm is still a matter of debate as it can be used as a secondary screen or a contingent screen or as primary screen. American College of Obstetricians and Gynaecologists (ACOG) recommends that NIPT is most widely used for secondary screening in women at high risk for fetus with aneuploidy such as advanced maternal age (> 35 years at delivery), ultrasound features indicating a high risk of Trisomy, history of previous pregnancy with Trisomy, a positive biochemical screening test and a parental balanced Robertsonian translocation with increased risk of Trisomy 21 or Trisomy 13.The advantage of using it as a secondary screen is that it aims to reduce the number of invasive procedures.

NIPT is also widely used as a contingent screen in low risk population in which the initial screening is done by conventional methods (biochemical and ultrasound), followed by a risk stratification into high, intermediate or low risk.

It lacks universal endorsement as a primary screen due to cost constraints and it is not recommended for the same. Thus, the current position of NIPT in the aneuploidy screening algorithm is outlined in Figure 4.

Timing of the Test:

An adequate fetal fraction is required for interpreting the results. Even though the cffDNA can be detected as early as 7 weeks, but the test is optimally performed after 11 weeks in order to get an adequate fetal fraction for reporting.

Interpretation of Cell-free fetal DNA-based testing (NIPT):

The test result can be reported as low-risk or high-risk for aneuploidy; positive or negative; aneuploidy detected or not detected.

a. **Negative test/ low risk 1:10000:** Routine antenatal care offered

b. **Positive test/ high risk >99%:** Following counselling, invasive testing with CVS or amniocentesis is strongly recommended before considering termination of pregnancy.

c. **No result: (Results that are not reported, indeterminate, or uninterpretable):**

The options after no result report is either a redraw sample for NIPT or invasive testing. Counselling about both options should be offered. In case no result is obtained, the rate of aneuploidy can be as

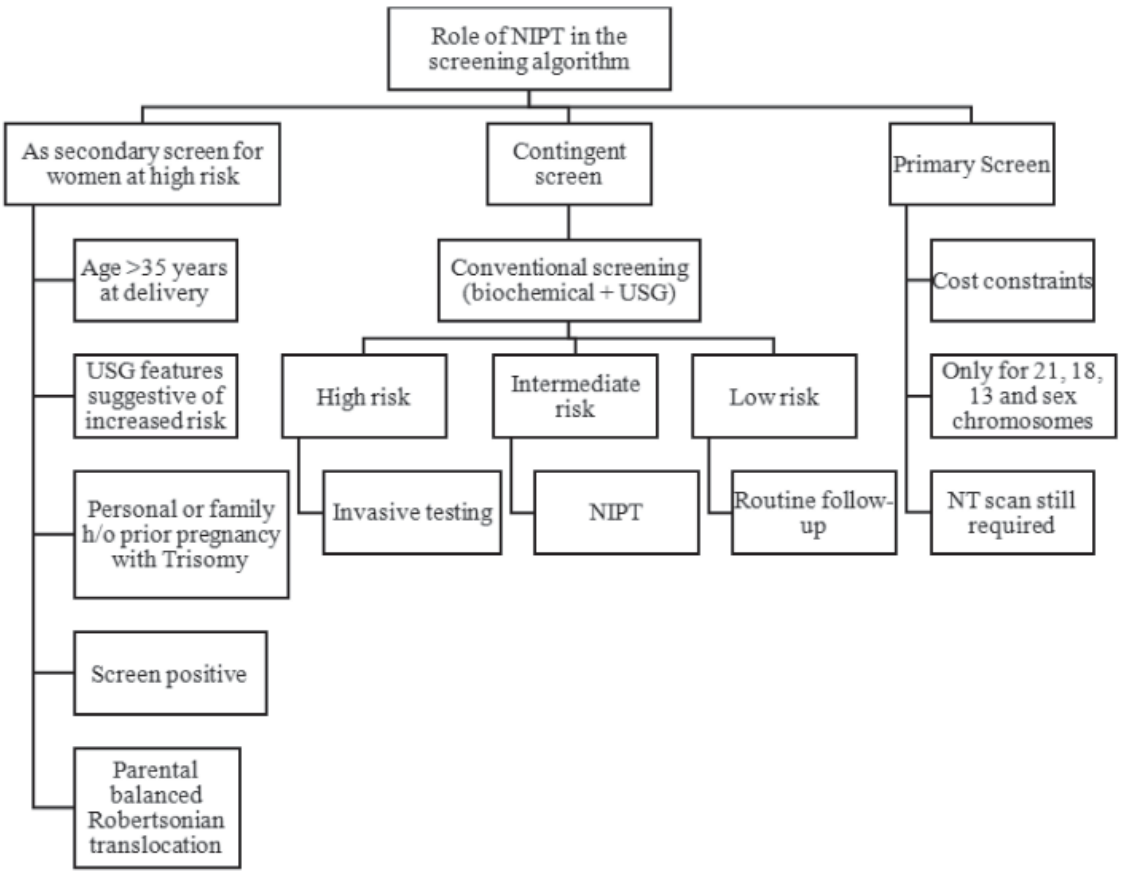

Figure 4: Role of NIPT in the Aneuploidy screening algorithm

high as 23% . Even though in such cases a repeat test can be done but it should be kept in mind the gestation age of the patient as repeat result may require 7-10 days, only 50-60% of repeat tests will provide a result and in case the result is positive it would further require invasive testing. Therefore, ACOG recommends counselling followed by detailed ultrasound evaluation and invasive testing with CVS or amniocentesis as the preferred option.

Factors affecting Performance of NIPT

Reasons for NIPT test failures

No result is considered a test failure and can be seen in 1-5% for autosomal trisomies and 4-7% for sex chromosome abnormalities based on technique being used. The most common reason for test failure is low fetalfraction (<4%) which in-turn could be due to early gestation age (< 10 weeks), obesity and fetalaneuploidy.

Reasons for imprecision in test results

The various reasons for false positive results are confined placental mosaicism, vanishing twin, maternal mosaicism,maternal cancer. The important reasons for falsenegative results could be placental mosaicism, borderline low fetal fraction or some technical problem.

Role of NIPT for other indications:

The use of NIPT for other indications is expanding. The other indications for performing NIPT can be:

1. Determination of fetal sex in women at risk of carrying fetuses with severe X-linked genetic disorders conditions like Duchenne Muscular Dystrophy.
2. Determination of fetal Rh-D status in Rh negative mother
3. Determination of a few selected microdeletion syndromes including Di George (22q), Wolf–Hirschhorn (4p-), Cri-du-Chat (5p-), Prader–Willi, Angelman and 1p36
4. Detection of the HPA-1a gene for detection of fetal or neonatal alloimmune thrombocytopenia (FNAIT)

Role of NIPT in twins

Preliminary data suggest that NIPT is a feasible test option for twin gestations. Due to the paucity of reported studies in multiple gestations, more studies are required before establishing it in practice.

Conclusion

Screening for aneuploidy is now an important part of routine obstetric care. One must understand carefully what various tests offer and goals of screening. The pregnant woman should be allowed to make an informed choice after appropriate counselling. NIPT offers a tremendous opportunity for screening for aneuploidy and it should be carefully selected in clinical practice.

Suggested Reading

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Journal Scan

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Outcomes of the first 50 patients with abnormally invasive placenta managed using the "Triple P Procedure" conservative surgical approach

Carrillo AP, Bhide A, Moore J, Hartopp R, Belli AM, Arulkumaran S, Thilaganathan B, Chandraharan E

Objective

To determine maternal outcomes for women with abnormally invasive placenta (AIP) managed using the Triple P Procedure and establish its safety as a conservative surgical management option.

Methods

A retrospective study of the outcomes of the first 50 patients who underwent the Triple P Procedure for AIP from September 2010 to May 2017 at St George's Maternity Unit. Maternity case notes and the database were reviewed to determine the volume of bleeding, procedure□related complications, hysterectomy rate, and postoperative hospitalization.

Results

Mean operative blood loss was 2318 mL (range, 400–7300 mL and the incidence of bladder and ureteric injuries was 2% (n=1) and 0%, respectively. Median length of hospital stay was 4 days (range, 2–8 days). Three women (6.0%) developed arterial thrombosis without any long term complications and none of the patients required peripartum hysterectomy.

Conclusion

The Triple P Procedure should be considered as a conservative, less risky alternative to a peripartum hysterectomy during counselling prior to surgery for women with AIP.

Comments

Abnormally invasive placenta (AIP), previously referred to as morbidly adherent placenta (MAP), is a rare but potentially life threatening condition. It is defined as the abnormal invasion of trophoblastic tissue beyond the decidua basalis into the myometrium, sometimes extending to the uterine serosa or even beyond it to infiltrate adjacent pelvic organs. It is classified depending on the degree of trophoblastic invasion into accreta (placenta invading the superficial myometrium), increta (invasion of the deeper myometrium), and percreta (the placenta perforates the uterine serosa and may infiltrate other pelvic organs)

The **Triple P procedure,** initially developed as a conservative surgical technique at St George's University Hospitals NHS Foundation is a three step surgical approach that includes perioperative localization of the placental edge and delivery of the fetus above the upper border of the placenta, pelvic devascularization, and placental nonseparation with myometrial excision and preserving about 2-cm margin of myometrium (even if there is some invading placental tissue) in the lower uterine lip to facilitate the repair of the myometrial defect.

"**Modified Triple P Procedure**" involved temporary clamping of the internal iliac arteries instead of insertion of occlusive balloon catheters and this modified procedure may be useful in centers with no access to interventional radiology.

The Triple P Procedure has been developed to minimize maternal morbidity and mortality associated with peripartum hysterectomy. It is recognized that there may be concerns surrounding the integrity of the uterine scar during a subsequent pregnancy after myometrial excision and uterine reconstruction. However, in 2017 the first case of pregnancy after the Triple P Procedure was reported with excellent maternal and perinatal outcomes. The Triple P Procedure may be considered for women who desire future pregnancies, after appropriate counseling on the possible risks of recurrence and complications, including uterine scar rupture.

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Archives of Gynecology and Obstetrics

A new approach to avoid ovarian failure as well function impairing adhesion formation in endometrioma infertility surgery

Torres LA, Roche DL, Devassy R, Wilde MS, Cezar C, Krentel H, Korell M, Wilde RL

Introduction

Deep ovarian endometriosis surgery is likely to be associated with diffuse bleeding, intraoperative ovarian tissue destruction and perioperative adhesion formation. A new surgical approach is hereby proposed to avoid the negative short-term impact of classic laparoscopic cystectomy on ovarian reserve.

Methodology

This is a preliminary observation of 10 cases which were followed by a second look laparoscopy, which was performed within the next 12–24 weeks of first surgery as part of their routinely endometrioma 3-step treatment.

Results

The need for intraoperative periovarian coagulation after endometrioma excision was avoided by combining the gold standard minimal-access endometrioma stripping technique with a purely plant-based medical product with high-hemostatic and antiadhesion barrier properties.

Conclusion

Endometrioma stripping followed by the application of a polysaccharide agent could avoid ovarian failure and at same time could reduce adhesion formation, thereby preserving tubo-ovarian function in endometrioma surgery. We encourage other surgically working groups to investigate middle- and long-term effects of this combined technique.

Comments

As a standard minimal access technique, the endometrioma is stripped out following an ante-mesenterial incision of the ovarian capsule, which usually leads to active bleeding of the stromal vessels requiring coagulation or suturing. Consequently, important ovarian tissue destruction could occur, affecting the oocyte function.

A new surgical approach is hereby proposed in this study to avoid the negative short-term impact of classic laparoscopic cystectomy on ovarian reserve during endometrioma surgery, especially in women of child-bearing age. Instead of drainage and electro coagulation of the endometrioma wall, the ante-mesenterial incision is kept opened with forceps and, afterwards, the entire endometrioma wound, the ventral surface and visceral fossa of the ovary are covered with the modified polysaccharide powder until complete hemostasis is achieved. For adhesion prevention, the coagulum and remaining white power are dripped with saline solution until obtaining a gel layer.

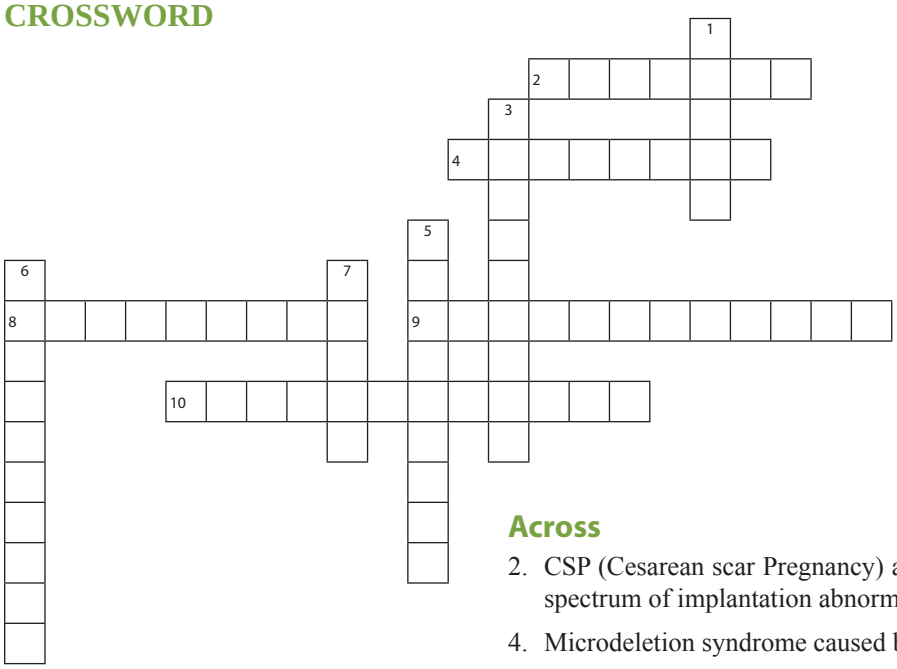
Routinely, during the whole of the surgery, no coagulative energy power is applied; only in case of a persistently oozing vessel, a punctual bipolar coagulation can become necessary. Irrespectively of endometrioma size, the modified polysaccharide powder was capable of achieving fast hemostasis of the diffuse bleeding, avoiding coagulation power after endometrioma stripping with a rapid formation of the antiadhesion gel layer.

In this study of 10 cases, 85% of patients had without or with a minor ovarian adhesion at a second look laparoscopy. Therefore, this study hypothesizes that this new approach could avoid unnecessary ovarian tissue destruction and preserve postoperative function of the tubo-ovarian unit, during and after endometrioma surgery.

The Maze of Knowledge

Kusum Lata
Assistant Professor, Department of Obstetrics & Gynaecology, All India Institute of Medical Sciences, New Delhi

CROSSWORD



Down

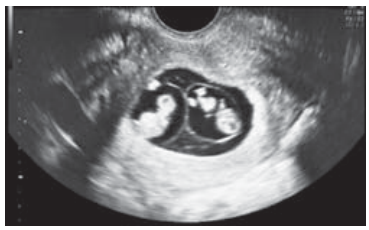
1. How many degrees of movements are possible in Robotics
3. Highest adverse effects in antenatal period are seen with this antiepileptic drug
5. Criteria for diagnosis of PCOS is
6. Poor neonatal adaptation syndrome is caused by
7. Puerperal psychosis usually develops with in …… days

Across

2. CSP (Cesarean scar Pregnancy) and……. are on a continuum spectrum of implantation abnormalities
4. Microdeletion syndrome caused by 11q23 deletion
8. This drug is used for OVI in PCOS
9. Free fetal DNA originates mainly from
10. Early recourse to……. is recommended for Placenta accreta

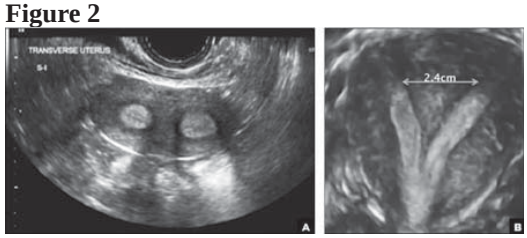
Pictorial Quiz

Figure 1



Q1. Give a diagnosis for the following image ?

Figure 2



Q2. Multiple miscarriages in a 29-year-old woman: Which type of Müllerian duct anomaly best fits the image below?

Refer page 41 for previous answer key.

Watsapp your answers to **9211656757.**
Names of first three correct entries will be mentioned in the next issue

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