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EDITORIAL

Intriguing Review and Topics in Fifth Issue of Thai Journal of Obstetrics and Gynaecology 2025

Vorapong Phupong, M.D., FRTCOG.*

** Editor in Chief, Thai J Obstet Gynaecol, The Royal Thai College of Obstetricians and Gynaecologists*

This fifth issue of Thai Journal of Obstetrics and Gynaecology 2025 contains many interesting articles. The special article is "Virtual fetal autopsy". The author reviewed postmortem imaging options including magnetic resonance imaging, ultrasound, computed tomography, microfocus computed tomography, and X-ray examination[1].

This issue also contains six original articles and one case report. Thirathanaboon performed a randomized controlled trial to compare the effect of weekly, three times per week, and daily iron supplementation on the hemoglobin and hematocrit levels in pregnant women and found a statistically significant decrease in hematocrit levels among all groups in the third trimester, with 28.57%, 14.28%, and 39.28% of participants in the daily iron supplement, thrice weekly iron supplement, and weekly iron supplement groups, respectively[2].

Ittipuripat et al performed a retrospective cohort study to investigate the association between meconium-stained amniotic fluid (MSAF) and obstetric perineal wound infections, and other puerperal infections. They found MSAF was not associated with an increased risk of obstetric perineal wound infection, and other puerperal infections[3].

Lersbuasin et al performed a cross-sectional study to evaluate the correlation of postvoid residual (PVR) measurement in pelvic organ prolapse patients by transabdominal sonography (TAS) and urinary catheterization. They found a high positive correlation of the PVR assessment by TAS and PVR assessment by urinary catheterization in pelvic organ prolapse patients[4].

Lertpongsaporn et al performed a randomized clinical trial to compare the knowledge of pertussis and influenza vaccines between pregnant women who received vaccine-related information through educational video and those who did not. They found pregnant women's knowledge score in the video group were significantly higher than those in the control group[5].

Tientong et al performed a retrospectively study examined the predictive value of preoperative body mass index (BMI) for progression-free survival (PFS) and overall survival (OS) of endometrial cancer (EC) patients, as well as the correlation between BMI and surgical outcomes. They found preoperative BMI affects surgical care and results. BMI did not affect PFS, however, it may preserve OS in EC patients[6].

Suntorn performed a randomized controlled trial to evaluate the effectiveness of telemedicine in managing and controlling gestational diabetes mellitus (GDM) among pregnant women. The result showed that telemedicine could be effective in helping pregnant women with GDM control their blood sugar levels without adverse effects on neonatal outcomes[7].

Regarding case report, Tapanwong reported three rare cases of spontaneous uterine perforation presenting with acute abdominal pain[8].

The RTCOG 40th annual meeting will be held during 28 - 31 October 2025 at Dusit Thani, Pattaya, Chonburi, Thailand. The theme of the meeting is "Next Gen & Next Trend in OB-GYN". Wish to see you at RTCOG Annual Meeting 2025 at Dusit Thani, Pattaya, Chonburi, Thailand

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SPECIAL ARTICLE

Virtual Fetal Autopsy

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ABSTRACT

Determining the cause of stillbirth is crucial for understanding preventable factors and managing future pregnancies. Currently, many parents decline conventional autopsy due to its invasive nature. To address this, less invasive autopsy methods based on imaging technology have been introduced as more accessible and acceptable options for parents. In addition to radiographs, other traditional clinical imaging techniques such as magnetic resonance imaging (MRI), ultrasound, and computed tomography have been used in postmortem investigations, especially for fetuses over 20 weeks of gestation. Advanced techniques like high-field MRI and micro-focus computed tomography have demonstrated higher diagnostic accuracy, though they remain limited by accessibility. This article aims to provide a perspective on "virtual fetal autopsy" from a pathologist's point of view to enhance obstetricians' understanding.

Keywords: fetal autopsy, virtual autopsy, postmortem, ultrasound, MRI, CT scan, micro-CT, radiographs.

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Stillbirth is a serious pregnancy complication and can be very traumatizing for any family. For obstetricians, identifying the cause of stillbirth is crucial to understanding preventable factors and managing future pregnancies. Typically, the evaluation of stillbirth includes a clinical history, perinatal autopsy, placental examination, and genetic testing[1]. Conventional autopsy is considered the gold standard because it can reveal more information through histological findings that cannot be seen with structural examination alone. However, some families find conventional autopsy invasive because they worry about body disfigurement and the removal of tissue needed for further analysis, which can reduce consent rates. In cases of stillbirth with severe maceration, a thorough evaluation via conventional autopsy is often not possible, especially for the fetal brain, which is delicate and tends to break during skull opening. The

very small fetus also poses problems for conventional autopsy, even when performed under direct microscopy. Additionally, the accuracy of findings from a conventional autopsy depends heavily on the skill of the pathologist examining it, which can typically be done only once and is often limited to documentation via photographs or videos. Conversely, imaging data from other methods can be stored and reviewed multiple times as needed, including for consultation with experts. It can also be viewed from different angles and used to create 3-dimensional structures for further analysis.

Noninvasive perinatal virtual autopsy using imaging techniques was introduced to address the limitations of conventional autopsy. Since the primary purpose of a traditional autopsy is to visually examine organs, any imaging method that provides a clear view of internal organs can serve as an alternative procedure. Postmortem imaging options include magnetic resonance imaging (MRI), ultrasound (US), computed tomography (CT), microfocus computed tomography (micro-CT), and X-ray examination[2-5].

Postmortem magnetic resonance imaging (MRI)

Postmortem MRI has been used since 1990[6] and is very popular in developed countries because it provides the clearest images compared to other imaging techniques[2]. The procedure should be performed as soon as possible for the best image quality[7]. The magnets commonly used in routine virtual autopsy are 1.5-Tesla (T) and 3-T, but the error rate is lower with 3-T magnets, especially in very small fetuses. Ultra-high magnetic field MRI with a strength of 7-T and higher has also been studied to produce detailed images of fetal anatomy, but it is mainly used for research due to instrument limitations and long scan times[8-11].

The cutoff for performing postmortem MRI varies depending on the type of MRI and techniques used. In earlier studies of 1.5-T MRI, a cutoff of 500 grams or 20 weeks of gestational age was suggested. Today, with advanced techniques and increased availability of 3-T MRI, it can be performed on early second-trimester fetuses with a weight of 300 grams. For very small fetuses, the image signal can be enhanced by placing the fetus in a saline bag or a 60 ml syringe filled with saline[12].

There are various protocols for the examination. If an MRI cannot be performed immediately after delivery, the fetus should be stored in a refrigerator at 4°C until the procedure, for up to 6 days. The fetus should be placed supine in an anatomically neutral position. The coil used must be adapted to the body size and as small as possible. Typically, a head coil is used for the brain and spine, while a body coil is used for overall body imaging[7]. T2 sequences are generally preferred because they provide better tissue contrast than T1 sequences. However, T1 and T2 signals in a deceased fetus may change due to cell death, maceration, decreased temperature, and preservation methods, which can lead to misinterpretation as pathological conditions[13]. T1 images generally have poor contrast and low signal, although high T1 signals are observed in the thyroid and bowel, related to meconium content[14].

Interpreting postmortem MRI is also difficult and can be misinterpreted due to autolytic changes. After fetal death, fluid buildup may occur, causing subcutaneous edema, pleural or pericardial effusion, and ascites. For heart imaging, it is common to see small pericardial effusions, intracardiac air, blood clots, and fluid–fluid levels in the heart and major vessels. The cardiac ventricles may appear thickened after death, which can be mistaken for ventricular hypertrophy[15]. Increased gas in the hepatobiliary system, distended bowel loops, and enlarged appearance of the normal fetal liver may be normal postmortem changes[16]. Skull deformities; brain ischemia indicated by edema, loss of gray-white matter differentiation, and low T2 signal in the basal ganglia; tonsillar descent; and small intraventricular hemorrhages without dilation can also be seen as postmortem changes[17].

The overall diagnostic accuracy of postmortem MRI ranges from 77% to 94%, depending on factors

such as protocol, gestational age, birth weight, organ system abnormalities, the reason for fetal death (if known), circumstances of death (pharmaceutical termination of pregnancy with or without feticide, spontaneous death, live birth, or stillbirth), organ system malformations, and the interval between death and MRI[15, 18-20]. When combined with ancillary investigations, such as placental examination and postmortem blood sampling, postmortem MRI can identify the cause of fetal death or major pathological abnormalities as effectively as conventional autopsy, with an accuracy of up to 89%[21]. The concordance rate improves with higher gestational age, especially in fetuses over 24 weeks' of gestation, reaching 95.7%. In the case of organ systems, postmortem MRI shows high diagnostic accuracy in the neurological, cardiovascular, pulmonary, and renal systems. Cerebral postmortem MRI has 87.5% sensitivity and 74.1% specificity for detecting overall brain pathology, and 88.4% sensitivity with 95.2% specificity for cerebral malformations. The detection of major intracranial bleeding achieved 100% sensitivity and 99.1% specificity[22]. The overall sensitivity of 3-T postmortem MRI for diagnosing fetal congenital heart disease is 78.2%, with a specificity of 85.4%[19]. The accuracy is notably lower in fetuses under 20 weeks and those with a birth weight below 100 grams. For non-cardiac thoracic abnormalities, postmortem MRI is highly sensitive in detecting pleural effusions (100% sensitivity) and lung or thoracic hypoplasia (60% sensitivity), but less effective for pulmonary infections and hemorrhages (12.5% and 33.3% sensitivity, respectively)[15]. Regarding abdominal abnormalities, postmortem MRI demonstrates 72.5% sensitivity and 90.8% specificity for overall abdominal pathology[18]. It performs well in identifying renal abnormalities (80% sensitivity and 98.6% specificity) and splenic abnormalities (100% sensitivity and 99.6% specificity), though its accuracy remains low (sensitivity of 50-55%) for the intestinal, liver, and adrenal gland.

Besides several advantages of postmortem MRI, there are some limitations, such as limited accessibility to MRI, the time-consuming procedures (around 60 minutes), the lack of trained radiographers to perform the procedure, especially for deceased fetuses, and the shortage of trained pediatric radiologists, particularly for postmortem MRI. The last point is very important because, beyond MRI technique skills, they must also have a good understanding of fetal anatomy, including congenital anomalies, which is significantly different from general MRI.

Postmortem ultrasound (US)

Compared to MRI and CT scans, ultrasound is much cheaper and more accessible, especially in developing countries. The procedure is straightforward: placing the fetus in a supine position inside a small tub and completely covering it with a 2 cm layer of water. The ultrasound probe is partially submerged in the water, making direct contact with the fetus[23].

The overall sensitivity ranges from 67% to 77%, and the specificity ranges from 74% to 90%[24, 25] Diagnostic accuracy is notably high in neurological abnormalities (84.3% sensitivity and 96.7% specificity) and abdominal abnormalities (78.4% sensitivity and 97.3% specificity), while lower in cardiothoracic abnormalities (52.1% sensitivity and 96.6% specificity[26]. This is because the brain and abdominal organs, especially the kidneys, are easier to assess. In contrast, many postmortem artifacts occur in the heart, leading to potential misdiagnoses. Longer intrauterine retention times increase autolytic changes, making it difficult to distinguish soft tissue planes. Postmortem intracardiac blood clots have echogenicities very similar to the myocardium. Air in the cardiac chambers is common in cases of fetal intracardiac injections used for pregnancy termination[27]. For fetuses after 20 weeks of gestation, postmortem ultrasound can clearly detect major anomalies in the four-chamber view, but it is much less effective in visualizing the great vessels[24]. When comparing postmortem 1.5-T MRI and ultrasound for non-invasive perinatal autopsy, ultrasound matched the MRI diagnosis in 86.8% of cases, with the highest agreement for spine (99.3%) and cardiac findings

(97.3%), while brain concordance was lower at 85.2%[27].

It appears that postmortem US is appropriate for assessing the fetal brain and abdomen, but it has limited diagnostic value for the fetal cardiovascular system. The main limitation is that the performance of postmortem US depends on the operator and requires specialized skills. Ideally, the sonographer should be a specialist in fetal medicine with extensive knowledge of fetal normal and abnormal anatomy.

Postmortem computed tomography (CT) Scan

Postmortem CT scans are more widely available, less expensive, and quicker to perform than MRI. However, the overall rate of concordance with conventional autopsy is only 38.1% in fetuses less than 24 weeks of gestation and 71.4% in fetuses greater than 24 weeks, with sensitivities of 27.8% and 50%, respectively[29]. Based on the body system, the sensitivity is highest in the musculoskeletal system (66.7%), and relatively low in the other systems. Compared to postmortem MRI, CT scans without contrast have a low success rate in examining the brain and thoracoabdominal organs. To improve the diagnostic accuracy of CT scans for identifying congenital cardiac malformations, CT angiography can be performed using contrast injection either through the umbilical cord or directly into the heart under ultrasound guidance. Direct injection into the heart achieved a 96% success rate in demonstrating major abnormalities of the four-chamber view and the great vessels[30].

A postmortem CT scan of a small fetus shows limited results due to the small size of the specimen and poor soft tissue contrast. Although postmortem CT is considered a very effective diagnostic tool for musculoskeletal abnormalities, another limitation to consider is limited ossification during early gestation.

Postmortem microfocus computed tomography (micro-CT)

Micro-CT is an X-ray-based technology similar to conventional CT, but instead of a rotating gantry, micro-CT scanners feature a fixed radiation source while samples are mounted on a rotating platform. Radiation source-to-sample distance and the sample-to-detector distance can be adjusted to achieve much higher resolutions, up to sub-micron (<μm) levels. Compared to conventional CT, micro-CT typically involves longer scan times and higher radiation doses[31]. Staining is only required when the researcher aims to study soft tissue. Without staining, micro-CT provides excellent spatial resolution for high-density structures (e.g., orbit, humerus, femur), even if these structures are not fully ossified yet[32].

For better visualization of soft tissue, staining is necessary before scanning. The fetus must be submerged in a staining solution[33]. The most commonly used staining solution is Lugol's solution, which is a water-based mixture containing two parts potassium iodide (KI) for every one part iodine (I2) or potassium triiodide (I2KI). This solution is preferred because it penetrates quickly and deeply, provides excellent contrast in all tissues, is non-toxic, and is relatively inexpensive[34]. However, the effectiveness of staining depends on fetal size, the concentration of the staining solution, and the duration of staining. As gestational age increases, fetal skin becomes less permeable to iodine, requiring longer incubation times. Higher concentrations can reduce staining time but may cause overstaining and loss of tissue differentiation. Since staining time correlates with diffusion speed, it takes longer in larger fetuses, ranging from hours to several weeks. For fetuses under 20 weeks of gestation, adequate staining usually takes between 3 and 10 days. Additionally, Lugol's solution may cause tissue shrinkage of up to 30%, which can be prevented by using buffer-prepared Lugol's solution (B-Lugol)[35].

The postmortem whole-body fetal micro-CT has high diagnostic accuracy in fetuses under 22 weeks of gestation, with 93.8% sensitivity and 100% specificity[36]. The performance of micro-CT can even be applied to embryos, which is an important advantage over conventional autopsy.

The limitation of postmortem micro-CT is dealing with large-sized fetuses (more than 20 weeks of gestation) that have sufficient iodine staining, as well as figuring out how to properly immobilize the fetal body during scanning. Since micro-CT scanners use fixed radiation sources and the specimen must be mounted vertically on an adjustable rotating platform, even though the fetus has been previously fixed in formalin, the fetal body's vertical axis can still collapse during the 20- to 30-minute scanning period[2].

The immersion of the fetus in iodine contrast can cause brown discoloration of the skin. Although there are techniques to reverse the staining, such as additional immersion in a sodium thiosulfate solution, this process requires an extra 1-2 days, which may be distressing for the parents. Additionally, this reversal may not be entirely effective[31]. These concerns should be discussed and the doctor should seek additional consent from the family before proceeding with the procedure.

Radiograph (X-ray examination)

A whole-body radiograph of the fetus, known as a babygram or skeletal survey, is usually performed in some centers as part of the routine examination of stillbirths. The main goal is to provide a general overview of fetal skeletal maturity, estimate gestational age, and diagnose genetic bone disorders. However, routine postmortem fetal radiography has been reported to be neither cost-effective nor enhances diagnostic value, except in specific cases of prenatally suspected skeletal abnormalities[37, 38]. It should only be done when a pathologist determines that it is necessary after external examinations.

A summary of postmortem imaging modalities is shown in Table 1.

Table 1. 1 Postmortem imaging modalities[39].

	Radiographs	Ultrasound	CT	MRI (3-T or 1.5-T)	Micro-CT	High-field MRI (7-T or more)
Availability	Easily available	Easily available	Easily available	Moderate	Limited	Limited
Cost	Cheap	Cheap	Moderate	Expensive	Same cost as CT scanner	Very expensive
Size of fetus	Any size	Any size	Any size	Better for larger fetuses (weight >300 or 500 g)	Small fetuses (<20 weeks of gestation) Up to 30 cm in length	Similar to micro-CT
Advantages	Easy to perform	Facilitates image-guided biopsies	High accuracy for musculoskeletal abnormalities	Multiple sequences, multiplanar reconstructions	Excellent resolution and soft tissue detail	Excellent resolution and soft tissue detail
Limitation	No internal soft tissue detail	• Operator dependent • Maceration may affect image quality	• Poor diagnostic accuracy • Poor soft tissue detail due to a lack of internal body fat	Poorer resolution in smaller fetuses	• Iodine contrast is required for soft tissue detail, which can cause tissue discoloration • Longer period of turnaround time due to pre-imaging staining process and removal	Long scanning times (hours)
Indication:	Consider musculoskeletal abnormalities	Assessment of soft tissue and internal organ detail	Consider musculoskeletal abnormalities	Assessment of soft tissue and internal organ detail	Small fetuses (<20 weeks gestation) where ultrasound and 1.5-T/3-T MRI non-diagnostic	Currently research tool only

Additional tissue sampling

There are four main types of postmortem investigation methods: conventional autopsy, less invasive autopsy (LIA), non-invasive autopsy (NIA), and minimally invasive autopsy (MIA) (Table 2)[40, 41].

Table 2. 1 Types of postmortem investigation methods[40, 41].

Term	Components	Placental examination	Histology	Genetics
Conventional autopsy or invasive autopsy	Review of the clinical history, external examination with photographs, and internal macroscopic examination	Yes	Yes, all target organs	Tissue samples from target organs for genetic testing
Less invasive autopsy (LIA) or virtopsy	Any autopsy procedure (including imaging) that is performed with smaller, less, or no incisions than conventional autopsy	Yes	Yes, most organs with focal biopsy via MIA approach	Tissue samples from target organs for genetic testing
Non-invasive autopsy (NIA) or imaging-only autopsy	External examination with postmortem cross-sectional imaging and ancillary testing	Yes	No	No
Minimally invasive autopsy (MIA)	Combination of imaging investigations and laparoscopic or image-guided needle-biopsy approach	Yes	Yes, most organs with focal biopsy	Tissue samples from target organs for genetic testing
MinImAL procedure (Minimally Invasive Autopsy with Laparoscopic-assisted sampling)	A type of MIA, using laparoscopic-assisted methods to visualize internal organs and acquire organ tissue sampling A single small incision (1 cm) at the left upper quadrant of the abdomen or epigastric region	Yes	Yes, most organs with focal biopsy	Tissue samples from target organs for genetic testing
INTACT procedure (INcision-less TArgeted Core Tissue)	A type of MIA, involving ultrasound-guided organ biopsies of fetuses via the umbilicus	Yes	Yes, most organs with focal biopsy	Tissue samples from target organs for genetic testing

In a traditional autopsy, which is considered the gold standard and involves routine tissue sampling from internal organs, the question arises whether this sampling should also be performed in virtual autopsy. Evidence shows that histological tissue can determine the cause of perinatal death in less than 1% of cases where death is unexplained after placental, clinical, or imaging examinations[42]. This suggests that when postmortem imaging shows no abnormalities, microscopic tissue sampling is unlikely to be beneficial. Centers with access to postmortem imaging may use it to guide the autopsy process. Conventional autopsy should be reserved only for cases where postmortem imaging uncovers unexpected abnormalities, non-diagnostic findings, or findings discordant with antenatal imaging[41].

If tissue sampling is necessary, whether for histology, additional genetics, or molecular studies, minimally invasive procedures with image guidance are currently recommended. Blind percutaneous

needle biopsies are not preferred due to their relatively low success rates in obtaining the targeted tissue, especially in deeply located organs that are small in size, such as the spleen, pancreas, kidney, adrenal glands, and heart[43]. Ultrasound-guided biopsies have a higher overall success rate (76.1%), with the highest success rates for the heart (93%) and lungs (91%) by individual organs, while the lowest success rate is for the spleen (11%)[44]. The biopsy can be performed via the umbilical vein, avoiding any body incisions (known as the 'INTACT' biopsy procedure). Laparoscopically guided tissue sampling (referred to as the "MinImAL" procedure) achieves the highest success rate in obtaining adequate histological samples in most major organs, such as 100% in the heart, lung, and kidney; 96.7% in the liver; 94.5% in the spleen; 89% in the adrenal glands; and 82.4% in the pancreas[43]. However, there are many limitations, including difficulty performing the procedure in small fetuses, the high costs of laparoscopic equipment, and the need for a specially trained operator.

Conclusion

Postmortem imaging has become a useful alternative to traditional autopsy. MRI appears to be the best in terms of image quality, but it is limited in availability, expensive, and not suitable for small fetuses. Postmortem ultrasound is helpful when MRI is not accessible, but it faces limitations with severe maceration and still requires further development of training programs. Radiographs and CT scans offer limited benefits in cases of suspected musculoskeletal issues. Micro-CT is a new postmortem imaging technique for small fetuses that provides excellent image quality, but it requires pre-scanning iodine staining and removal, which delays results and is not feasible for larger fetuses. Availability is also restricted, similar to high-field MRI, which is mainly used for research.

Although there are many limitations to noninvasive perinatal virtual autopsy by imaging technique, we are now in a new era of developing technology. It may be time to move from traditional invasive autopsy, which is gradually declining among parents, to these new postmortem investigative methods.

Potential conflicts of interest

The authors declare no competing interests.

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OBSTETRICS

A Comparative Study of the Efficacy of Daily and Intermittent Iron Supplementation in Pregnant Women: A randomized controlled trial

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ABSTRACT

Objectives: This study aimed to compare the effect of weekly, three times per week, and daily iron supplementation on the hemoglobin and hematocrit levels in pregnant women. A secondary objective included assessing urine iodine levels in conjunction with the adverse effects associated with the use of iron supplements in various formulations.

Materials and Methods: A randomized controlled trial was conducted using 84 pregnant women receiving antenatal care at Somdejprasangkharach 17th Hospital. Participants were randomly divided into three groups: group 1 was daily iron supplement (DIS), received one tablet of triferdine daily; group 2 was thrice weekly iron supplement (TIS), received one tablet of triferdine every other day; group 3 was weekly iron supplement (WIS), received one tablet of triferdine, ferrous fumarate, and ½ tab of folic acid once a week. To determine the efficacy, venous blood samples were collected for complete blood count and iron studies at the initial presentation and at 32–36 weeks of gestation. Any adverse effects of medication, such as abdominal pain, nausea, and vomiting, were monitored using questionnaires every 4 weeks. Medication adherence was also assessed, and participants were asked to bring their medication to each hospital visit for pill counting.

Results: The study found a statistically significant decrease in hematocrit levels among all groups in the third trimester, with 28.57%, 14.28%, and 39.28% of participants in the DIS, TIS, and WIS groups, respectively, meeting the criteria for iron deficiency anemia in the third trimester. The study found no statistically significant differences between the groups ($p = 0.064$). However, ferritin levels decreased significantly and differently between the groups ($p = 0.033$), with the lowest values observed in the WIS group. The prevalence of low serum ferritin was 46.4%, 64.3%, and 71.4% in the DIS, TIS, and WIS groups, respectively. There were no significant differences in side effects among groups.

Conclusion: The results of this study indicated a reduction in hematocrit levels across all study groups throughout the third trimester. Although comparisons between groups revealed no significant differences in hematocrit and hemoglobin level, the WIS group had the highest incidence of iron deficiency anemia. Based on the study results, we concluded that the TIS group demonstrated the highest efficacy in preventing iron deficiency anemia during pregnancy

Keywords: iron supplement, pregnancy, iron deficiency anemia, antenatal care, hemoglobin.

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การศึกษาเปรียบเทียบประสิทธิภาพของการเสริมธาตุเหล็กแบบทุกวันและแบบเป็นระยะในหญิงตั้งครรภ์: การทดลองแบบสุ่มที่มีกลุ่มควบคุม

พรศักดิ์ ถิรธนบูรณ์

บทคัดย่อ

วัตถุประสงค์: *เพื่อเปรียบเทียบผลของการให้ยาเสริมธาตุเหล็กแบบให้สัปดาห์ละครั้ง แบบให้ 3 ครั้งต่อสัปดาห์ และแบบให้ทุกวันต่อระดับฮีโมโกลบินและระดับฮีมาโตคริตในสตรีตั้งครรภ์ และมีวัตถุประสงค์รองเพื่อศึกษาปริมาณไอโอดีนในปัสสาวะและอาการไม่พึงประสงค์ของการให้ยาแต่ละแบบ*

วัสดุและวิธีการ: *เป็นการศึกษาทดลองแบบสุ่มที่มีกลุ่มควบคุม ในผู้หญิงตั้งครรภ์ที่มาเข้ารับการฝากครรภ์ที่โรงพยาบาลสมเด็จพระสังฆราชองค์ที่ 17 จำนวน 84 ราย โดยอาสาสมัครถูกแบ่งออกเป็น 3 กลุ่มแบบสุ่ม ได้แก่ กลุ่มที่ได้รับยากลุ่มที่ 1 daily iron supplement (DIS) ได้รับ triferdine รับประทานวันละ 1 เม็ด กลุ่มที่ 2 thrice weekly iron supplement (TIS) ได้รับ triferdine รับประทาน 1 เม็ด วันเว้นวัน และกลุ่มที่ 3 weekly iron supplement (WIS) ได้รับ triferdine รับประทาน 1 เม็ด และ ferrous fumarate 1 เม็ด และ folic acid ครึ่งเม็ด สัปดาห์ละ 1 ครั้ง ประเมินประสิทธิภาพของการได้รับยาโดยเจาะเลือดตรวจระดับ CBC และ iron study ที่แรกรับและอีกครั้ง ที่อายุครรภ์ 32-36 สัปดาห์ จากนั้นติดตามสอบถามอาการไม่พึงประสงค์ของการใช้ยา เช่น อาการปวดท้อง คลื่นไส้ อาเจียน เป็นต้น โดยใช้แบบสอบถาม ทุก ๆ 4 สัปดาห์ รวมถึงการสอบถามความสม่ำเสมอของการรับประทานยา และให้นำยามาด้วยทุกครั้งเมื่อมาที่โรงพยาบาลเพื่อนับเม็ดยา*

ผลการศึกษา: *จากผลการศึกษาพบว่าระดับฮีมาโตคริตลดลงอย่างมีนัยสำคัญทางสถิติในทุกกลุ่มตัวอย่างที่ไตรมาสที่ 3 และเข้าเกณฑ์ภาวะโลหิตจางจากการขาดธาตุเหล็กในไตรมาสที่ 3 ร้อยละ 28.57, 14.28 และ 39.28 ในกลุ่ม DIS, TIS และ WIS ตามลำดับ ไม่พบมีความแตกต่างกันอย่างมีนัยสำคัญระหว่างกลุ่ม ($p = 0.064$) ในขณะที่ระดับ ferritin มีค่าลดลงแตกต่างกันอย่างมีนัยสำคัญระหว่างกลุ่ม ($p = 0.033$) โดยพบค่าน้อยที่สุดในกลุ่มตัวอย่างกลุ่ม WIS และพบภาวะ serum ferritin ต่ำ คิดเป็น ร้อยละ 46.4, 64.3 และ ร้อยละ 71.4 ในกลุ่ม DIS, TIS และ WIS ตามลำดับ ไม่พบอาการข้างเคียง*

สรุป: *จากผลการศึกษาพบว่าระดับฮีมาโตคริตลดลงในไตรมาสที่ 3 ทั้ง 3 กลุ่ม ถึงแม้ว่าไม่พบความแตกต่างของระดับฮีมาโตคริตและฮีโมโกลบินระหว่างกลุ่มอย่างมีนัยสำคัญ แต่พบความชุกของภาวะซีดจากการขาดเหล็กในกลุ่มที่ได้รับยาหนึ่งครั้งต่อสัปดาห์ ผลการศึกษาสรุปได้ว่าการได้รับยาแบบ TIS มีประสิทธิภาพสูงที่สุดในการป้องกันภาวะโลหิตจางจากการขาดธาตุเหล็กในหญิงตั้งครรภ์*

คำสำคัญ: *การเสริมธาตุเหล็ก, ตั้งครรภ์, โลหิตจางการขาดธาตุเหล็ก, ฝากครรภ์, ฮีโมโกลบิน*

Introduction

Anemia is a prevalent illness among pregnant women that can impact the health of both the mother and the fetus[1]. It may result from various circumstances, including starvation, illness, and genetic disorders[2]. Several micronutrients, including iron, folate, vitamins A, B12, and C[3], contribute to anemia, with iron deficiency being the most prevalent cause.

The prevalence among pregnant women worldwide ranges between 29.0-42.7%[4]. In Southeast Asia, the prevalence is as high as 48%. In Thailand, approximately 6.92 – 30% of pregnant women have anemia at first antenatal care (ANC)[5–7], Thongperm et al[8] reported that the prevalence of anemia among pregnant women in Trang province was found to be 17.2% at the first visit, which increased to 22.5% and 50% in the second and third trimesters, respectively. The predominant reasons were attributed to thalassemia, with only 5% resulting from iron deficiency. According to statistical data compiled from the record at Somdejprasangkharach 17th Hospital, the prevalence of anemia among pregnant women was around 23.6%, 17.58%, and 19.51% in 2020, 2021 and 2022, respectively.

Iron deficiency is the most important cause of anemia during pregnancy, with an incidence of 18-19% in the United States. Pregnancy requires iron to meet the physiological demands of the fetus and promote blood flow as well as tissue development in the body[9,10]. The maternal demand for iron grows from 1 to 2.5 mg per day during the first trimester, reaching 6.5 mg per day in the third trimester. The body necessitates approximately 1 gram of iron throughout pregnancy, with 360 mg allocated for the fetus and placenta, and 450 mg designated for the synthesis of red blood cells in the mother. Of the remaining 240 mg, it is excreted by feces, urine, and perspiration[11]. During pregnancy, untreated iron deficiency is associated with an increased risk of iron deficiency anemia, placental hypertrophy, and maternal hypothyroidism[12]. If serum ferritin is below 15 µg/L, it signifies iron deficiency, and it is classified as iron deficiency anemia[13] when accompanied by hemoglobin levels under 11 g/dL.

The World Health Organization (WHO) characterizes pregnant women as having anemia when their Hb levels are less than 11 g/dl in the first and third trimesters, and Hb is less than 10.5 g/dl in the second trimester[14,15]. In 2012, the WHO recommended daily oral iron and folic acid supplementation as a crucial component of prenatal care[16]. Subsequently, the WHO guidelines in 2016 suggested a weekly iron supplementation regimen of 120 mg combined with 2,800 micrograms (2.8 mg) of folic acid for pregnant women when daily iron intake is impractical. This recommendation acknowledges the intestinal mucosa's rapid turnover, occurring every 5 to 6 days. The rationale for weekly administration is to optimize intestinal iron absorption and minimize the potential for free radical formation associated with excessive iron accumulation within the intestinal tract[17]. Moreover, prior research indicated that administering iron supplements weekly yielded no distinct effects on anemia in near-term pregnant women, low birth weight infants, and premature births compared to daily administration. Additionally, side effects from iron supplementation were less frequent, and pregnant women were more compliant with continuous intake[18,19]. Following the iron supplement, hepcidin, a liver-cell-derived protein that is crucial to regulating iron metabolism, would be elevated. This elevation inhibits intestinal iron absorption within 24 hours. Previous research suggested that iron supplementation exceeding 60 mg promoted intestinal iron absorption if administered with a 48-hour interval[20], contrary to the World Health Organization's recommendation of weekly administration.

The study by Bouzari et al[21] revealed that daily iron supplementation and weekly iron supplementation were equally effective in preventing anemia among pregnant women. However, the study provided only 50 milligrams of iron in the group that received it once a day and every other day, allowing 100 milligrams of iron in the form of 1 time per week, with 60 milligrams of iron, which is different from the 60 milligrams of iron supplement provided in Thailand. In addition, the

previous study has indicated that iron supplementation in non-anemic pregnant women leads to elevated blood iron levels and is associated with an increased risk of preterm birth, low birth weight, and gestational diabetes mellitus[22, 23].

Goonewardene et al[24] likewise reported that a group receiving iron supplements once weekly and thrice weekly had a greater risk of iron deficiency compared to a group receiving daily supplements, with no variation in side effects from the medications. Thus, it is advisable to consume iron supplements daily, as this is more efficacious in preventing anemia.

The primary objective of this study was to examine the comparative efficacy of intermittent iron supplementation administered once a week, thrice a week, and daily.

To evaluate the efficacy, blood samples were collected for complete blood count and iron studies at the initial presentation and at 32-36 weeks of gestation. As commercially available iron supplements are fortified with iodine, different supplementations may have variable effects on maternal iodine levels. Consequently, the secondary objective of this study was to assess urine iodine levels in conjunction with adverse effects, such as nausea, abdominal pain or constipation, to determine the most appropriate iron supplementation for pregnant women.

Materials and Methods

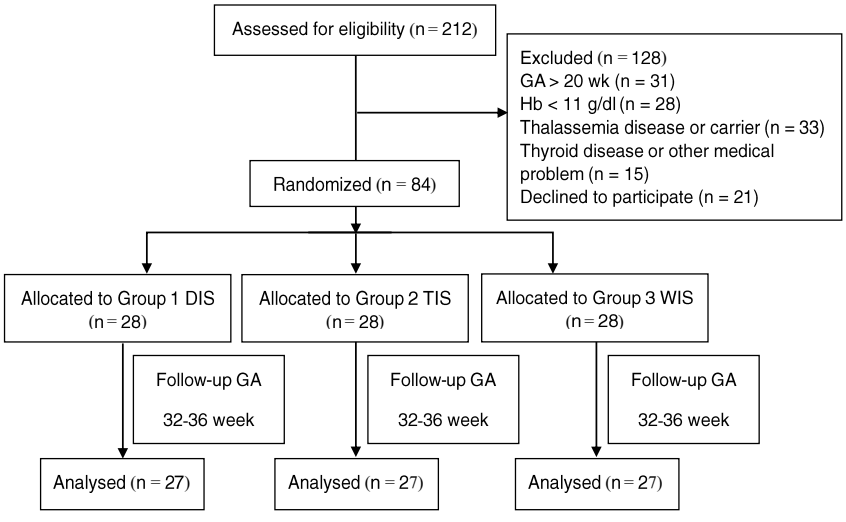
This open-label randomized controlled study was conducted among pregnant women seeking antenatal care at Somdejprasangkharach 17th Hospital from April 2023 to March 2024. The study was approved by the Human Research Ethics Committee of the Public Health Office, Suphan Buri Province. The trial was prospectively registered in the Thai Clinical Trials Registry (TCTR20230310002) on 10 March 2023. The pregnancies of those who had a body mass index (BMI) ≥ 18.5 kg/m^2, were aged between 18 and 50 years, had a gestational age of less than 20 weeks, and had hemoglobin (Hb) ≥ 11 g/dl or hematocrit (Hct) ≥ 33%, no history of iron deficiency anemia or taking iron supplements were included. Pregnant women were excluded if they had a history of diseases related to the blood system and iron metabolism, anemia, chronic diseases affecting iron absorption, malabsorption, bariatric surgery, or complications during pregnancy such as preterm labor, preterm premature rupture of membranes (PPROM), and infections.

The participants who met the inclusion criteria were randomly assigned to one of three groups, including group 1, daily iron supplement (DIS), group 2, thrice a week iron supplement (TIS), and group 3, weekly iron supplement (WIS)) using a computer-generated block randomization method. Random numbers were assigned in opaque envelopes after the participants provided written informed consent.

All participants were asked about demographic information, including age, chronic illnesses, and obstetric history. Baseline venous blood specimens were collected for complete blood count (CBC), iron studies, and C-reactive protein (CRP). Urine samples were obtained for iodine assessment. Urine iodine concentrations were measured using the Sandell-Kolthoff method. Results were expressed in µg/L, with intra-assay and inter-assay coefficients of variation of 3-5% and 6-12%, respectively. Afterward, the participants in group 1 (DIS) received daily triferdine (potassium iodide 196 mcg, ferrous fumarate 185 mg, and folic acid 400 mcg). Group 2 (TIS) received triferdine every other day, while group 3 (WIS) received weekly triferdine plus ferrous fumarate (200 mg), and a half tablet of folic acid (5 mg). In the WIS group, additional ferrous supplementation was required. Since triferdine contains iodine, ferrous fumarate 200 mg was selected as the supplementary iron source to avoid excessive iodine exposure in participants. Treatment initiation occurred following confirmation of inclusion and exclusion criteria and patient consent to participate in the study. Treatment was discontinued under two conditions: 1) anemia was detected in the second blood assessment, or 2) when the second blood results were normal, medication was continued until delivery. Follow-up blood and urine samples were collected at 32 to 36 weeks of gestation. All participants were provided with medications that were placed in

plastic bags with drug administration labeled by hospital pharmacists to increase patient compliance and prevent dosage errors.

Participants were instructed to bring all medication containers to each scheduled antenatal visit (every 4 weeks). At each visit, pill counts were conducted to calculate the number of tablets consumed and the remaining quantity to assess medication adherence. Side effects of iron supplementation, such as abdominal pain, nausea, and vomiting, were recorded by a questionnaire administered every four weeks, which also evaluated adherence to the supplementation schedule. Additionally, participants were systematically questioned about any abnormal bleeding symptoms at every 4 weeks, as we would like to detect if there was any other cause of anemia during the study period. Information regarding birth history, including delivery method, gestational age, and neonatal weight, was collected. The flow of the participants is summarized in Fig. 1.



DIS: Daily iron supplement, TIS: Thrice a week iron supplement, WIS: Weekly iron supplement

Fig. 1. Study flow diagram.

The sample size was calculated for a three-group by analysis of variance (ANOVA) design[25] using the following parameters: $\alpha = 0.05$, $\beta = 0.05$, and effect size = 0.5330[21]. This determined a minimum of 22 participants per group. Adjusting for an expected 20% attrition rate, the final sample size was calculated as 28 participants per group (n = 22/0.8 = 28). Data analysis was conducted on a computer using SPSS version 27. Descriptive data were analyzed for both qualitative and quantitative variables. ANOVA and Bonferroni's post hoc test were employed to evaluate continuous variables, both within and between groups, before and after supplementation.

Results

A total of 84 pregnant women participated, and they were randomly assigned into 3 groups of 28 volunteers each. Table 1 presents the general information of participants in each group. No statistically significant variations were seen in terms of maternal age, gestational age at initial visit, body mass index, hemoglobin concentration, hematocrit, mean corpuscular volume, serum iron, serum ferritin, transferrin saturation, total iron binding capacity (TIBC), and CRP among the groups. Nonetheless, a statistically significant disparity in urine iodine levels was observed, with group 2 exhibiting markedly greater levels than the other groups (p = 0.01), and

no anemia was detected upon initial admission.

Upon follow-up at gestational ages of 32 to 36 weeks, no significant differences were observed in the levels of hemoglobin, hematocrit, MCV, serum iron, transferrin saturation, total iron binding capacity, urine iodine, and CRP among the groups. However, a statistically significant disparity in ferritin levels was observed between the groups. Post-hoc analysis utilizing the Bonferroni technique revealed a statistically significant difference between group 1 DIS and group 3 WIS (p = 0.028), as illustrated in Table 2.

Table 1. Participant's demographic data.

	DIS (n = 28)	TIS (n = 28)	WIS (n = 28)	p value
Age (years)	24.07 ± 6.06	24.82 ± 5.23	22.71 ± 3.83	0.301
GA at first visit (weeks)	14.04 ± 2.72	13.50 ± 2.50	13.96 ± 2.55	0.703
BMI (kg/m^2)	22.58 ± 6.56	24.53 ± 5.81	23.63 ± 5.89	0.491
Hemoglobin (g/dl)	12.57 ± 0.85	12.59 ± 0.84	12.50 ± 0.96	0.919
Hematocrit (%)	38.06 ± 2.09	38.04 ± 2.46	37.72 ± 2.69	0.840
MCV (fl)	85.26 ± 4.65	83.93 ± 5.80	84.55 ± 5.55	0.650
Serum iron (µg/dl)	78.54 ± 31.38	80.45 ± 31.75	81.32 ± 23.97	0.936
Serum ferritin (ng/ml)	108.832 ± 100.17	100.68 ± 78.46	79.89 ± 59.94	0.393
TIBC(µg/dl)	315.29 ± 50.67	305.11 ± 72.13	299.86 ± 91.36	0.726
Transferin saturation (%)	25.79 ± 11.40	26.29 ± 11.80	25.95 ± 11.00	0.981
CRP (mg/l)	12.15 ± 16.86	8.97 ± 9.87	5.10 ± 3.33	0.076
Duration of supplement (days)	116 ± 9.89	132.5 ± 10.60	126 ± 19.79	0.853
Urine iodine (µg/L)	165.03 ± 86.10	268.43 ± 186.45	158.85 ± 82.13	0.002*

DIS: daily iron supplement, TIS: thrice weekly iron supplement, WIS: weekly iron supplement, GA: gestational age, BMI: body mass index, MCV: mean corpuscular volume, TIBC: total iron binding capacity, CRP: C-reactive protein
Data expressed as mean ± standard deviation.
*statistical significance at $p < 0.05$ when analyzed with ANOVA.

Table 2. Comparative data of the results of the second blood test between groups.

	DIS (n = 27)	TIS (n = 27)	WIS (n = 27)	p value
Hemoglobin (g/dl)	12.72 ± 5. 11	12.58 ± 3.67	11.32 ± 0.92	0.306
Hematocrit (%)	35.53 ± 2.28	35.90 ± 2.92	34.30 ± 2.52	0.064
MCV (fl)	84.19 ± 15.43	85.62 ± 5. 45	84.77 ± 5.36	0.865
Serum iron (µg/dl)	91.37 ± 47.08	85.07 ± 50.22	66.89 ± 68.82	0.256
Serum ferritin (ng/ml)	35.95 ± 22.15	29.70 ± 21.94	21.71 ± 13.60	0.033*
TIBC(µg/dl)	438.41 ± 55.50	451. 54 ± 61.02	469.89 ± 50.24	0.121
Transferrin saturation (%)	21.30 ± 11.52	18.93 ± 10.55	14.48 ± 15.22	0.136
Urine iodine (µg/L)	204.17 ± 213.19	180.52 ± 131. 71	173.70 ± 118.36	0.763
CRP (mg/l)	4.81 ± 5.31	7.58 ± 10.18	5.80 ± 5.69	0.380

DIS: daily iron supplement, TIS: thrice weekly iron supplement, WIS: weekly iron supplement, GA: gestational age, BMI: body mass index, MCV: mean corpuscular volume, TIBC: total iron binding capacity, CRP: C-reactive protein
Data expressed as mean ± standard deviation.
* statistical significance at $p < 0.05$ when analyzed with ANOVA statistics.

The follow-up blood test (during the third trimester of pregnancy) revealed iron deficiency anemia (Hb < 11) in 8 (28.57%), 4 (14.28%), and 11 (39.28%) subjects in the DIS, TIS, and WIS groups, respectively. Despite its higher prevalence in the WIS group compared to the other groups, the difference was not statistically significant (p = 0.109). The prevalence of low serum ferritin levels (< 30 µg/L) in the DIS, TIS, and WIS groups was 46.4%, 64.3%, and 71.4%, respectively. Despite its higher prevalence in the WIS group compared to the other groups, the difference was not statistically significant (p = 0.143).

No significant difference in urinary iodine concentrations was observed between groups at the second assessment.

Significant decreases in hematocrit and serum ferritin accompanied by increased TIBC were observed uniformly across treatment groups post-intervention, with no detectable changes in hemoglobin, MCV, or serum iron concentrations. (Table 3)

Table 3. Mean difference of pre and post blood test within group.

	Group		mean ± SD	mean difference ± SD	95%CI		p value
Hematocrit (%)	DIS	pre	38.06 ± 2.09	2.48 ± 2.17	1.62	3.34	< 0.001*
		post	35.53 ± 2.28				
	TIS	pre	38.04 ± 2.46	2.14 ± 3.12	0.93	3.35	0.001*
		post	35.90 ± 2.92				
	WIS	pre	37.72 ± 2.69	3.51 ± 1.98	2.73	4.29	< 0.001*
		post	34.30 ± 2.52				
Hemoglobin (g/dl)	DIS	pre	12.57 ± 0.85	-0.17 ± 5.03	-2.16	1.81	0.856
		post	12.72 ± 5. 11				
	TIS	pre	12.59 ± 0.84	0.01 ± 3.72	-1.42	1.45	0.984
		post	12.58 ± 3.67				
	WIS	pre	12.50 ± 0.96	1.22 ± 0.67	0.96	1.49	< 0.001*
		post	11.32 ± 0.92				
MCV (fl)	DIS	pre	85.26 ± 4.65	0.98 ± 15.06	-4.97	6.93	0.738
		post	84.19 ± 15.43				
	TIS	pre	83.93 ± 5.80	-1.68 ± 2.93	-2.82	-0.54	0.005*
		post	85.62 ± 5. 45				
	WIS	pre	84.55 ± 5.55	0.48 ± 3.63	-0.95	1.92	0.495
		post	84.77 ± 5.36				
Serum iron (µg/dl)	DIS	pre	78.54 ± 31.38	-12.07 ± 48.68	-31.33	7.18	0.209
		post	91.37 ± 47.08				
	TIS	pre	80.45 ± 31.75	-4.60 ± 50.90	-24.34	15.13	0.636
		post	85.07 ± 50.22				
	WIS	pre	81.32 ± 23.97	15.22 ± 63.06	-9.72	40.17	0.221
		post	66.89 ± 68.82				
Serum ferritin (ng/ml)	DIS	pre	108.832 ± 100.17	56.80 ± 43.56	39.56	74.03	< 0.001*
		post	35.95 ± 22.15				
	TIS	pre	100.68 ± 78.46	70.97 ± 66.86	45.05	96.90	< 0.001*
		post	29.70 ± 21.94				
	WIS	pre	79.89 ± 59.94	55.00 ± 51.81	34.50	75.50	< 0.001*
		post	21.71 ± 13.60				
TIBC (µg/dl)	DIS	pre	315.29 ± 50.67	-120.70 ± 50.32	-140.61	-100.79	< 0.001*
		post	438.41 ± 55.50				
	TIS	pre	305.11 ± 72.13	-146.42 ± 70.56	-173.79	-119.06	<0.001*
		post	451. 54 ± 61.02				
	WIS	pre	299.86 ± 91.36	-171.95 ± 99.05	-211.14	-132.76	<0.001*
		post	469.89 ± 50.24				
Transferrin saturation (%)	DIS	pre	25.79 ± 11.40	4.59 ± 12.46	-0.33	9.52	0.067
		post	21.30 ± 11.52				
	TIS	pre	26.29 ± 11.80	7.35 ± 13.81	1.99	12.71	0.009*
		post	18.93 ± 10.55				
	WIS	pre	25.95 ± 11.00	11.62 ± 15.02	5.68	17.57	<0.001*
		post	14.48 ± 15.22				

Table 3. Mean difference of pre and post blood test within group. (Cont.)

	Group		mean ± SD	mean difference ± SD	95%CI		p value
Urine Iodine (µg/L)	DIS	pre	165.03 ± 86.10	-38.93 ± 224.70	-127.82	49.95	0.376
		post	204.17 ± 213.19				
	TIS	pre	268.43 ± 186.45	87.91 ± 190.26	14.13	161.68	0.021*
		post	180.52 ± 131. 71				
	WIS	pre	158.85 ± 82.13	-15.49 ±129.47	-66.71	35.72	0.540
		post	173.70 ± 118.36				
CRP (mg/l)	DIS	pre	12.15 ± 16.86	7.33 ± 15.38	1.25	13.42	0.020*
		post	4.81 ± 5.31				
	TIS	pre	8.97 ± 9.87	1.39 ± 5.56	-0.76	3.54	0.197
		post	7.58 ± 10.18				
	WIS	pre	5.10 ± 3.33	-0.86 ± 5.43	-3.01	1.28	0.415
		post	5.80 ± 5.69				

DIS: daily iron supplement, TIS: thrice weekly iron supplement, WIS: weekly iron supplement, GA: gestational age, BMI: body mass index, MCV: mean corpuscular volume, TIBC: total iron binding capacity, CRP: C-reactive protein, SD: standard deviation, CI: confidence interval
* statistical significance at $p < 0.05$ when analyzed with paired t-test

Between-group analysis revealed no statistically significant differences in the incidence of adverse gastrointestinal events, including nausea, vomiting, constipation, diarrhea, and flatulence. Similarly, no significant differences were observed in the frequency of taste disturbances between treatment groups.

There was no evidence of preterm labor or perinatal death in any of the groups. All infants had normal Apgar scores. No statistically significant differences were observed between the groups concerning hematocrit levels, thyroid-stimulating hormone (TSH) levels, or birth weight. (Table 4)

Table 4. Neonatal outcomes.

	Group 1 DIS (n = 20)	Group 2 TIS (n = 23)	Group 3WIS (n = 17)	p value
Hematocrit (%)	53.36 ± 6.97	51.67 ± 5.03	50.35 ± 4.64	0.276
BW < 2,500 g	3 (15%)	3 (13.4%)	1 (5.88%)	0.780
Birthweight	3043.50 ± 395.35	2982.17 ± 500.30	2995.29 ± 389.83	0.894
TSH levels	3.14 ± 2.31	2.49 ± 2.28	3.27 ± 3.26	0.586

DIS: daily iron supplement, TIS: thrice weekly iron supplement, WIS: weekly iron supplement, BW: birth weight, TSH: thyroid-stimulating hormone

Discussion

The results of the study indicated a significant reduction in hemoglobin levels across all sample groups throughout the third trimester, with incidences of iron deficiency anemia recorded at 28.57%, 14.28%, and 39.28% in groups 1 DIS, 2 TIS, and 3 WIS, respectively. No substantial difference existed between the groups. Simultaneously, the ferritin levels exhibited a substantial decline throughout the groups, with group 3 WIS recording the lowest value and ferritin levels at 46.4%, 64.3%, and 71.4% in groups 1 DIS, 2 TIS, and 3 WIS, respectively.

Anemia is a prevalent condition affecting from 19.3% to 57.4% of the population[6,19,26]. The prevalence seen in this study was comparable. This occurs because, during pregnancy, the quantity of red blood cells rises by 25%, while the plasma volume expands by 50%. The altered proportion led to a reduction in hemoglobin levels, causing anemia accompanied by iron depletion during pregnancy. Inadequate iron intake increased the risk of anemia[12].

Anemia is associated with several maternal and

newborn symptoms, including maternal fatique, early birth, low birthweight, postpartum hemorrhage, infant anemia, and potential impacts on brain function[5, 27–31]. Thus, anemia monitoring is essential for pregnant women. The hemoglobin level alone is insufficient to determine the quantity of stored iron. Consequently, ferritin levels provide a more precise and sensitive evaluation[32, 33]. The sensitivity of ferritin levels is 89%, whereas that of hemoglobin levels is 29%. Utilizing a cut-off threshold of < 30 ng/ml, the sensitivity and specificity for the diagnosis of iron deficiency anemia are 92% and 98%, respectively. The study revealed that the proportion of individuals with low ferritin levels exceeded that of those with low hemoglobin levels. The disparity in ferritin levels across the three experimental groups indicates that assessing ferritin levels may serve as a superior screening method for iron deficiency anemia compared to evaluating hemoglobin levels alone. Nonetheless, inflammation in the body may influence ferritin levels. Therefore, data should be taken cautiously in the presence of inflammation.

This study revealed a significant decrease in the levels of hematocrit and serum ferritin with an increase in the TIBC level in all three groups despite unchanged hemoglobin levels, indicating that iron deficiency anemia is still present after iron supplementation. While serum iron levels were maintained because of active supplementation, the presence of iron deficiency markers suggests inadequate therapeutic response. This suboptimal outcome is probably due to two factors: the physiological plasma volume expansion during pregnancy and the possibility of iron malabsorption or lower bioavailability, which limits utilization[34]. These findings aligned with previous studies. Srimaneesiri et al[35] conducted a study to evaluate the effect of vitamin C for daily iron supplementation in pregnant women with high-risk anemia. They found that hemoglobin and hematocrit levels decreased at the 8-week follow-up, which might have been due to physiological plasma volume expansion, inadequate nutrition, or insufficient iron supplementation. In the WIS group, a combination of Triferdine and ferrous fumarate was used to achieve 120 mg of elemental iron while avoiding excessive iodine intake. However, despite this approach, the WIS group demonstrated markedly reduced ferritin levels compared to the other two groups suggesting that daily or alternate-day iron supplementation diminishes the prevalence of anemia. Nevertheless, an examination of the ferritin levels revealed that only the cohort receiving daily iron supplements exhibited an average ferritin level within the normal range. This finding aligned with the research conducted by Ridwan et al[36], which indicated that the group administering iron daily had elevated ferritin levels compared to those receiving it weekly. According to Bumrungpert et al[37], which compared the administration of 120 mg ferrous bisglycinate and folinic acid with 200 mg ferrous fumarate once daily in pregnant women, the findings revealed that although serum iron levels increased in both groups, the group receiving ferrous bisglycinate and folinic acid demonstrated higher serum iron concentrations despite receiving a lower iron dosage. This phenomenon can be attributed to the co-administration of iron with folic acid, which plays important roles in supporting the absorption and metabolism of iron, hemoglobin, and erythrocytes. In contrast, a study by Sadaf et al[38] concluded that weekly supplementation provided an equivalent protective effect to daily intake. In the study by Sadaf et al, the cohort that ingested iron weekly received 130 mg, surpassing the amount in this study. The measurement was evaluated based on Hb and Hct values rather than ferritin values.

The study by Bouzari et al[21], which examined iron administration patterns to prevent anemia in pregnant women, revealed no differences in hemoglobin and ferritin levels across the three groups, despite all groups exhibiting decreased ferritin levels. This may have resulted from variations in ethnicity and nutritional status, which were not evaluated in this study. The study by Nisar et al[40] demonstrated that both daily and weekly iron supplementation could elevate blood concentration and ferritin levels in both groups. Both participants acquired knowledge

regarding the significance of iron supplementation and an appropriate diet, which may account for the increase in hemoglobin and ferritin levels in both groups.

The research conducted by Abdelgawad et al[39] indicated that administering iron once weekly could aid in the prevention of anemia. However, the participants were administered 200 mg of iron weekly, exceeding the 120 mg provided in this study. The study was constrained by the small sample size in each group, potentially resulting in a lack of statistically meaningful differences. Nevertheless, it was determined that weekly iron supplementation was unlikely to adequately moderate the prevalence of anemia.

Furthermore, Bhatla et al[40] demonstrated that pregnant women receiving daily iron supplementation showed significantly elevated lipid peroxidation levels compared to controls. This increased oxidative stress and subsequent membrane damage from lipid peroxidation has been implicated in the development of serious pregnancy complications, including preeclampsia and intrauterine growth restriction. These findings suggest that excessive iron supplementation during pregnancy may potentially compromise both maternal and fetal health outcomes. Adequate iodine intake is crucial for thyroid hormone synthesis and fetal neurodevelopment, yet achieving optimal iodine status remains challenging. In this study, the TIS group showed significantly higher baseline urinary iodine levels compared to other groups, but no significant between-group differences were observed at the second assessment. Additionally, infant thyroid function parameters showed no significant differences between groups. These findings suggest that iron supplementation does not substantially disrupt iodine homeostasis in pregnant women. However, larger studies with extended follow-up are needed to definitively establish the safety of iodine-containing iron supplements during pregnancy This open label randomized controlled trial aimed to evaluate various iron supplement formulations with comprehensive long-term follow-up through delivery, providing significant insights into intermittent iron supplementation in the Thai population. However, limitations should be addressed. First, the sample size in this study may have been insufficient to identify clinically significant differences. Second, nutritional factors were not evaluated, which could have influenced iron absorption. Finally, the open-label design of this study constitutes a limitation, as the lack of blinding may have introduced observer and participant bias. Further research should investigate other dosage regimens or combinations with other nutrients that may improve iron absorption and efficacy with larger sample sizes, conducting thorough nutritional assessments.

Conclusion

The results of this study indicated a reduction in hematocrit levels across all study groups throughout the third trimester. Although between-group comparisons revealed no significant differences, the WIS group was found to have the highest incidence of iron deficiency anemia. Based on the study results, we concluded that the TIS group demonstrated the highest efficacy in preventing iron deficiency anemia during pregnancy.

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Potential conflicts of interest

The author declares no conflicts of interest.

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OBSTETRICS

Association Between Meconium-stained Amniotic Fluid and Obstetric Perineal Wound Infection

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ABSTRACT

Objectives: Meconium-stained amniotic fluid (MSAF) has been associated with higher rates of surgical site infection. The present study aimed to investigate the association between MSAF and obstetric perineal wound infections, and other puerperal infections, to inform the preventive strategies.

Materials and Methods: This retrospective cohort study reviewed medical records of women delivered at King Chulalongkorn Memorial Hospital from January 1, 2018 to December 31, 2020. Women who underwent vaginal delivery with episiotomy or had an obstetric perineal wound and were followed up at 6 weeks postpartum were included. The cohort comprised of pregnancies complicated by MSAF (n = 366) and those without MSAF (n = 1,464). The primary outcomes were the incidence of infected episiotomy wounds and wound dehiscence. Percentages and 95% confidence intervals (CI) were calculated for categorical variables and odds ratios (OR) with 95% CI were used for comparisons between groups.

Results: A total of 1,830 patients were included, with a mean age of 29.5 years. The rate of infected episiotomy wound in the MSAF group (3.55%, 95% CI 1.89 to 6.07) did not significantly differ from that of the non-MSAF group (3.55%, 95% CI 2.65 to 4.66), yielding an OR of 1.00 (95% CI 0.54 to 1.86). Similarly, there was no significant difference in the rate of wound dehiscence, chorioamnionitis, and other puerperal infections between the groups.

Conclusion: Our findings suggested that MSAF was not associated with an increased risk of obstetric perineal wound infection. Therefore, antibiotic prophylaxis to prevent such infections in women with MSAF may not be necessary.

Keywords: infected episiotomy wound, meconium-stained amniotic fluid, obstetric perineal wound infection

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ความสัมพันธ์ของภาวะมีขี้เทาในน้ำคร่ำกับแผลฝีเย็บติดเชื้อ

ศิรารัศม์ อิทธิภูริพัฒน์, สุรสิทธิ์ ชัยทองวงศ์วัฒนา

บทคัดย่อ

วัตถุประสงค์*: น้ำคร่ำที่มีขี้เทาเพิ่มความเสี่ยงต่อการติดเชื้อของแผลผ่าตัดอย่างมีนัยสำคัญ การศึกษานี้มีวัตถุประสงค์เพื่อหาความสัมพันธ์ของภาวะมีขี้เทาในน้ำคร่ำกับการติดเชื้อของแผลฝีเย็บและการติดเชื้อหลังคลอดอื่นๆ ของมารดา เพื่อหาวิธีป้องกันแผลฝีเย็บติดเชื้อในรายที่มีน้ำคร่ำมีขี้เทา*

วัสดุและวิธีการ*: การศึกษาจากเหตุไปหาผลแบบย้อนหลังนี้ดำเนินการโดยทบทวนเวชระเบียนของสตรีตั้งครรภ์ซึ่งคลอดบุตรทางช่องคลอดที่โรงพยาบาลจุฬาลงกรณ์ ตั้งแต่ 1 มกราคม พ.ศ. 2561 ถึง 31 ธันวาคม พ.ศ. 2563 คัดเลือกสตรีที่มีแผลฝีเย็บและมาตรวจติดตามที่ 6 สัปดาห์หลังคลอด เป็นรายที่มีขี้เทาในน้ำคร่ำ 366 ราย กับรายที่ไม่มีขี้เทาในน้ำคร่ำ 1,464 ราย ผลลัพธ์หลัก ได้แก่ อุบัติการณ์แผลฝีเย็บติดเชื้อและแผลแยก โดยแสดงในรูปแบบร้อยละและช่วงความเชื่อมั่นร้อยละ 95 (95% CI) และเปรียบเทียบระหว่างกลุ่มด้วย Odds ratio (OR) และช่วงความเชื่อมั่น ร้อยละ 95*

ผลการศึกษา*: สตรีตั้งครรภ์รวม 1,830 ราย มีอายุเฉลี่ย 29.5 ปี อัตราการเกิดแผลฝีเย็บติดเชื้อในกลุ่มที่มีขี้เทาในน้ำคร่ำ (ร้อยละ 3.55, 95% CI 1.89 ถึง 6.07) ไม่มีความแตกต่างกันอย่างมีนัยสำคัญกับกลุ่มที่ไม่มีขี้เทาในน้ำคร่ำ (ร้อยละ 3.55, 95% CI 2.65 ถึง 4.66) และมี OR 1.00, 95% CI 0.54 ถึง 1.86 และไม่พบความแตกต่างระหว่างกลุ่มอย่างมีนัยสำคัญของอัตราการเกิดแผลแยก (OR 0.74, 95% CI 0.28 ถึง 1.93)*

สรุป*: การศึกษานี้ไม่พบความสัมพันธ์ของภาวะมีขี้เทาในน้ำคร่ำกับความเสี่ยงของแผลฝีเย็บติดเชื้อ ดังนั้น ในสตรีที่มีขี้เทาในน้ำคร่ำจึงไม่จำเป็นต้องให้ยาปฏิชีวนะเพื่อป้องกันการติดเชื้อดังกล่าว*

คำสำคัญ*: แผลฝีเย็บติดเชื้อ, ภาวะมีขี้เทาในน้ำคร่ำ, การติดเชื้อแผลฝีเย็บทางสูติกรรม*

Introduction

Meconium-stained amniotic fluid (MSAF), resulting from the passage of fetal colonic contents into the amniotic fluid, is reported in approximately 8-25% of all deliveries[1]. In term pregnancies, the incidence of MSAF ranges from 15-20% and increases to 30-40% in postterm pregnancies[2]. MSAF can lead to adverse outcomes for both mother and fetus, including meconium aspiration syndromes, respiratory distress, neonatal sepsis, and neonatal intensive care unit admission[3]. Pregnant women with MSAF are at risk of complications, such as chorioamnionitis, endometritis, surgical site infection, and puerperal infection[4-6]. While the exact pathogenesis remains unclear, some studies suggest a higher prevalence of positive amniotic fluid cultures in the MSAF group[7-9], indicating meconium as a risk factor for microbial invasion of the amniotic cavity. Additionally, meconium may inhibit bacteriostatic properties of amniotic fluid and negatively impact host defense systems[7, 9,10], potentially leading to increased bacterial growth and the risk of chorioamnionitis.

Episiotomy, a surgical enlargement of the posterior aspect of the vagina performing in the last part of the second stage of labor[11], is one of the most common procedures performed in modern obstetrics[12]. However, there are insufficient objective evidence-based criteria to recommend routine episiotomy[11], leading to a decline in its rate in developed countries. Nevertheless, episiotomy remains common in the Asian population due to shorter perineum and stronger tissue, which predispose Asian women to higher risks of large perineal lacerations during vaginal delivery[18]. Adverse outcomes of episiotomy may include perineal wound infection, wound dehiscence, dyspareunia, urinary incontinence, and fecal incontinence[13]. The incidence of episiotomy wound infection ranges from 0.5 to 2.8%[14]. Several maternal and intrapartum factors have been identified as potential risk factors, including obesity, diabetes mellitus, primiparity, fetal macrosomia, prolonged rupture of membranes, prolonged second stage of labor, operative vaginal delivery, multiple vaginal examinations before delivery, operator experience, and poor perineal hygiene[19-23]. These complications can have negative effects on postpartum physical, psychological and sexual recovery, often requiring additional treatment such as antibiotics, pain controller, re-admission, and wound debridement, leading to increased costs.

Previous studies have shown that MSAF is significantly associated with positive cultures compared to clear amniotic fluid, increasing the risk of puerperal complications such as chorioamnionitis, endometritis, and surgical site infection following cesarean delivery[4-6]. The primary objective of the present study is to investigate the association between MSAF and obstetric perineal wound infection, as well as episiotomy wound dehiscence among women who underwent vaginal delivery to inform prevention strategies. Secondary outcomes include intrapartum fever, maternal infection, and other puerperal infections.

Materials and Methods

This retrospective cohort study was approved by the Research Ethics Committee of the Faculty of Medicine, Chulalongkorn University (IRB No. 0029/65). Electronic medical records of women who delivered at King Chulalongkorn Memorial Hospital, Bangkok, Thailand, from January 2018 to December 2020 were reviewed. Inclusion criteria comprised women who underwent vaginal delivery of a fetus with a gestational age greater than 22 weeks or a birth weight exceeding 500 grams, with episiotomy or obstetric perineal wound and followed up at 6-week postpartum. According to the protocol of postpartum wound care, the persons who did perineorrhaphy were the obstetricians, obstetric residents or nurse midwives.

Due to sample size calculation utilized the formula for cohort studies for binary data without

continuity correction[15], based on the incidence of obstetric perineal wound infection of 1% (0.5 – 2.8%[14] and the relative risk of puerperal infection in pregnancies with MSAF (RR = 2)[4-5], with alpha and beta error set at 0.05 and 0.2, respectively, using a ratio 1:4 (MSAF: non-MSAF) ratio, determining a requirement of 366 pregnancies complicated by MSAF and 1464 cases without MSAF to detect significant differences. After institutional review boards provided ethical approval for the study, the data were collected. Due to the high loss follow-up rate at 6-week postpartum clinic (37.8%), the ratio of participant inclusion was amended from a 1:2 (MSAF: non-MSAF) ratio to a 1:4 ratio to deal with the limited sample size. The duration of data collection may affect the primary outcome because medical practice may be changed with time.

Definition of obstetric perineal wound infection is the infection at the incision site that occurs within 30 days after surgery and involves skin, subcutaneous tissue, or muscle located above the fascial layer and any of the following: 1 Purulent drainage from incision or drain located above the fascial layer. 2. Organism isolated from culture of fluid from wound 3. Wound dehiscence 4. Surgeon's or physician's diagnosis of infection[16]. Wound dehiscence is defined as a persistent gap between wound edges > 0.5 cm in the period of surgical site infection, involving the vaginal mucosa or the perineal muscle layers[16-17]. Each outcome in this study was collected from medical records as reported by the surgeon or physician, who made a diagnosis; however, in some cases, diagnosis including the culture result was more accurate. The identification of eligible women with MSAF was done using ICD-10 (International Classification of Diseases 10th Revision) codes, including: O800 – O809 spontaneous vertex delivery; O810 – O819 instrumental delivery; O830 – O839 breech assisted delivery; and O681 – O682 labor and delivery complicated by meconium in amniotic fluid. When reviewing the case in sequence according to the date and time of delivery and starting with the indexed case, two women who delivered without MSAF before and after the indexed case served as controls. The medical records were reviewed until the 6-week postpartum visit to confirm the occurrence of obstetric perineal wound infection and wound dehiscence and the wound healing by history taking and physical examination. Exclusion criteria included: no obstetric perineal laceration; prior maternal infection before delivery; incomplete medical records; and loss to follow-up at the postpartum visit.

Data collection involved baseline characteristics such as maternal age, parity, gestational age at delivery, number of antenatal care (ANC) visits, body mass index (BMI), along with mode of delivery, types of perineal wound (episiotomy or spontaneous tear), amniotic fluid characteristics, and maternal and neonatal outcomes. Primary outcomes were infected obstetric perineal wound and wound dehiscence, while secondary outcomes included intrapartum fever and other puerperal infections.

Statistical analysis was performed using SPSS version 22 (IBM, New York, USA). Categorical variables were presented as percentages and 95% confidence intervals (CI) and compared between groups using chi-square or Fisher exact tests, with odds ratio (OR) and 95% CI. Continuous variables were assessed for normality with Kolmogorov-Smirnov test and described as mean and standard deviation (SD) or median and interquartile range (IQR) as appropriate. Parametric data were compared using the independent t-test, while nonparametric data were compared using the Mann-Whitney U test. A p value < 0.05 was considered statistically significant.

Results

A total of 2,780 medical records were assessed for eligibility, and 950 of them met the exclusion criteria (Fig. 1). The study included 1,830 eligible women (366 cases with MSAF and 1464 controls) with a mean age of 29.5 years and a mean gestational age at delivery of 38.6 weeks (Table 1).

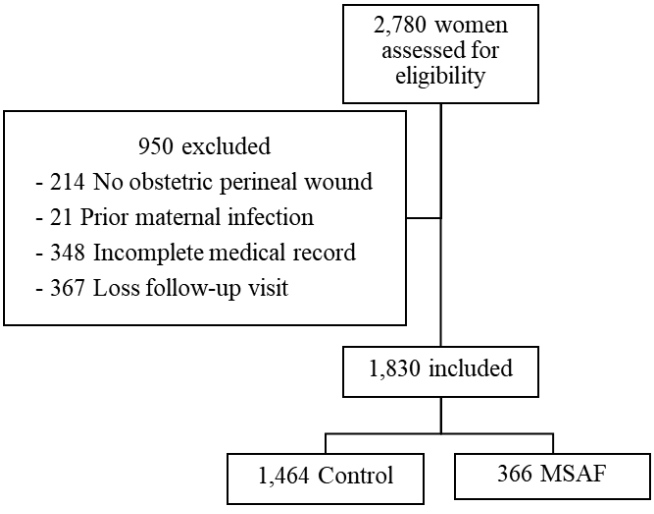

Fig. 1. Participant flow chart

MSAF: meconium-stained amniotic fluid

Table 1. Demographic data (n = 1830).

Characteristics		
Age (years)		29.5 ± 5.8
Gestational age at delivery (weeks)		38.6 ± 1.6
Number of antenatal care (times)		9.1 ± 2.6
Body mass index (kg/m^2)		21.9 ± 4.1
Parity	Nulliparous	1,161 (63.4%)
	Parous	669 (36.6%)
Mode of delivery	Spontaneous vertex delivery	1,770 (96.7%)
	Forceps extraction	48 (2.6%)
	Vacuum extraction	10 (0.5%)
	Breech assisted delivery	2 (0.1%)
Episiotomy type	None (Perineal tear)	134 (7.3%)
	Median	463 (25.3%)
	Mediolateral	1,233 (67.4%)

Data presented as mean ± standard deviation or n (%).

The majority of participants were nulliparous (63.4%), delivered by spontaneous vertex delivery (96.7%), and underwent mediolateral episiotomy (67.4%). No differences between the groups were demonstrated regarding maternal age, mode of delivery, or type of episiotomy (Table 2). However, women with MSAF had significantly higher proportions of nulliparous, term pregnancy, and poor ANC compared to the control group. The rate of infected obstetric perineal wound in the MSAF group (3.6%, 95% CI 1.89 to 6.07) was not different from that of the non-MSAF group (3.6%, 95% CI 2.65 to

4.66) with an OR of 1.0 (95% CI 0.54 to 1.86) (Table 3). Similarly, no significant difference was demonstrated in the rate of wound dehiscence between the groups (OR 0.74, 95% CI 0.28 to 1.93). Although women in the MSAF group had a significantly higher rate of intrapartum fever than those in the non-MSAF group (OR 2.95, 95% CI 1.18 to 7.38), no significant differences were observed between the groups in terms of chorioamnionitis (suspected and confirmed chorioamnionitis), and other puerperal infections (endomyometritis and septic pelvic thrombophlebitis).

Among a total of 366 patients, 336 had thin MSAF, of whom 11 developed obstetric perineal wound infection (3.27%), whereas 30 patients had thick MSAF, with 2 cases of obstetric perineal wound infection (6.67%). Wound cultures were obtained from 10 of the 13 affected women in the MSAF group. Escherichia coli was the most frequently isolated pathogen (4 cases, 40%), followed by Streptococcus agalactiae (3 cases, 30%). Klebsiella pneumoniae and Staphylococcus aureus were each isolated in 2 cases (20%), while Staphylococcus lugdunensis was detected in 1 case (10%). No growth was observed in 1 case (10%), and mixed organisms were identified in 3 cases, as previously described.

In addition, data were collected on pregnancy complications that may be related to infection; however, these were not found to significantly increase the risk of infected episiotomy wounds. These included gestational diabetes mellitus (OR 1.89, 95% CI 0.80 to 4.50), obesity (OR 0.39, 95% CI 0.05 to 2.85), and premature rupture of membranes (PROM) (OR 2.28, 95% CI 0.29 to 17.82).

Table 2. Comparison between MSAF and non-MSAF groups.

Characteristics	MSAF (n = 366)	Non-MSAF (n = 1,464)	p value
Age (years)	29.5 ± 6.0	29.4 ± 5.8	0.314
Gestational age at delivery (weeks)	39.0 ± 1.3	38.5 ± 1.6	0.001
Preterm (GA < 37 weeks)	14 (3.8%)	152 (10.4%)	< 0.001
Term (GA ≥ 37 weeks)	352 (96.2%)	1,312 (89.6%)	
Number of antenatal care visit			
Poor ANC (< 4 times)	17 (4.6%)	26 (1.8%)	0.001
Adequate ANC (≥ 4 times)	349 (95.4%)	1,438 (98.2%)	
Parity			
Nulliparous (P = 0)	256 (69.9%)	905 (61.8%)	0.004
Parous (P ≥ 1)	110 (30.1%)	559 (38.2%)	
Mode of delivery			
Spontaneous vertex delivery	349 (95.4%)	1,421 (97.1%)	0.101
Operative deliveries[a]	17 (4.6%)	43 (2.9%)	
Episiotomy type			
Perineal tear	25 (6.8%)	109 (7.4%)	
Median episiotomy	86 (23.5%)	377 (25.8%)	0.578
Mediolateral episiotomy	255 (69.7%)	978 (66.8%)	

Data presented as mean ± standard deviation or n (%).
a including forceps extraction, vacuum extraction, and breech-assisted deliveries
GA: gestational age, ANC: antenatal care, P: parity, MSAF: meconium-stained amniotic fluid

Table 3. Perineal wound infection, wound dehiscence, other maternal and puerperal infections.

Complications	MSAF (n = 366)	Non-MSAF (n = 1,464)	Odds ratio	95% CI
Obstetric perineal wound infection	13 (3.6%)	52 (3.6%)	1.0	0.54, 1.86
Wound dehiscence	5 (1.4%)	27 (1.8%)	0.74	0.28, 1.93
Intrapartum fever	8 (2.2%)	11 (0.9%)	2.95	1.18, 7.38
Chorioamnionitis	1 (0.27%)	3 (0.20%)	1.33	0.14, 12.86
Endometritis	1 (0.27%)	9 (0.61%)	0.44	0.06, 3.51
Other puerperal infections[a]	1 (0.27%)	10 (0.68%)	0.40	0.05, 3.12

[a] including endometritis and septic pelvic thrombophlebitis
MSAF: meconium-stained amniotic fluid, CI: confidence interval

Discussion

There have been no previous studies investigating the association of MSAF with complications of episiotomy wound or intrapartum fever. This study found that perineal wound infection or dehiscence did not significantly differ between women with MSAF and those in the non-MSAF group. In contrast to findings in women undergoing cesarean delivery, MSAF was found to increase the risks of chorioamnionitis and puerperal infections including endomyometritis, and postcesarean surgical site infection[4-6]. The inconsistency in the results between this study and previous ones may be related to differences in the route of delivery. While infections of episiotomy wound and postcesarean surgical wound may present similar clinical findings, they likely have distinct contributing factors. Therefore, a direct comparison of these wound infections is not feasible, and further studies are warranted to identify factors associated with episiotomy wound infection. The higher incidence of perineal wound infection in this study (3.6%), compared to the previous studies (0.5-2.8%)[14], may be the result of the persons who performed the perineorrhaphy including the training of obstetric residents.

In contrast to Wertheimer et al. (2020), who reported that MSAF in pregnancies complicated by PPROM was associated with higher rates of neonatal intensive care unit admission, chorioamnionitis, and placental abruption[24], this study did not demonstrate an increased risk of perineal wound infection or wound dehiscence among women with MSAF. The discrepancy may be attributed to differences in study populations and outcomes; PPROM represents a high-risk setting for intrauterine infection, whereas this study mainly involved term vaginal deliveries with localized surgical site complications. These findings suggest that the clinical significance of MSAF may vary according to gestational age and obstetric context.

Women with MSAF had a significantly higher rate of intrapartum fever than those in the non-MSAF group. However, meconium may be either a cause or a result of intrapartum fever, and this study was unable to establish causality. Previous studies have found that women with MSAF had a significantly higher rate of puerperal infections, including chorioamnionitis and endometritis compared to those without MSAF[4-6], while the present study demonstrated did not show any difference in the rate of puerperal infections between the groups. These inconsistent results may be attributed to various factors, including differences in populations and hospital settings.

The strengths of this study include a clear definition of both exposures and outcomes, standardized electronic medical records recorded by obstetricians, pediatricians, and nurses, and longitudinal data collection from delivery to the 6-week postpartum follow-up visit. However,

information bias may occur due to the retrospective nature of the study. The completeness of the information in the medical records depended on how thoroughly the documentation was recorded. Some details, such as the diagnostic criteria for each maternal or puerperal infection, may not be consistently approached, potentially leading to misinformation. The confounding factors such as duration of delivery, duration of membrane rupture, underlying condition that increases the risk of infection were not analyzed in this study. Only the term pregnancies recruitment may reduce the confounding factors such as infections or other stress that can cause fetal meconium release in an earlier period; therefore, this can be applied in the further studies. Additionally, differences between women with MSAF and controls in terms of gestational age at delivery, number of antenatal care visits, and parity should be considered, although these factors may not affect the primary outcome. As a hospital-based study, the findings may not be generalizable to the entire population in Thailand. These are the limitations of the study.

Despite aiming to determine whether MSAF posed a risk of obstetric perineal wound infection to inform prevention strategies, this study found no evidence of such an association. Although a significant association between MSAF and intrapartum fever was demonstrated, this factor did not increase the risks of chorioamnionitis, puerperal infections or endomyometritis. Therefore, the study suggests that MSAF does not elevate the risk of obstetric perineal wound infections. Consequently, the use of antibiotic prophylaxis in women with MSAF who deliver vaginally is not supported, and rational drug use is encouraged instead. Further prospective studies are required to support these findings.

Conclusion

The findings of this study indicated that MSAF was not associated with an increased risk of obstetric perineal wound infection or wound dehiscence. Therefore, the use of prophylactic antibiotics for vaginal delivery with MSAF is not supported.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Correlation of Transabdominal Ultrasound and Catheterization for the Assessment of Postvoid Residual Urine in Pelvic Organ Prolapse Patients

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ABSTRACT

Objectives: The aim of this study was to evaluate the correlation of postvoid residual (PVR) measurement in pelvic organ prolapse patients by transabdominal sonography (TAS) and urinary catheterization.

Materials and Methods: During November 2021 - March 2022, a cross-sectional study was conducted in newly diagnosed as pelvic organ prolapse (POP) patients stage 1-4 patients at Female Pelvic Medicine and Reconstructive Surgery (FPMRS) clinic, King Chulalongkorn Memorial hospital, Thailand. The PVR was determined by TAS and urinary catheterization. TAS was independently performed by two investigators. Each investigator performed ultrasound twice. After completed ultrasound evaluation, urinary catheterization was immediately performed.

Results: Seventy-seven POP patients were included. The mean ± standard deviation of age was 70.65 ± 9.15 years. Fifty-one percent of patients had advanced stage of prolapse. The correlation coefficients (r) of TAS and catheterization by 2 evaluators were 0.74 ($p < 0.001$) and 0.79 ($p < 0.001$). The intra-rater reliability of PVR measurement by TAS of both evaluators were 0.93 and 0.95. The inter-rater reliability of PVR measurement by TAS were 0.78 (1st measurement) and 0.79 (2nd measurement).

Conclusion: There was a high positive correlation of the PVR assessment by TAS and PVR assessment by urinary catheterization in POP patients. This technique can be used as the alternative choice for PVR measurement in patients with POP.

Keywords: transabdominal ultrasound, postvoid residual urine, pelvic organ prolapse.

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ความสัมพันธ์ระหว่างการคลื่นเสียงความถี่สูงทางหน้าท้องและการสวนปัสสาวะในการประเมินปริมาณปัสสาวะตกค้างหลังขับถ่ายในผู้ป่วยที่มีภาวะอวัยวะอุ้งเชิงกรานหย่อน

พรทิตา เลิศบัวสิน, อธิวัฒน์ ทรงศิริพันธุ์, ปุริม เรือนภู่, กีรติ เชียงทอง, สุวิทย์ บุณยะเวชชีวิน

บทคัดย่อ

วัตถุประสงค์: *เพื่อประเมินความสัมพันธ์ระหว่างการวัดปัสสาวะตกค้างหลังขับถ่าย ในผู้ป่วยที่มีภาวะอุ้งเชิงกรานหย่อนด้วยวิธีการตรวจคลื่นเสียงความถี่สูงทางหน้าท้องและการสวนปัสสาวะ*

วัสดุและวิธีการ: *การศึกษาชนิดนี้เป็นแบบตัดขวาง ในผู้ป่วยที่มีภาวะอวัยวะอุ้งเชิงกรานหย่อนรายใหม่ที่รับบริการในคลินิกเวชศาสตร์เชิงกรานสตรีและศัลยกรรมซ่อมเสริม โรงพยาบาลจุฬาลงกรณ์ ประเทศไทย ในช่วงระหว่างเดือนพฤศจิกายน 2021 ถึง มีนาคม 2022 โดยทำการวัดปริมาตรปัสสาวะตกค้างหลังการถ่ายปัสสาวะ โดยตรวจคลื่นเสียงความถี่สูงทางหน้าท้อง และการสวนปัสสาวะ การตรวจคลื่นเสียงความถี่สูงทางหน้าท้อง ดำเนินการโดยนักวิจัยสองคนแยกกัน โดยแต่ละคนทำการตรวจคลื่นเสียงความถี่สูงทางหน้าท้องสองครั้ง หลังจากประเมินด้วยคลื่นเสียงความถี่สูงทางหน้าท้องแล้ว ทำการการสวนปัสสาวะทันที*

ผลการศึกษา: *มีผู้ป่วยที่มีภาวะอวัยวะอุ้งเชิงกรานหย่อนเข้าร่วมจำนวน 77 ราย อายุเฉลี่ย ± ส่วนเบี่ยงเบนมาตรฐาน คือ 70.65 ± 9.15 ปี ร้อยละ 51 ของผู้ป่วยอยู่ในระยะที่รุนแรง ค่าสัมประสิทธิ์ความสัมพันธ์ (r) ระหว่าง การตรวจคลื่นเสียงความถี่สูงทางหน้าท้อง และการสวนปัสสาวะโดยผู้ประเมินทั้งสองอยู่ที่ 0.74 ($p < 0.001$) และ 0.79 ($p < 0.001$) ความเที่ยงของผู้ประเมินในการวัด ปัสสาวะตกค้างหลังขับถ่าย ด้วยคลื่นเสียงความถี่สูงทางหน้าท้อง อยู่ที่ 0.93 และ 0.95 ความเที่ยงของผู้ประเมินในการวัดปัสสาวะตกค้างหลังขับถ่าย ด้วยคลื่นเสียงความถี่สูงทางหน้าท้อง อยู่ที่ 0.78 (การวัดครั้งแรก) และ 0.79 (การวัดครั้งที่สอง)*

สรุป: *การประเมินปริมาณปัสสาวะตกค้างหลังขับถ่ายด้วยคลื่นเสียงความถี่สูงทางหน้าท้อง มีความสัมพันธ์ทางบวกในระดับสูงกับการประเมินโดยการสวนปัสสาวะในผู้ป่วยที่มีภาวะอวัยวะภายในอุ้งเชิงกรานหย่อน ซึ่งวิธีนี้สามารถใช้เป็นทางเลือกในการวัดปัสสาวะตกค้างหลังขับถ่าย ในผู้ป่วยที่มีภาวะอวัยวะอุ้งเชิงกรานหย่อน*

คำสำคัญ: *การตรวจคลื่นเสียงความถี่สูงทางหน้าท้อง, ปริมาณปัสสาวะตกค้างหลังขับถ่าย, อวัยวะอุ้งเชิงกรานหย่อน*

Introduction

Postvoid residual volume (PVR) is the volume of urine left in the bladder at the end of micturition which is a key marker of bladder function[1]. High PVR can be used as a diagnostic tool in evaluation of lower urinary tract dysfunction such as bladder outlet obstruction, underactive, or acontractile detrusor[1-3]. The prevalence of abnormal PVR ranges from 6-30% in patients with pelvic organ prolapse (POP)[4]. Urethral kinking caused by prolapse leads to incomplete bladder emptying and urinary retention. Apart from signs and symptoms of lower urinary tract dysfunction in women presenting with POP, PVR should be determined for early detection of lower urinary tract dysfunction.

The gold standard method for PVR measurement is urinary catheterization[5]. The disadvantages of this method include patient discomfort, infection, or an increase in the risk of urethral trauma. Because of these limitations, an alternative non-invasive method using transabdominal ultrasound (TAS) may be considered. However, the result is operator-dependent, the reliability of these diagnostic modality in women with POP should be examined. Currently, there is no study reported of the accuracy and the inter- and intra-rater reliabilities of TAS for measurement PVR in POP patients. The primary purpose of this study was to evaluate the correlation between TAS and urinary catheterization for measurement of PVR in POP patients. The secondary purposes were to assess the inter- and intra-rater reliabilities of TAS for PVR assessment in POP patients.

Materials and Methods

A cross-sectional study was conducted at female pelvic medicine and reconstructive surgery (FPMRS) clinic, King Chulalongkornkorn Memorial hospital between November 2021 - March 2022. The study protocol was approved by Institutional review board, faculty of medicine, Chulalongkorn university (IRB No 921/63). Inclusion criteria were the Thai women who was more than 20 years old, newly diagnosed as POP stage 1-4 and agree to participate this study. Pregnant women and patients who cannot follow the instruction were excluded.

After informed consent were obtained, the demographic data including age, occupation, underlying conditions, parity and route of delivery were recorded. Lower urinary tract symptoms (LUTS) such as difficult to urinate, stress urinary incontinence, urgency and urgency incontinence were also recorded. The participants were evaluated for severity of POP by pelvic organ prolapse quantification (POP-Q) system by two investigators (LP: evaluator 1 and SA: evaluator 2). Before the evaluations, both evaluators underwent the same 30 hours training to standardize the evaluation procedure. The standardization included the order of the sequences of measurements, the position of the probe, and verbal commands. The evaluation was conducted in a private examination room with low light to facilitate visualization. All cases of POP voided without any treatment or manual reduction. The TAS was immediately done after the voiding act, and the patients was taken to the examination room. The patients were asked to remove their clothes from the infra-abdominal region. Subsequently, a gel was applied to the ultrasound-conducting probe, and it was placed on the lower abdomen to locate the bladder. The probe was moved from side to side to find the bladder's largest cross-sectional and sagittal diameter. TAS was performed within 1 minute after patient voiding. Evaluator 2 performed TAS immediately after evaluator 1 finished. The evaluators did not have access to the values of each other's measurements. While one evaluator performed the TAS, the other remained outside the examination room. Urinary catheterization was done within 5 minutes from patient finished voiding by Foley catheterization 12 French unit.

Method of PVR measurement and ultrasound apparatus

A Samsung 2D, sonocare R7 model ultrasound

(Samsung Medison Co., Ltd, Seoul, Korea) was used. The procedure for measuring the residual volume of the bladder was conducted following the prolate ellipsoid method. Each investigator performed ultrasound twice. Maximum width and height in cross-sectional and sagittal planes were measured and recorded without prolapse reduction. Residual urine volume obtained by ultrasound were calculated by formula; volume = width x depth x height x 0.52[6].

After completed ultrasound examination, urinary catheterization was immediately performed for the accuracy of PVR volume. The volume from catheterization were also recorded. All processes finished within 10 minutes.

Statistical Analysis

All demographic data was analyzed by descriptive statistics. Mean ± standard deviation (SD) was used in continuous variable data. For categorial data, frequency and percentage were reported. The correlations of PVR measurement by TAS and urinary catheterization were evaluated by the Pearson's test for correlation (r). The correlation coefficients was classified as very high positive (r > 0.9-1), high positive (r = 0.7 - 0.9), moderate positive (r = 0.5 - 0.7), low positive (r = 0.3 - 0.5), negligible (r < 0.3)[7]. The inter- and intra-rater intra-class correlations (ICCs) were calculated and tested at a significant level of 5%. The determination of the ICC ≥ 0.75 was classified as excellent, 0.40 ≤ ICC < 0.75 as satisfactory and ICC < 0.40 as poor[8]. The sample size estimation was calculated from the correlation coefficient of 0.66 from the pilot study (performed with 10 prolapse participants). Assuming statistic significant difference of p value = 0.05 and 80% power, the total sample size number of 70 patients were needed. To prevent data errors, 10% of participants were added. A total of 77 participants were required in this study.

Results

The mean ± SD of age, parity, vaginal delivery, and cesarean section were 70.65 ± 9.15 years, 2.6 ± 1.58, 2.5 ± 1.58 times, 0.09 ± 2.9 times, respectively. Most patients had the POP- Q stage of 2-4 (Table 1). The number (%) of the anterior, middle, and posterior compartment prolapse stage ≥ 3 were 48.1, 42.9 and 18.2. The mean ± SD of the volume obtained from TAS and urine catheterization were 41.68 ± 29.28 and 50.09 ± 36.92, respectively (Table 1). Mean evaluation time for evaluator 1(LP) and evaluator 2(SA) were 1.56 and 1.50 minutes, respectively. The mean time from the patient finished voiding to urinary catheterization was 4.06 minutes.

There were high positive correlation coefficients (r) of the PVR measured by TAS with the PVR measured by urine catheterization (r = 0.74 (evaluator 1 (LP)) and 0.79 (evaluator 2 (SA)) (p< 0.001)) (Fig.1). A Bland-Altman plot showed agreement between two techniques with mean ± SD of the difference at 8.41 (evaluator 1 (LP)) and 10.37 (evaluator 2 (SA)) (Fig. 2).

The intra-rater reliability of TAS measurement of bladder residual urine volume was 0.93 (Evaluator 1 (LP)) and 0.95 (Evaluator 2 (SA)) (Table 2). Inter-rater reliability for PVR measurement between evaluators (SA and LP) was 0.79 (Table 3).

Table 1. Baseline characteristic of the participants (n = 77).

Characteristics	mean ± SD	minimum - maximum
Age (years)	70.65 ± 9.15	49-93
Parity (births)	2.60 ± 1.58	0-7
Vaginal delivery (times) (n = 72)	2.50 ± 1.58	1-7
Operative vaginal delivery (times)	0.25 ± 0.52	0-2
Body mass index (kg/m2)	25.39 ±4.85	14.89-39.95
Transabdominal ultrasound volume (ml)	41.68 ±29.28	3.01-129.93
Urine catheterization volume (ml)	50.09 ± 36.92	1.00-160.00
	median	**Q1, Q3**
Cesarean delivery (times) (n = 7)	1	(1, 1)
	n (%)	
Pelvic organs prolapse (Stages)		
1	2 (2.6)	
2	28 (36.4)	
3	26 (33.8)	
4	21 (27.3)	
Symptoms related with POP		
Voiding difficulty	30 (39.0)	
Reduce mass of for urinate	29 (37.6)	
Stress Urinary Incontinence	18 (23.4)	
Urgency	36 (46.8)	
Urge Urinary Incontinence	31 (40.3)	
Constipation	17 (22.1)	

SD: standard deviation, POP: pelvic organ prolapse

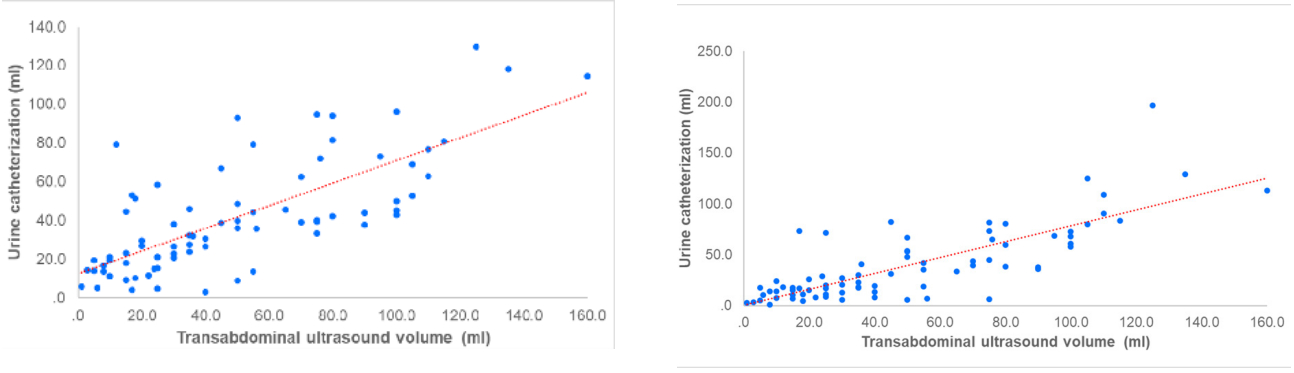

Fig. 1. Scatter plot showing the correlation coefficients (r) of postvoid residual measurement by transabdominal sonography versus urine catheterization by 2 evaluators (evaluator 1, r = 0.74 and evaluator 2, r = 0.79).

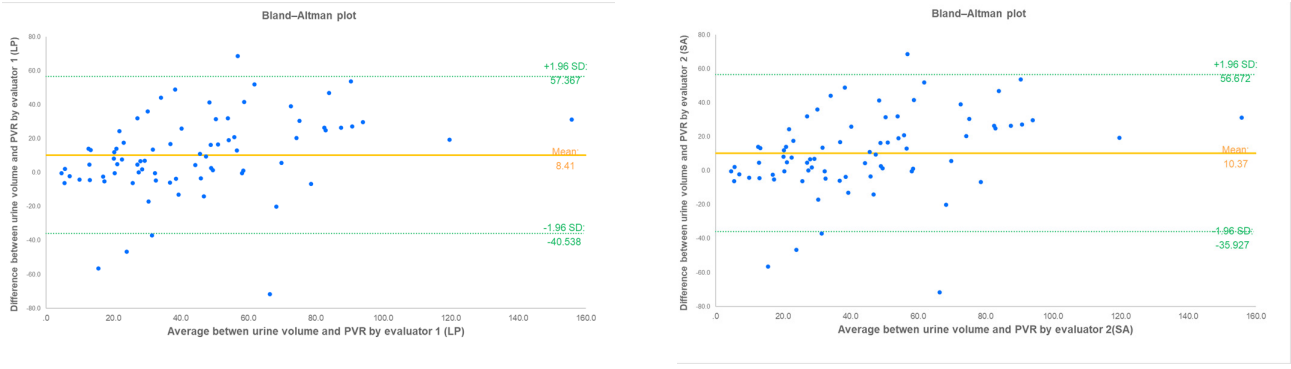

Fig. 2. Bland-Altman analysis of catheterization and transabdominal sonography volume (ml).

Table 2. Intra-rater reliability of bladder dimension measurement and transabdominal sonography volume.

Evaluator	Measure	Minimum to maximum	mean ± SD	ICC	p value
Evaluator 1	Cross-sectional plane				
	1st width (cm)	1.75-8.56	4.97 ± 1.44	0.83	< 0.001
	2nd width (cm)	1.41-8.07	4.82 ± 1.49		
	1st height (cm)	1.13-6.58	3.65 ± 1.18	0.86	< 0.001
	2nd height (cm)	1.10-7.33	3.67 ± 1.15		
	Sagittal plane				
	1st width (cm)	1.07-5.73	2.51 ± 1.01	0.76	< 0.001
	2nd width (cm)	1.00-5.88	2.51 ± 1.12		
	1st height (cm)	1.19-7.13	3.73 ± 1.22	0.81	< 0.001
	2nd height (cm)	1.24-6.44	3.68 ± 1.13		
	1st volume (ml)	2.73-120.79	42.14 ± 28.69	0.93	< 0.001
	2nd volume (ml)	3.29-142.27	41.21 ± 28.69		
Evaluator 2	Cross-sectional plane				
	1st width (cm)	1.22-8.83	4.62 ± 1.77	0.83	< 0.001
	2nd width (cm)	1.39-8.54	4.70 ± 1.76		
	1st height (cm)	1.20-6.71	3.40 ± 1.18	0.91	< 0.001
	2nd height (cm)	1.05-7.01	3.44 ± 1.30		
	Sagittal plane				
	1st width (cm)	0.87-5.88	2.81 ± 1.14	0.82	< 0.001
	2nd width (cm)	1.20-5.51	2.82 ± 0.99		
	1st height (cm)	1.22-6.70	3.40 ± 1.21	0.89	< 0.001
	2nd height (cm)	1.47-6.95	3.59 ± 1.20		
	1st volume (ml)	1.29-178.63	38.55 ± 34.85	0.95	< 0.001
	2nd volume (ml)	1.28-214.58	40.89 ± 38.76		

SD: standard deviation, ICC: inter- and intra-rater intra-class correlations

Table 3. Inter-rater reliability of bladder dimension measurement and transabdominal sonography volume.

Evaluator/ measurement	Minimum to maximum	mean ± SD	ICC	p value
Cross-sectional plane				
Evaluator 1/1st width(cm)	1.75-8.56	4.99 ± 1.45	0.59	< 0.001
Evaluator 2/1st width(cm)	2.22-8.83	4.62 ± 1.77		
Evaluator 1/2nd width(cm)	1.41-8.07	4.82 ± 1.49	0.60	< 0.001
Evaluator 2/2nd width(cm)	1.39-8.54	4.70 ± 1.76		
Evaluator 1/1st height(cm)	1.13-6.58	3.65 ± 1.18	0.61	< 0.001
Evaluator 2/1st height(cm)	1.20-6.71	3.40 ± 1.18		
Evaluator 1/2nd height(cm)	1.10-7.33	3.67 ± 1.15	0.69	< 0.001
Evaluator 2/2nd height(cm)	1.05-7.01	3.44 ± 1.30		
Sagittal plane				
Evaluator 1/1st width(cm)	1.07-5.73	2.51 ± 1.01	0.45	< 0.001
Evaluator 2/1st width(cm)	0.87-5.88	2.81 ± 1.14		
Evaluator 1/2nd width(cm)	1.00-5.88	2.51 ± 1.12	0.56	< 0.001
Evaluator 2/2nd width(cm)	1.20-5.51	2.82 ± 0.99		
Evaluator 1/1st height(cm)	1.19-7.13	3.73 ± 1.22	0.65	< 0.001
Evaluator 2/1st height(cm)	1.22-6.70	3.41 ± 1.21		
Evaluator 1/2nd height(cm)	1.24-6.36	3.68 ± 1.26	0.57	< 0.001
Evaluator 2/2nd height(cm)	1.47-6.95	3.59 ± 1.20		
Evaluator 1/ 1st volume(ml)	2.73-120.79	42.14 ± 28.69	0.78	< 0.001
Evaluator 2/1st volume(ml)	1.29-178.63	38.55 ± 34.85		
Evaluator 1 /2nd volume(ml)	3.29-142.27	41.21 ± 28.69	0.79	< 0.001
Evaluator 2/2nd volume (ml)	1.28-214.58	40.89 ± 38.76		

SD: standard deviation, ICC: inter- and intra-rater intra-class correlations

Discussion

This study demonstrated the good correlation coefficient between TAS and urinary catheterization in PVR assessment. The reliability of PVR measured by TAS was excellent. From our study, we noticed the high prevalence of LUTS in women with pelvic organ prolapse. The PVR is a key marker for bladder function assessment in this group of women and can be used for prediction of lower urinary tract dysfunction. Evaluation of residual urine volume is ideally useful for screening the patients with POP for further appropriate treatment.

From previous studies by Lertbunnaphong[9] and Yip[10], TAS had high correlation coefficient with urinary catheterization when used to determine PVR in patients without prolapse. They reported the ICC at 0.93 and 0.96, respectively. Patients with POP can have the anatomical change and lead to high PVR. The study to confirm the accuracy and reliability of using the TAS to measure the PVR in women with POP is necessary. The result from our study confirms the accuracy and reliability of TAS for PVR measurement in patients with POP. Our results were similar to previous study by Prapaspongsa et al[11]. They reported the high correlation of PVR assessed by transvaginal ultrasound with urinary catheterization.

The correlation coefficient was 0.99. Cassado et al[12] also reported the application of translabial ultrasound in POP patients for PVR measurement (ICC: 0.739-0.777).

The inter- and intra-rater reliability of transabdominal ultrasound in this study was at an excellent level. These results were similar to the previous study in non-prolapse women by Padilha et al[13]. They reported similar results (the residual inter-test volume was 0.96 and intra-test volume was 0.99).

There was a report of poor correlation of the measurement of residual urine volume by transabdominal ultrasound with the urine catheterization when the volume was lower than 100 ml[14, 15]. We found good correlations in the case of volume less than 100 ml in this study. This can be explained by the different formulas used in those reports to the formula used in this study.

PVR measured by urinary catheterization can cause infection and trauma to urethra. While the PVR measured by TAS is non-invasive and less discomfort than urinary catheterization. The TAS is simple, non-invasive, and easy to perform. It is more convenient than a transvaginal or translabial approach. Patients can re-void if the residual volume remains high. This is particularly useful because incomplete bladder emptying may not be caused solely by prolapse or bladder outlet obstruction but could also be due to some degree of bladder dysfunction. This method is advocated to use as the alternative choice for PVR measurement in patients with POP. There might be some limitations of utilizing the ultrasound measurement for residual urine in the center that the ultrasound machine was not available at the outpatient clinic. Or the service charge of using the ultrasound machine was expensive.

The strength of this study was that we compared this technique with the gold standard method (urinary catheterization). Both accuracy and reliability study were included in this study.

The limitation of this study was that there was small number of patients with advanced stage of POP (stage 4). The anatomy of advanced stage POP may be distorted more than the early stage (stage 1-2). The PVR in these patients can be higher than early stage prolapse. Further study to evaluate the accuracy of this tool in patients with advance stage of POP patients is needed to confirm the accuracy of TAS using for PVR measurement. The second limitation of this study was that there was no comparison for the measurement of PVR between reduced prolapse and non-reduced prolapse condition. Reduced prolapse may increase the accuracy of measurement PVR by TAS in POP patients. Further study to compare the correlation between reduction versus non-reduction technique in women with POP is advocated.

Conclusion

There was a high positive correlation of the PVR assessment by transabdominal ultrasound and PVR assessment by urinary catheterization in POP patients. The PVR measurement by TAS in women with POP is reliable and accurate. This technique can be used as the alternative choice for PVR measurement in patients with POP.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Effectiveness of an Educational Video on the Knowledge of Influenza and Pertussis Vaccination among Pregnant Women: A randomized controlled trial

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ABSTRACT

Objectives: To compare the knowledge of pertussis and influenza vaccines between pregnant women who received vaccine-related information through educational video and those who did not.

Materials and Methods: A randomized clinical trial was conducted at the antenatal care clinic at Siriraj Hospital. A total of 270 pregnant women, between 20-36 weeks of gestation, were randomly assigned to either receive (video group, n = 135) or not receive (control group, n = 135) information about pertussis and influenza vaccination via educational video. A questionnaire was administered before and after the intervention to assess knowledge of pertussis and influenza vaccines. Knowledge scores were compared between the two groups.

Results: The baseline characteristics of the two groups were similar, except that women in the control group were more likely to have prior knowledge about the pertussis vaccine than those in the video group ($p = 0.027$). Although pre-test knowledge scores were comparable, the post-test scores in the video group were significantly higher than those in the control group (11 vs 8 for pertussis and 8 vs 7 for influenza vaccination, $p < 0.001$). A higher proportion of women in the video group exhibited good knowledge (score ≥ 8/15 for pertussis and ≥ 6/11 for influenza vaccination) compared to the control group (88.1% vs 60% for pertussis and 91.1% vs 73.3% for influenza vaccination, $p < 0.001$). Vaccination rates were similar between the two groups: 94.4% for influenza, 96.3% for pertussis and 91.1% for both vaccines.

Conclusion: Incorporating an educational video on pertussis and influenza vaccination into routine antenatal care significantly increased pregnant women's knowledge score.

Keywords: educational video, pertussis vaccine, influenza vaccine, knowledge.

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ผลของการให้ความรู้หญิงตั้งครรภ์เกี่ยวกับวัคซีนไอกรนและวัคซีนไข้หวัดใหญ่ผ่านทางวีดิทัศน์: การทดลองแบบสุ่มและมีกลุ่มควบคุม

อรอุษา เลิศพงศาภรณ์, ภัทรวรรณ หลิ่มศิริ, ธนาภา เรขาวศิน พินนิงตัน, สุพิชญา สุรเสรีวงษ์

บทคัดย่อ

วัตถุประสงค์*: เพื่อศึกษาเปรียบเทียบความรู้เกี่ยวกับวัคซีนไอกรนและไข้หวัดใหญ่ในหญิงตั้งครรภ์กลุ่มที่ได้ดูและไม่ได้ดูวีดิทัศน์*

วัสดุและวิธีการ*: การทดลองแบบสุ่มนี้ดำเนินการที่หน่วยฝากครรภ์โรงพยาบาลศิริราช ในหญิงตั้งครรภ์จำนวน 270 ราย ที่มีอายุครรภ์ระหว่าง 20-36 สัปดาห์โดยแบ่งออกเป็นสองกลุ่ม กลุ่มที่ได้ดูวีดิทัศน์จำนวน 135 คนและกลุ่มควบคุมที่ไม่ได้ดูวีดิทัศน์จำนวน 135 คน โดยมีการตอบแบบสอบถามก่อนและหลังการทดลองเพื่อประเมินความรู้เกี่ยวกับการฉีดวัคซีนป้องกันไข้หวัดใหญ่และไอกรน*

ผลการศึกษา*: ลักษณะพื้นฐานของผู้เข้าร่วมทั้งสองกลุ่มมีความคล้ายคลึงกัน แต่ในกลุ่มควบคุมรู้จักวัคซีนป้องกันไอกรนมากกว่ากลุ่มวีดิทัศน์ ($p = 0.027$) แม้ว่าคะแนนความรู้ก่อนการทดลองจะไม่แตกต่างกัน แต่คะแนนความรู้หลังการทดลองของกลุ่มวีดิทัศน์สูงกว่ากลุ่มควบคุมอย่างมีนัยสำคัญ (11 เทียบกับ 8 สำหรับวัคซีนไอกรน และ 8 เทียบกับ 7 สำหรับวัคซีนไข้หวัดใหญ่, $p < 0.001$) นอกจากนี้พบว่าสัดส่วนของผู้ที่มีความรู้ดีโดยมีคะแนน ≥ 8/15 สำหรับวัคซีนไอกรน และ ≥ 6/11 สำหรับวัคซีนไข้หวัดใหญ่ในกลุ่มวีดิทัศน์มากกว่ากลุ่มควบคุมอย่างมีนัยสำคัญ (ร้อยละ 88.1 เทียบกับ 60 สำหรับวัคซีนไอกรน และ ร้อยละ 91.1 เทียบกับ 73.3 สำหรับวัคซีนไข้หวัดใหญ่, $p < 0.001$) อัตราการฉีดวัคซีนไข้หวัดใหญ่และไอกรนอยู่ที่ร้อยละ 94.4 และ 96.3 ตามลำดับ และหญิงตั้งครรภ์ที่ได้รับวัคซีนทั้งสองชนิดอยู่ที่ร้อยละ 91.1 โดยอัตราการฉีดวัคซีนทั้งสองกลุ่มไม่แตกต่างกัน*

สรุป*: การให้ความรู้เกี่ยวกับวัคซีนไอกรนและไข้หวัดใหญ่ผ่านทางวีดิทัศน์ระหว่างการฝากครรภ์สามารถเพิ่มความรู้ของหญิงตั้งครรภ์ได้อย่างมีนัยสำคัญ*

คำสำคัญ*: วีดิทัศน์, วัคซีนไอกรน, วัคซีนไข้หวัดใหญ่, ความรู้*

Introduction

Vaccination programs for pregnant women are designed to enhance immunity and prevent diseases, as the immune system weakens during pregnancy, increasing the risk of severe symptoms and infections. Immunity can also be transferred to fetuses, helping protect newborns from diseases before they receive their own vaccines[1]. The Advisory Committee on Immunization Practices (ACIP) and the American College of Obstetricians and Gynecologists (ACOG) recommend that all pregnant women receive an annual influenza vaccine during flu season and a pertussis vaccine between 27–36 weeks' gestation[2].

Influenza is a respiratory infection caused by influenza viruses[3]. While many recover without complications or severe symptoms, certain groups, such as individuals with underlying diseases, the elderly, small children, and pregnant women are at higher risk of severe or lethal infections[4]. In pregnant women, influenza can lead to complications and adverse effects on fetuses, such as premature labor, fetal arrhythmia, or fetal mortality[5]. The primary objective of influenza vaccines in pregnant women is to prevent infection.

Pertussis, or whooping cough, is a respiratory infection caused by the bacterium Bordetella pertussis, resulting in persistent coughing, breathing difficulties, or apnea in neonates[6]. Although the disease affects individuals of all ages, it is most prevalent and lethal in infants and young children[7, 8]. Diphtheria, tetanus, and pertussis (DTP) vaccines have been part of Thailand's expanded program of immunization (EPI) since 1977, with a reported coverage rate nearing 100%[9]. However, between 2011 and 2021, Thailand saw a steady increase in pertussis cases, primarily in neonates under two months who had not yet met vaccination requirements[10]. Studies suggest that vaccinating pregnant women can significantly reduce the risk of pertussis in neonates[11].

Despite global recommendations for influenza and pertussis vaccination in pregnant women, coverage rates for these two vaccines remain moderate. In the United States, surveys from 2020 showed vaccination rates of only 61.2% for influenza and 56.6% for pertussis, respectively. These findings suggest that vaccination rates could be improved through physician recommendations[12]. In Thailand, a survey conducted by King Chulalongkorn Memorial Hospital revealed that in 2017, only 40.5% of pregnant women accepted influenza vaccine, with physician recommendations being the most influential factor[13]. Meanwhile, the acceptance rate of pertussis vaccines in 2020 was 45.5%, but it could potentially rise to 81.9% if physician recommendations and assurances of fetal safety are guaranteed[14]. One contributing factor to moderate acceptance rates of influenza and pertussis vaccines in Thailand is insufficient information regarding the benefits of these vaccines for expectant women.

A variety of methods were employed to provide patients with recommendations, including counseling, informational brochures, and educational videos. In Thailand, numerous studies have demonstrated that educational videos can enhance patients' understanding of various topics, such as adolescent contraception and colposcopic examinations[15, 16]. Notably, a study comparing methods of nutritional counseling for pregnant women found that video-based education was equally effective as traditional face-to-face counseling[17]. However, limited research has been conducted on the use of educational videos to improve pregnant women's understanding of vaccines.

Consequently, we aimed to investigate whether educational videos on influenza and pertussis vaccines can improve knowledge and increase vaccine acceptance rates among expectant women. Furthermore, the study sought to assess pertussis and influenza vaccination rates to enhance the antenatal care system.

Materials and Methods

This prospective randomized controlled trial was conducted between August and December 2023. Women who were pregnant and visited Siriraj Hospital for antenatal care were recruited. This study was

approved by the Siriraj Institutional Review Board (IRB) on August 4, 2023 (COA No. SI 591/2023), in accordance with the ethical principles of the Declaration of Helsinki, the Belmont Report, and the CIOMS Guidelines. The clinical trial registration number was TCTR20240811002.

The study included pregnant women aged 18 years or older, between 20 and 36 weeks of gestation, who had visited an antenatal care facility. Individuals with intellectual or mental disabilities were excluded. Participants were randomly assigned to either the control group or the video intervention group using a mixed block randomization technique. To minimize bias, and maintain a consistent research environment, antenatal care and vaccine recommendations were provided obstetricians who were unaware of the study.

A two-part pre-test questionnaire was administered to both groups. Part 1 collected baseline data, such as age, gestational age, occupation, and income. Part 2 consisted of questions assessing knowledge of the influenza vaccine (11 points) and the pertussis vaccine (15 points). Each question had three potential responses: "Incorrect," "Correct," and "Uncertain." Participants were awarded one point for each correct. Good knowledge was defined as a score of more than 50% on each section of the questionnaire ($\geq$ 8 points for pertussis vaccine knowledge and $\geq$ 6 points for influenza vaccine knowledge). The questionnaire's validity was confirmed by three experts in infectious diseases of the female reproductive system, infectious diseases of medicine, and maternal-fetal medicine. A pilot study involving 20 participants assessed its reliability, resulting in Cronbach's alpha values of 0.79 for the influenza vaccine and 0.73 for the pertussis vaccine, respectively.

The control group received routine vaccine recommendations from clinicians, covering four critical topics: the importance of vaccinations, the optimal gestational age for vaccination, potential side effects, and the cost of vaccinations. Although the content may differ depending on the physician on duty at the time, these fundamental topics were consistently addressed to all. Individual counseling sessions lasted approximately 10 minutes. The video group received the same recommendations, along with access to an 11-minute educational video. Participants could view the video by scanning a QR code on any device, regardless of whether they had received physicians' recommendations or not. The video provided detailed information on pertussis and influenza, including outbreaks, the advantages of vaccination, the optimal timing during pregnancy, and contraindications.

After the interventions, both groups completed a post-test questionnaire identical to the pre-test, with an additional query regarding the prevalence of influenza and pertussis vaccination. The entire process is summarized in a flow diagram (Fig. 1). During the same appointment, participants were required to complete the post-test questionnaire promptly after receiving the recommendations, regardless of whether they had viewed the educational video. Participants in the video group were subsequently allowed to revisit the video and share it with others.

In this study, the sample size for the pertussis vaccine group was calculated to be 84 participants per group, with 80% power and a 5% significance level. This calculation was based on a study by Ratanasaengsuang et al (2022)[14], which revealed that 66.9% of participants had a high level of knowledge about pertussis vaccines. It was hypothesized that delivering information through a video could increase the proportion of participants who possessed a high level of knowledge of pertussis vaccines to 85%. For the influenza group, the sample size was determined to be 62 patients per group, based on a findings of a 2021 study by Leewongtrakul et al[13], which found that 78.5% of participants had a high level of knowledge of influenza vaccines. It was hypothesized that video-based information could raise this to 95%. The sample size was calculated to compare proportions between two independent groups, utilizing the formula for a two-proportion z-test. A total of 270 participants, including a 10% allowance for incomplete or missing questionnaires, were recruited.

Statistical analyses were performed using IBM SPSS Statistics version 23 for Windows (IBM Corp., Armonk, NY, USA). Quantitative data were presented as means and standard deviations, while qualitative data were presented as percentages. In contrast, the pre- and post-test knowledge scores were non-parametric in nature and therefore were reported as medians. The primary outcome was a comparison of the understanding of influenza and pertussis vaccines between pregnant women who received information from an educational video and those who received information from routine care. A Mann-Whitney test was used to compare the median scores between groups. The McNemar's test assessed the percentage of individuals with good knowledge levels within groups, while the chi-square test was used to compare these percentages, vaccination rates, and baseline characteristics between the two groups. Statistical significance was defined as a p value of less than 0.05.

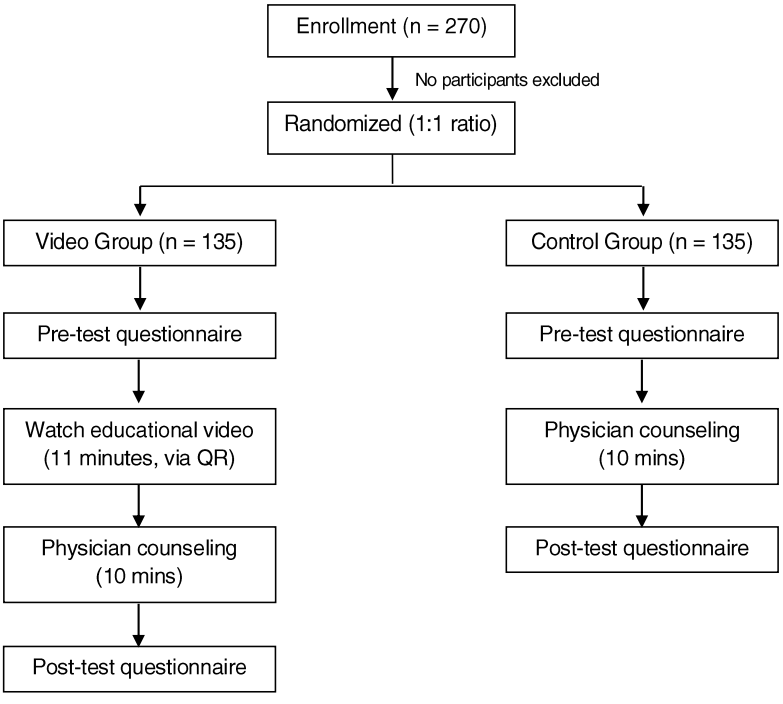

Fig. 1. Flow diagram of the randomized controlled trial.

Results

All 270 pregnant women who participated in the study submitted their questionnaires. Table 1 displays participants' characteristics, which were comparable between the two groups, including their awareness of influenza vaccination. However, awareness of pertussis vaccination was significantly higher in the control group (58.5% vs 43%, p = 0.015). Table 2 Comparisons of pre- and post-test knowledge scores on pertussis and influenza vaccines between the two groups. While the pre-test scores were similar, the study group, which received the educational video achieved substantially higher scores on the post-test for both pertussis (11 vs 8, $p < 0.001$) and influenza vaccines (8 vs 7, $p < 0.001$). The study group also possessed a considerably higher proportion of participants with good knowledge (88.1% vs 60% for pertussis, 91.1% vs 73.3% for influenza, $p < 0.001$). Significant post-test enhancements were observed in both groups ($p < 0.001$).

Table 1. Comparisons of baseline characteristics between the two groups.

Characteristics	Video group (n = 135)	Control group (n = 135)	p value
Mean age ± SD (years)	30.3 ± 6.3	30.7 ± 6.0	0.609
Mean gestational age ± SD (weeks)	28.5 ± 4.1	28.4 ± 4.0	0.812
Nulliparous	69 (51.1%)	69 (51.1%)	1.0
Education			0.280
Primary	3 (2.2%)	7 (5.2%)	
Secondary	64 (47.4%)	49 (36.3%)	
Bachelor degree	57 (42.2%)	69 (51.1%)	
Master degree	11 (8.1%)	10 (7.4%)	
Income (Baht)			0.974
< 10,000	12 (8.9%)	13 (9.6%)	
10,000 - 19,999	44 (32.6%)	47 (34.8%)	
20,000 - 39,999	52 (38.5%)	52 (38.5%)	
40,000 – 100,000	23 (17%)	20 (14.8%)	
> 100,000	4 (3%)	3 (2.2%)	
Occupation			0.935
Housewife	20 (14.8%)	22 (16.3%)	
Private practice	20 (14.8%)	20 (14.8%)	
Employee	74 (54.8%)	69 (51.1%)	
Medical personnel	5 (3.7%)	4 (3%)	
Government officer	16 (11.9%)	20 (14.8%)	
Awareness of influenza vaccination	119 (88.1%)	120 (88.9%)	0.84
Awareness of pertussis vaccination	58 (43%)	79 (58.5%)	0.015
Vaccines acquisition in previous pregnancy	**n = 66**	**n = 66**	0.378
Tdap vaccine only	19 (28.7%)	13 (19.7%)	
Influenza vaccine only	5 (7.6%)	5 (7.6%)	
Tdap and Influenza vaccine	21 (31.9%)	32 (48.5%)	
Uncertain vaccine	18 (27.3%)	13 (19.7%)	
No vaccine	3 (4.5%)	3 (4.5%)	

SD: standard deviation

Table 2. Comparisons of pre- and post-test knowledge scores on pertussis and influenza vaccines between the two groups.

	Video group (n = 135)	Control group (n = 135)	p value
Pertussis vaccine			
Median pretest scores (min, max)	6 (0, 13)	6 (0, 12)	0.275[a]
Median posttest scores (min, max)	11 (0, 14)	8 (0, 14)	< 0.001[a]
Median change (min, max)	4 (-4, 14)	2 (-4, 11)	< 0.001[a]
Pretest good knowledge scores (Scores > 8)	47 (34.8%)	51 (37.8%)	0.704[c]
Posttest good knowledge scores (Scores > 8)	119 (88.1%)[b]	81 (60%)[b]	< 0.001[c]
Influenza vaccine			
Median pretest scores (min, max)	6 (0, 10)	5 (0, 10)	0.679[a]
Median posttest scores (min, max)	8 (0, 11)	7 (0, 11)	< 0.001[a]
Median change (min, max)	3 (-3, 10)	1 (-4, 7)	< 0.001[a]
Pretest good knowledge scores (Scores > 6)	68 (50.4%)	62 (45.9%)	0.46[c]
Posttest good knowledge scores (Scores > 6)	123 (91.1%)[b]	99 (73.3%)[b]	< 0.001[c]

[a] p values (Mann-Whitney test), [b] significantly higher than pretest scores, all p values < 0.001 (McNemar's test), [c] p values (Chi-square test)

The pre-test scores of the participants suggested that most participants were aware of the pertussis vaccine's safety, but lacked knowledge about the disease and its transmission (69.6% and 2.2% correct answers in the pertussis pretest, respectively). Many were unaware that pertussis can be transmitted from family members to neonates and some believed that those vaccinated in childhood would never contract the disease (15.9% and 13%). In comparison to the control group, the study group's participants demonstrated a better understanding of pertussis infection (68.1% vs. 33.3%). The most commonly missed question in both groups concerned the transmission of pertussis from mothers to fetuses (4.1% of correct responses post-test). Regarding influenza, most participants were aware that outbreaks are prevalent in Thailand annually and believed that the vaccine is safe for expectant women (86.3% and 68.1%, respectively). The study group's participants exhibited a higher level of awareness regarding the risk of influenza vaccine allergies in people with egg allergies compared to the control group after watching the educational video (83.7% vs 48.9%). However, a common misconception persisted in both groups: that influenza cannot be transmitted from infected mothers to their infants (5.6% of correct responses post-test).

The influenza vaccination rate was 94.4%, while the pertussis vaccination rate was 96.3%. Table 3 shows the actual vaccination rates among expectant women during the study. Although the differences were not statistically significant, the study group had higher vaccination rates than the control group, particularly for pertussis (98.5% vs 94%, p = 0.264) and for those receiving both vaccines (94.1% vs 88.1%, p = 0.134).

Subgroup analyses demonstrated that the study group achieved significantly higher post-test scores than the control group, despite the control group's higher initial awareness of pertussis. The educational video significantly increased the proportion of participants with adequate knowledge among those already aware of the vaccine (from 55.2% to 96.6%, p < 0.001).

Table 3. Comparison of pertussis and influenza vaccination rates among participants during pregnancy.

Vaccination	Video group (n = 135)	Control group (n = 135)	p value
Influenza	128 (94.8%)	127 (94%)	0.857
Trivalent	74 (57.8%)	72 (56.7%)	
Tetravalent	54 (42.2%)	55 (43.3%)	
Pertussis	133 (98.5%)	127 (94%)	0.264
Tdap vaccine	117 (88%)	117 (92.1%)	
aP vaccine	16 (12%)	10 (7.9%)	
Influenza and pertussis	127 (94.1%)	119 (88.1%)	0.134

aP: acellular pertussis vaccine
Tdap: tetanus, diphtheria, and pertussis vaccine

Discussion

The results of this study demonstrated that knowledge and comprehension of pertussis and influenza vaccines among pregnant women substantially improves with the implementation of an educational video. Previous studies in Thailand and other countries have reported low vaccination coverage among expectant women. According to the health belief model, knowledge plays a key role in motivating individuals to adopt disease prevention practices[18]. Several studies have suggested that providing additional recommendations can improve coverage rates[13, 14, 19]. According to a US study, the primary reason for not receiving vaccines was a lack of knowledge, and that physician recommendations could potentially increase vaccination coverage rates[12]. In the same vein, a study conducted at King Chulalongkorn Memorial Hospital demonstrated that

patients' intention to receive pertussis vaccines was influenced by their beliefs in the safety and benefits of the vaccines[14].

Counselling, educational videos, and information brochures are some of the many methods used to provide recommendations to patients. Suthasmalee et al (2015) found that educational videos were more effective than brochures in improving patients' understanding of the colposcopic examinations[15]. Similarly, research conducted at King Chulalongkorn Memorial Hospital demonstrated that an educational video was more effective in enhancing patients' adoption of advance care plans than standard verbal advice[20]. In comparison to conventional care, a study conducted at Ramathibodi Hospital also found that educational videos could alleviate patients' anxiety during electroconvulsive therapy[21].

In contrast, a study conducted at Maharat Nakhon Ratchasima Hospital showed no significant difference between individual counseling and video-based group counseling in educating adolescents about contraception[16]. This may be due to the shorter guidance provide to the video group compared to the individual counseling group.

The use of educational videos to improve knowledge of expectant women regarding vaccines has not been investigated in Thailand. One challenge to increasing vaccination coverage through advice alone is that obstetricians typically provide antenatal care, and the content and duration of their recommendations depends on the patient. Consequently, an educational video may serve as an effective alternative to conventional counseling.

The present study's findings regarding knowledge of pertussis vaccine indicated that the percentage of individuals with good pre-intervention knowledge scores (36.3%) was lower than that observed in a study by Ratanasaengsuang et al (2022), which was conducted at King Chulalongkorn Memorial Hospital (66.9%)[14]. Similarly, the percentage of individuals with high knowledge scores in this study regarding the influenza vaccine (48.2%) was lower than in the study conducted at King Chulalongkorn Memorial Hospital by Leewongtrakul et al (2021) (78.5%)[13]. The varying results could be attributed to the higher level of education of participants in previous studies. Additionally, those studies were administered at tertiary referral hospitals using different questionnaires and individual knowledge assessments. The baseline knowledge scores in our study were significantly low, with only one-third demonstrating adequate knowledge about pertussis vaccination despite knowledge playing a critical role in maternal immunization. Despite the assessment being conducted at the beginning of the third trimester (meaning gestation 28 weeks), a period during which pregnant women are generally expected to have sufficient knowledge regarding their pregnancy and delivery. However, video-based education proved more effective in providing comprehensive information to expectant mothers, leading to substantial improvement in vaccine knowledge, nearly doubling their scores.

The highest response rates in both pre- and post-tests were related to the efficacy and safety of pertussis and influenza vaccines, indicating that public education initiatives were effective and likely contributed to high vaccination rates among participants. Along with national vaccination policies, maternal knowledge, beliefs, and attitudes play a crucial role in vaccine adoption[16].

In contrast, the lowest correct response rates were tied to misconceptions about in-utero transmission of influenza and pertussis, which can cause unnecessary anxiety. Although this misunderstanding may inadvertently increase vaccination rates, it necessitates correction. Neither the educational video nor physician advice improved understanding of this concept in this study, suggesting that these methods should be revised in future interventions.

Additionally, participants had limited baseline knowledge about the simultaneous administration of influenza and pertussis vaccines (7.0%) and the role of family members as primary sources of pertussis transmission to neonates (15.9%, respectively). Nevertheless, the educational video significantly

improved comprehension in these areas, highlighting its potential as an effective tool for enhancing vaccine-related knowledge.

With vaccination coverage rates of 94.4% for influenza, 96.3% for pertussis and 91.1% for both vaccines, this study showed notably higher vaccination coverage rates of influenza and pertussis vaccines among pregnant women, compared to previous studies in the United States (94.4% vs 61.2% for influenza vaccine; 96.3% vs 56.6% for pertussis vaccine)[12] and Thailand (94.4% vs 40.5% for influenza vaccine; 96.3% vs 45.5% for pertussis vaccine)[13, 14]. Although both the control and study groups exhibited high vaccination rates, the study group exhibited a higher vaccination rate for both pertussis and influenza vaccines compared to the control group, particularly for pertussis vaccination, though this difference was not statistically significant, likely due to the small sample size. Furthermore, the high baseline vaccination rates observed in both groups may have been influenced by standardized local vaccination protocols.

Myers et al (2016) emphasized the significant correlation between vaccine acceptance and provider recommendations, especially from obstetric providers[22]. In a survey of women in their third trimester, healthcare provider recommendations were identified as the most trusted source of information (89.1%), with a vaccine acceptance rate of 87%[23]. Our results emphasize the value of educational videos, although the high vaccination rates in this study during pregnancy may have been influenced by physician recommendations, which remain irreplaceable. This study emphasizes the critical role of education in enhancing vaccine comprehension, showing that educational videos can be a valuable addition to provider guidance, helping expectant women make informed decisions.

The study's randomized controlled trial design, along with pre- and post-tests allowed for a clear comparison of outcomes, such as vaccination rates and knowledge gains associated with each method of advice. These are key strengths of the study. The questionnaire was meticulously developed using standardized data generated by experts, and its validity was verified through a pilot study. This ensured the reliability of the collected data and helped identify specific knowledge deficits that necessitate further investigation. Additionally, the questionnaire also identified areas in which misconceptions persisted, offering valuable insights for future educational materials.

Despite significant effort in designing and developing the educational video, the study's findings emphasize the need for ongoing refinement. The questionnaire results helped pinpoint deficiencies in the current educational content, which in turn may guide future revisions to enhance its effectiveness.

However, there were some limitations. Although the counseling topics were comparable for both groups, the level of detail provided by physicians may have varied. Additionally, baseline characteristics indicated that the control group had a more comprehensive understanding of the pertussis vaccine. Yet, subgroup analysis revealed that the video was particularly effective in improving knowledge for those who already had some background on the vaccines. This suggests that a foundational level of knowledge can improve the efficacy of educational interventions.

This study emphasizes that educational videos can be an effective aid for improving vaccine comprehension and uptake, even though vaccination rates in the control group were generally high, likely due to established hospital vaccination protocols. The standardized approach in our hospital setting may have limited the ability to fully assess the video's impact on vaccination rates.

Various healthcare settings can incorporate educational videos on pertussis and influenza vaccines into antenatal care management. This approach can reduce the workload of healthcare personnel by providing a reliable and time-saving method of communicating critical information. For smaller institutions with limited resources, implementing such videos can be a practical, time-

saving alternative. In larger institutions and tertiary care settings, especially among populations with a basic understanding of vaccines, these videos can complement existing initiatives, significantly enhancing vaccine education, supporting informed decision-making, and potentially increasing vaccination rates among pregnant women.

Conclusion

The inclusion of educational videos on pertussis and influenza vaccination in routine antenatal care markedly enhanced the knowledge scores of pregnant women.

Potential conflicts of interest

The authors declare no conflicts of interest.

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GYNAECOLOGY

The Association between Preoperative Body Mass Index and Survival Outcome in Endometrial Cancer

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ABSTRACT

Objectives: This research examined the predictive value of preoperative body mass index (BMI) for progression-free survival (PFS) and overall survival (OS) of endometrial cancer (EC) patients, as well as the correlation between BMI and surgical outcomes.

Materials and Methods: EC patients who had surgery between January 2016 and October 2022 were retrospectively analyzed. Survival rates, surgical specifics, and clinicopathological features were evaluated. Survival studies employed Cox proportional hazards models and Kaplan-Meier curves.

Results: Of 252 EC patients studied, 31% were obese (BMI ≥ 30 kg/m^2). In obese individuals, endometrioid G1 histology and early-stage disease were favorable clinicopathological characteristics. Most obese people were not given adjuvant therapy. Obese individuals had a lessened paraaortic lymphadenectomy frequency. Adjuvant radiation treatment and an Eastern Cooperative Oncology Group performance level of 1 were the only significant predictors of PFS in the multivariate analysis. Age, advanced stage, histology, and surgical quality predicted OS. Patients with BMI < 30 and ≥ 30 kg/m^2 showed comparable PFS, per Kaplan–Meier curves. Obese individuals had a slightly higher 5-year OS rate.

Conclusion: EC patients' preoperative BMI affects surgical care and results. Technical difficulties during surgery reduce the frequency of full staging in obese individuals. BMI did not affect PFS, however, it may preserve OS in EC patients.

Keywords: endometrial cancer, obesity, surgical outcomes, survival.

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ความสัมพันธ์ระหว่างดัชนีมวลกายก่อนการผ่าตัดและผลลัพธ์การรอดชีวิตในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูก

พลอยทราย ตั้งอมตะกุล, กมัยธร เทียนทอง

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความสัมพันธ์ระหว่างดัชนีมวลกายก่อนการผ่าตัดต่อการรอดชีวิตปลอดโรค และการรอดชีวิตรวมในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูก รวมถึงศึกษาความสัมพันธ์ระหว่างดัชนีมวลกายก่อนการผ่าตัดและผลลัพธ์การผ่าตัด*

วัสดุและวิธีการ: *การวิเคราะห์ข้อมูลแบบย้อนหลังในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกที่ได้รับการผ่าตัดระหว่างเดือนมกราคม พ.ศ. 2559 ถึงเดือนตุลาคม พ.ศ. 2565 โดยประเมินอัตราการรอดชีวิต รายละเอียดการผ่าตัด ลักษณะทางคลินิกและพยาธิวิทยา ใช้แบบจำลองความเสี่ยงสัมพัทธ์แบบ Cox และกราฟ Kaplan-Meier เพื่อทำนายการรอดชีวิต*

ผลการศึกษา: *ในกลุ่มผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกจำนวน 252 ราย พบว่าร้อยละ 31 มีภาวะอ้วน (ค่าดัชนีมวลกายก่อนการผ่าตัด ≥ 30 กิโลกรัมต่อตารางเมตร) ในกลุ่มผู้ป่วยที่อ้วนพบว่ามีลักษณะทางคลินิกและพยาธิวิทยาที่ไม่รุนแรง เช่น พยาธิวิทยาของเนื้อเยื่อประเภท endometrioid เกรด 1 และระยะโรคในระยะแรก ผู้ป่วยส่วนใหญ่ในกลุ่มนี้ไม่ได้รับการรักษาเสริม และพบว่ามีอัตราการผ่าตัดเอาน้ำเหลืองหลอดเลือดเออร์ตาต่ำ การวิเคราะห์หลายตัวแปรพบว่า การรักษาเสริมด้วยรังสีรักษาและระดับสมรรถภาพทางร่างกายของ Eastern Cooperative Oncology Group (ECOG) ที่ระดับ 1 เป็นตัวพยากรณ์ที่สำคัญสำหรับการรอดชีวิตปลอดโรค นอกจากนี้ อายุ ระยะของโรคที่รุนแรง พยาธิวิทยาของเนื้อเยื่อและคุณภาพการผ่าตัดเป็นตัวการพยากรณ์ที่สำคัญสำหรับการรอดชีวิต การวิเคราะห์ Kaplan-Meier พบว่า ไม่มีความแตกต่างที่มีนัยสำคัญในการรอดชีวิตปลอดโรค ระหว่างผู้ป่วยที่มีค่าดัชนีมวลกายก่อนการผ่าตัด < 30 กิโลกรัมต่อตารางเมตร และผู้ป่วยที่มีค่าดัชนีมวลกายก่อนการผ่าตัด ≥ 30 กิโลกรัมต่อตารางเมตร อย่างไรก็ตาม ผู้ที่มีภาวะอ้วนมีอัตราการรอดชีวิตรวมที่ 5 ปีสูงขึ้นเล็กน้อย*

สรุป: *ค่าดัชนีมวลกายก่อนการผ่าตัดในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกส่งผลต่อการดูแลและผลลัพธ์การผ่าตัด ผู้ที่มีภาวะอ้วนมีความยากลำบากทางเทคนิคในระหว่างการผ่าตัด ทำให้การผ่าตัดเพื่อกำหนดระยะของโรคไม่สมบูรณ์ ค่าดัชนีมวลกายก่อนการผ่าตัดไม่มีผลกระทบต่อการรอดชีวิตปลอดโรค แต่มีแนวโน้มเพิ่มการรอดชีวิตรวมในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูก*

คำสำคัญ: *มะเร็งเยื่อบุโพรงมดลูก, ภาวะอ้วน, ผลลัพธ์การผ่าตัด, การรอดชีวิต*

Introduction

Over the past ten years, endometrial cancer (EC), the sixth most common cancer globally, has increased in frequency. Although incidence rates in Asian nations are generally lower than those in Western nations[1], new data from Cancer in Thailand Vol. 10 represent a 6.7 age-standardized incidence rate per 100,000 women (2016–2018). Consequently, EC has surpassed cervical cancer to become the second most common gynecologic cancer[2].

Multiple risk factors for EC have been identified, including obesity, advanced age, unopposed estrogen exposure, and nulliparity. Among all cancers, EC has the strongest association with obesity[3]. Epidemiologic and histologic evidence suggests that EC can be stratified into types I and II[4]. Type I EC is primarily estrogen-dependent and associated with excess endogenous estrogen secondary to obesity. It typically exhibits low-grade histology and carries a more favorable prognosis than type II EC[5].

Individuals with an obesity-related body mass index (BMI) (> 25 kg/m^2) are twice as likely to develop EC as those with a normal BMI. A BMI of 30 kg/m^2 or higher is considered obese. Additionally, for women with severe obesity (BMI of ≥ 35 kg/m^2), the risk is even higher, at 4.7 times higher. Furthermore, linked to a number of comorbid conditions are cardiovascular disease, diabetes mellitus, obstructive sleep apnea, and hypertension. Patients with EC may have worse prognoses as a result of these conditions, which also raise the risk of perioperative complications[6].

Currently, combined with or without a lymphadenectomy, total hysterectomy and bilateral salpingo-oophorectomy, are the standard treatments for EC. This surgical procedure can be performed through traditional laparotomy or minimally invasive approaches without compromising survival outcomes. When high-grade histology or an advanced disease stage is detected, pelvic and paraaortic lymphadenectomy is necessary to guide appropriate adjuvant therapies such as radiotherapy, chemotherapy, or both. However, performing surgery on obese patients presents challenges, including difficulties operating in a deep operative field, a heightened risk of surgical complications, a prolonged hospital stay, and increased healthcare costs. Because of these challenges, surgeons may even opt to avoid complete surgical staging, including lymphadenectomy[7]. Obesity can also pose obstacles to the delivery of adjuvant treatments. Consequently, patients with obesity may receive inadequate treatment, potentially impacting their survival outcomes[8].

This study's main goal was to determine the predictive value of preoperative BMI in order to forecast patients with EC's overall survival (OS) and progression-free survival (PFS). The second objective was to investigate the association between preoperative BMI and surgical outcomes in this particular patient population.

Materials and Methods

From January 2016 to October 2022, one super-tertiary hospital served as the site of this retrospective cohort study. We got institutional review board ethical approval from Rajavithi Hospital, Thailand (IRB number 056/2022). EC-diagnosed patients who had undergone bilateral salpingo-oophorectomy and total hysterectomy, with or without lymphadenectomy, were included in the registry. Surgeons specializing in gynecologic oncology at our hospital carried out the surgeries using laparoscopic or traditional laparotomy techniques. Individuals who had incomplete medical records and synchronous cancer were not allowed to participate in the research. The patient selection process is illustrated in Fig. 1. The staging system for surgery was determined by applying the 2009 revision of the International Federation of Gynecology and Obstetrics (FIGO). According to FIGO staging and the likelihood of recurrence, postoperative adjuvant therapies, such as chemotherapy, radiotherapy, or a combination of the two, were given.

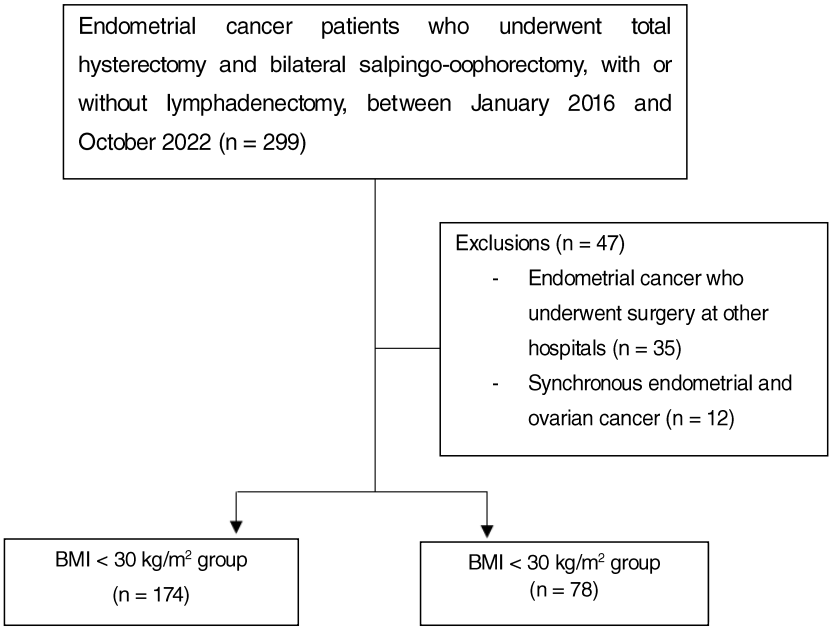

Fig. 1. Flowchart of patient selection.

Clinicopathological data were obtained from the medical records and included baseline characteristics (age at cancer diagnosis, performance status according to the Eastern Cooperative Oncology Group [ECOG], preoperative BMI, comorbidities, and currently taking medications), preoperative serum albumin level, histologic subtype, grading, and nodal status. Surgical details were also collected, including the operation date, operative findings, surgical procedure, operative duration, estimated blood loss, and residual tumor status. Other recorded variables included FIGO staging, intraoperative and postoperative complications occurring within 30 days after the operation, type and date of postoperative adjuvant treatment, and length of hospital stay. Patients were divided into two groups according to their preoperative BMI: non-obese patients (BMI of < 30 kg/m^2) and the obese group (BMI of ≥ 30 kg/m^2). The World Health Organization's international classification served as the basis for this classification of adult obesity.

The patients' care team from the gynecological oncology department routinely checked them in as outpatients after their treatment. Imaging studies were conducted on patients suspected to have recurrent disease. For such patients, treatment decisions were made based on the site and extent of the disease. Follow-up data, including the date of recurrence, site of recurrent disease, and last follow-up period, were obtained from the medical records. Disease recurrence was confirmed either histologically or clinically based on imaging findings. Both the imaging study date and the histopathological confirmation date were used to determine the date of recurrence. Through civil registration databases, the death date and cause were discovered.

In this study, PFS and OS were the main survival outcomes that were examined. The PFS was calculated by measuring the interval between the date of the operation and the date of any cause's recurrence or demise, whichever occurred first. From

the date of the operation until the patient's death from any cause or, if they were still alive at the conclusion of the study, the last follow-up date, OS was defined.

Using reference numbers from a study by Gaballa et al, the formula for testing two independent proportions served as the basis for calculating the sample size[9]. Patients with EC with a BMI of < 30 and ≥ 30 kg/m^2 had 5-year PFS rates of 78% and 58%, respectively, in the reference study. With a ratio of 2:1, the power was set to 80%, the type I error at 0.05, and the sample size was calculated to be 124 patients in the non-obese group and 62 patients in the obese group. The study aimed to include at least 137 patients with EC in the non-obese group and 69 in the obese group, taking into account a dropout rate of 10% statistical evaluation.

Statistical analysis

The chi-square test was used to analyze the categorical variables comparing patients with EC with a BMI of < 30 versus ≥ 30 kg/m^2. Frequencies and percentages of the outcomes were displayed. For normally distributed data, which were reported as mean ± standard deviation, the continuous data were evaluated using the student's t-test; for non-normally distributed data, which were reported as median and range, the Mann-Whiney U test was utilized. The Kaplan–Meier method was used to estimate the survival curves for OS and PFS. To evaluate the relationship between variables and survival outcomes, univariate and multivariate Cox regression analyses were run, taking into account covariates with a p value of < 0.1 from the univariate analysis. For the entire cohort, risk ratios (HRs) and 95% confidence intervals (CI) were provided. The statistical analyses conducted with Stata version 17 (StataCorp, College Station, TX, USA) revealed a statistically significant difference when p values of < 0.05 or when the null hypothesis was excluded by 95% CI.

Results

The study included 252 patients with EC who underwent surgery at a single super-tertiary hospital between January 2016 and October 2022. 78 (31%) and 174 (69%) of these patients had BMIs of ≥ 30 kg/m^2 and < 30 kg/m^2, respectively. The average BMI values for the obesity and non-obesity groups were 34.83 kg/m^2 and 24.11 kg/m^2, respectively. According to BMI, Table 1 displays the clinicopathological features of the patients. Individuals who had a BMI of 30 kg/m^2 or higher were considerably younger (mean age, 54.83 ± 11.52 vs 58.79 ± 9.93 years; p=0.006) and exhibited a greater occurrence of hypertension (64.1% vs 47.1%, p=0.013) and additional comorbidities like cardiovascular or thyroid conditions (15.4% vs 6.3%, p=0.021). Additionally, a greater percentage of patients with a BMI of 30 kg/m^2 were assigned to FIGO stage I (75.6% vs 60.3% compared to 60.9%, p = 0.023) and had endometrioid G1 histology (60.3% vs 38.5%, p = 0.001). Furthermore, the proportion of patients who did not receive adjuvant treatment was significantly higher in the obese group (47.4% vs 27%, p < 0.002).

The operative data and surgical complications are shown in Table 2 based on BMI. The laparotomy technique was used for surgery in 82% of the cases. Less frequently than patients with a BMI of < 30 kg/m^2, patients with a BMI of ≥ 30 kg/m^2 underwent paraaortic lymph node sampling, bilateral pelvic lymph node dissection, bilateral salpingo-oophorectomy, and total hysterectomy (35.9% vs 67.2%, p < 0.001). Furthermore, no discernible variations were found in terms of the amount of residual illness, the estimated blood loss, the length of the operation, the hospital stay, or the intraoperative complications. Postoperative complications, including fever, bowel ileus, and surgical site infection, were rare and failed to identify any statistically significant distinctions between the two groups.

Table 1. Clinicopathological characteristics according to BMI.

	BMI < 30 kg/m² (n = 174)	BMI ≥ 30 kg/m² (n = 78)	p value
Age (years)	58.79 ± 9.93	54.83 ± 11.52	0.006*
Co-morbidity			
No	99 (56.9%)	52 (66.7%)	0.143
DM	47 (27%)	25 (32.1%)	0.413
HT	82 (47.1%)	50 (64.1%)	0.013*
DLP	41 (23.6%)	26 (33.3%)	0.105
Other	11 (6.3%)	12 (15.4%)	0.021*
Current medication			
ASA	22 (12.6%)	10 (12.8%)	0.969
MFM	43 (24.7%)	23 (29.5%)	0.426
Statin	47 (27%)	30 (38.5%)	0.068
Other	77 (44.3%)	46 (59%)	0.031*
Preoperative Albumin (g/dL)	4.32 ± 0.45	4.33 ± 0.38	0.811
Previous abdominal surgery	26 (14.9%)	10 (12.8%)	0.656
ECOG			
0	127 (73%)	61 (78.2%)	0.379
1	47 (27%)	17 (21.8%)	0.379
Preoperative adjuvant treatment			
No	173 (99.4%)	78 (100%)	0.502
Radiation	1 (0.6%)	0 (0%)	0.502
FIGO Stage			
I	106 (60.9%)	59 (75.6%)	0.023*
II	18 (10.3%)	5 (6.4%)	0.316
III	38 (21.8%)	12 (15.4%)	0.235
IV	12 (6.9%)	2 (2.6%)	0.165
Histology			
Endometrioid G1	67 (38.5%)	47 (60.3%)	0.001*
Endometrioid G2	35 (20.1%)	21 (26.9%)	0.229
Endometrioid G3	41 (23.6%)	4 (5.1%)	<0.001*
Carcinosarcoma	12 (6.9%)	1 (1.3%)	0.063
Serous carcinoma	5 (2.9%)	2 (2.6%)	0.890
Clear cell carcinoma	14 (8%)	3 (3.8%)	0.219
Adjuvant treatment			
No	47 (27%)	37 (47.4%)	0.002*
Radiation	46 (26.4%)	24 (30.8%)	0.478
Chemotherapy	61 (35.1%)	11 (14.1%)	0.001*
Chemotherapy and Radiation	20 (11.5%)	6 (7.7%)	0.359

DM: Diabetes Mellitus, HT: Hypertension, DLP: Dyslipidemia, ASA: Aspirin, MFM: Metformin

Table 2. Operative data and surgical complications according to BMI.

	BMI < 30 kg/m² (n = 174)	BMI ≥ 30 kg/m² (n = 78)	p value
Type of operation			
TAH with BSO	8 (4.6%)	14 (17.9%)	0.001*
TAH with BSO with BPND	39 (22.4%)	26 (33.3%)	0.067
TAH with BSO with BPND with PANS	98 (56.3%)	22 (28.2%)	< 0.001*
TLH with BSO	1 (0.6%)	3 (3.8%)	0.055
TLH with BSO with BPND	9 (5.2%)	7 (9%)	0.253
TLH with BSO with BPND with PANS	19 (10.9%)	6 (7.7%)	0.428
Residual disease			
No	160 (92%)	76 (97.4%)	0.099
< 1 cm	4 (2.3%)	1 (1.3%)	0.593
≥ 1 cm	10 (5.7%)	1 (1.3%)	0.109
Estimated blood loss (ml)	546.26 ± 268.54	313.33 ± 217.42	0.367
Operative time (minutes)	172.19 ± 46.77	169.04 ± 49.23	0.627
Hospital stays (days)	4.9 ± 2.75	4.46 ± 1.53	0.192
Intraoperative complications			
Blood transfusion	19 (10.9%)	3 (3.8%)	0.066
Bowel injury	2 (1.1%)	1 (1.3%)	0.929
Other	4 (2.3%)	0 (0%)	0.177
Postoperative complications			
Surgical site infection	4 (2.3%)	1 (1.3%)	0.593
Postoperative fever	2 (1.1%)	1 (1.3%)	0.929
Other	0 (0%)	1 (1.3%)	0.135

TAH: Total abdominal hysterectomy, TLH: Total laparoscopic hysterectomy, BSO: Bilateral salpingo-oophorectomy, BPND: Bilateral pelvic lymph node dissection, PANS: Paraaortic lymph node sampling

In Table 3, the PFS univariate and multivariate analysis results are displayed. The univariate analysis revealed that non-endometrioid histology, high-grade histology, adjuvant radiation therapy, adjuvant combined chemotherapy and radiation, low preoperative albumin level (< 3.5 g/dL), ECOG performance status of 1, FIGO stage III/IV, and non-optimal surgery were independent poor prognostic factors for PFS. When aspirin was taken, the chance of recurrence was also significantly decreased. The only significant prognostic factors for PFS that remained in the multivariate analysis, however, were an ECOG performance status of 1 (adjusted HR [95% CI] 2.71 [1.31–5.6]; p = 0.007) and adjuvant radiation therapy (adjusted HR [95% CI] 4.03 [1.22–13.29]; p = 0.022).

Table 4 displays the OS univariate and multivariate analysis results. An age > 60 years, a low preoperative albumin level (< 3.5 g/dL), ECOG performance status of 1, FIGO stage III/IV, non-endometrioid histology, high-grade histology, adjuvant chemotherapy, adjuvant combined chemotherapy and radiation, lymphadenectomy, were found to be separate poor prognostic factors for OS, as was suboptimal surgery. Hypertension and aspirin use were linked to a significantly lower risk of death among patients with a BMI of ≥ 30 kg/m². In the multivariate analysis, an age of > 60 years, non-endometrioid histology, FIGO stage III/IV, and suboptimal surgery continued to be highly unfavorable prognostic factors for OS. Furthermore, in the multivariate analysis, hypertension significantly reduced the risk of death.

Table 3. Univariate and multivariate analysis of prognostic factors for PFS.

Characteristics	Univariate		Multivariate	
	HR (95% CI)	p value	Adjusted HR (95% CI)	p value
BMI (kg/m^2)				
< 30	1			
≥ 30	0.8 (0.39, 1.66)	0.552		
Age (years)				
< 60	1			
≥ 60	1.48 (0.77, 2.82)	0.238		
Underlying disease				
No	1.31 (0.69, 2.5)	0.411		
DM	0.91 (0.44, 1.89)	0.806		
HT	0.6 (0.31, 1.16)	0.131		
DLP	0.89 (0.42, 1.88)	0.754		
Current medication				
ASA	0.17 (0.02, 1.27)	0.084*	0.16 (0.02, 1.17)	0.071
MFM	1.04 (0.5, 2.15)	0.919		
Statin	0.84 (0.41, 1.73)	0.635		
Preoperative albumin (g/dL)				
≥ 3.5	1		1	
< 3.5	3.78 (1.34, 10.69)	0.012*	2.86 (0.81, 10.19)	0.104
ECOG				
0	1		1	
1	3.52 (1.85, 6.71)	<0.001*	2.71 (1.31, 5.6)	0.007*
FIGO Stage				
I/II	1		1	
III/IV	2.81 (1.47, 5.37)	0.002*	1.3 (0.56, 3.03)	0.539
Histology				
Endometrioid	1		1	
Non-endometrioid	2.81 (1.39, 5.69)	0.004*	1.85 (0.75, 4.55)	0.181
Adjuvant treatment				
No	1		1	
Radiation	3.51 (1.12, 11.04)	0.031*	4.03 (1.22, 13.29)	0.022*
Chemotherapy	1.66 (0.3, 9.04)	0.56		
Chemotherapy and radiation	6.91 (2.36, 20.24)	<0.001*	0.81 (0.14, 4.73)	0.818
Type of operation				
Laparotomy	1			
Laparoscopy	1.13 (0.5, 2.58)	0.768		
Lymphadenectomy				
No	1			
BPND	0.98 (0.31, 3.03)	0.966		
BPND and PANS	0.96 (0.33, 2.79)	0.939		
Optimal surgery				
Yes	1		1	
No	2.65 (1.03, 6.81)	0.043*	1.03 (0.32, 0.33)	0.96

DM: Diabetes Mellitus, HT: Hypertension, DLP: Dyslipidemia, ASA: Aspirin, MFM: Metformin, BPND: Bilateral pelvic lymph node dissection, PANS: Paraaortic lymph node sampling

Table 4. Univariate and multivariate analysis of prognostic factors for OS.

Characteristics	Univariate		Multivariate	
	HR (95% CI)	p value	Adjusted HR (95% CI)	p value
BMI (kg/m^2)				
< 30	1		1	
≥ 30	0.46 (0.22, 0.94)	0.035*	0.84 (0.37, 1.9)	0.676
Age (years)				
< 60	1		1	
≥ 60	2.37 (1.33, 4.23)	0.003*	2.79 (1.43, 5.43)	0.003*
Underlying disease				
No	1.32 (0.75, 2.29)	0.334		
DM	1.06 (0.58, 1.94)	0.854		
HT	0.57 (0.32, 1.01)	0.053*	0.41 (0.2, 0.83)	0.014*
DLP	0.76 (0.39, 1.48)	0.417		
Current medication				
ASA	0.26 (0.06, 1.05)	0.058*	0.27 (0.06, 1.2)	0.085
MFM	0.96 (0.51, 1.81)	0.91		
Statin	0.88 (0.47, 1.63)	0.677		
Pre-operative albumin (g/dL)				
≥ 3.5	1		1	
< 3.5	6.11 (2.6, 14.36)	<0.001*	2.28 (0.75, 6.91)	0.145
ECOG				
0	1		1	
1	2.64 (1.51, 4.61)	0.001*	1.98 (0.97, 4.07)	0.062
FIGO Stage				
I/II	1		1	
III/IV	3.05 (1.75, 5.32)	<0.001*	2.74 (1.06, 7.12)	0.038*
Histology				
Endometrioid	1		1	
Non-endometrioid	4.12 (2.29, 7.41)	<0.001*	2.67 (1.18, 6.03)	0.018*
Adjuvant treatment				
No	1		1	
Radiation	1.91 (0.83, 4.41)	0.13		
Chemotherapy	2.45 (0.87, 6.87)	0.09*	0.6 (0.18, 1.97)	0.397
Chemotherapy and radiation	3.08 (1.41, 6.73)	0.005*	0.64 (0.2, 2.05)	0.449
Type of operation				
Laparotomy	1			
Laparoscopy	0.8 (0.4, 1.6)	0.527		
Lymphadenectomy				
No	1		1	
BPND	3.78 (1.17, 12.23)	0.027*	1.32 (0.39, 4.52)	0.656
BPND and PANS	8.29 (3.85, 17.85)	<0.001*	1.09 (0.34, 3.48)	0.88
Optimal surgery				
Yes	1		1	
No	6.24 (3.18, 12.21)	<0.001*	2.72 (1.12, 6.61)	0.027*

DM: Diabetes Mellitus, HT: Hypertension, DLP: Dyslipidemia, ASA: Aspirin, MFM: Metformin, BPND: Bilateral pelvic lymph node dissection, PANS: Paraaortic lymph node sampling

The Kaplan-Meier survival analyses for overall PFS is presented in Fig. 2a. The overall 5-year PFS rates were 85.6% (95% CI 79.4%–90.0%) in the non-obese group and 87.2% (95% CI 77.5%–92.9%) in the obese group, with a median follow-up period of 68 months. Although the obese group exhibited a slightly higher PFS rate than the non-obese group, the difference was not statistically significant (p = 0.552). When stratified by disease stage, as illustrated in Fig. 3, early-stage patients had 5-year PFS rates of 89.5% (95% CI 82.6%–93.8%) in the non-obese group and 92.9% (95% CI 82.2%–96.7%) in the obese group (p = 0.367). Although the trend suggests a slightly better PFS in obese patients, no statistically significant difference was observed. Furthermore, advanced-stage patients exhibited lower 5-year PFS rates, with the non-obese group at 75.5% (95% CI 61.0%–85.3%) and the obese group at 64.3% (95% CI 34.3%–83.3%), though this difference was not statistically significant (p = 0.457).

The Kaplan-Meier survival analyses for overall OS is shown in Fig. 2b. The overall 5-year OS rate was significantly higher in the obese group (88.5%, 95% CI 79.0%–93.8%) compared to the non-obese group (79.2%, 95% CI 72.4%–84.5%), with a statistically significant correlation observed (p = 0.03) via Cox proportional hazards regression analysis. When stratified by stage as shown in Fig. 4, early-stage patients had 5-year OS rates of 84.7% (95% CI, 77.0%–89.9%) in the non-obese group and 93.8% (95% CI, 84.2%–97.6%) in the obese group (p = 0.026). However, in advanced-stage disease, OS rates were comparable between the two groups (65.4%, 95% CI 50.4%–76.9% for non-obese vs 64.3%, 95% CI 34.3%–83.3% for obese), with no statistically significant difference (p = 0.876).

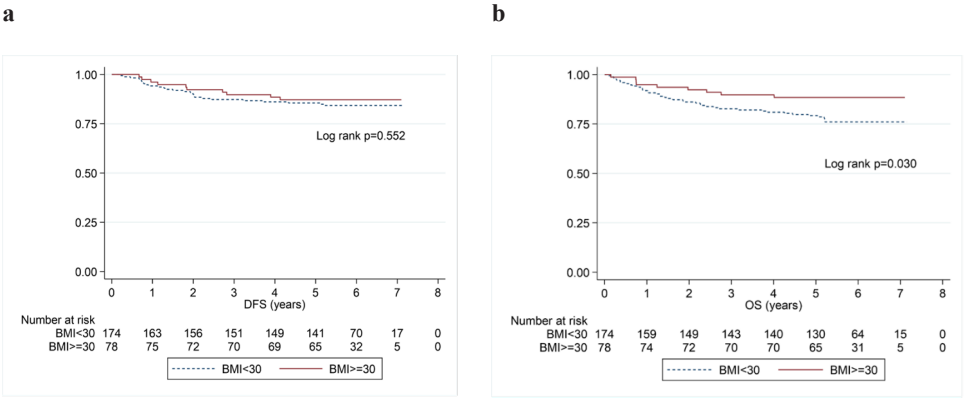

Fig. 2. Kaplan Meier Curves of overall PFS (a) and OS (b).

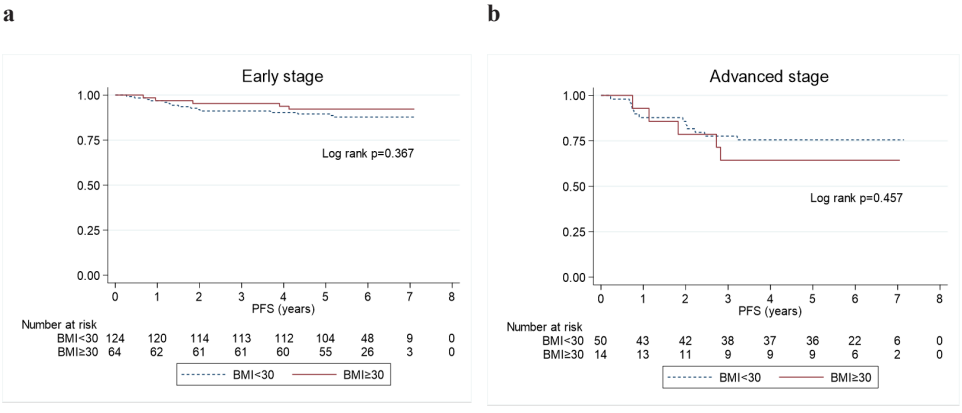

Fig. 3. Kaplan Meier Curves of PFS stratified by early (a) and advanced disease stages (b).

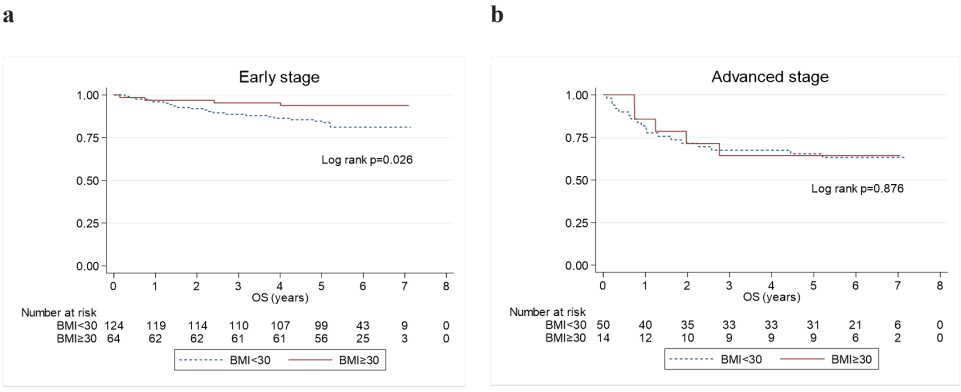

Fig. 4. Kaplan Meier Curves of OS stratified by early (a) and advanced disease stages (b).

Discussion

As an established risk factor for several metabolic diseases and cancers, including EC, obesity is a well-known public health concern. There are two subsets of EC: type I and type II. Eighty percent of EC cases are type I tumors, which are often dependent on estrogen, have low-grade endometrioid histology, and often develop against a backdrop of hyperplasia. On the other hand, type II tumors are commonly associated with high-grade features, arise within atrophic endometrium, and are less likely to be estrogen dependent. Obesity has been linked to a 2.7-time increase in type I tumor development and a 1.8-time increase in type II tumor development in women. Furthermore, individuals with metabolic syndrome a condition characterized by the co-occurrence of abdominal obesity, diabetes mellitus, hypertension, and dyslipidemia—have a two fold increased risk of developing EC[10].

Numerous mechanisms mediate the hormonal impact of obesity on EC. Adipocytes in the peripheral fat of obese people use aromatase to convert androgens to estrone and estradiol. Additionally, sex hormone-binding globulin levels are linked to decreased in obesity, which raises levels of bioactive estrogen. Estrogen metabolites function as mutagens, forming adducts with DNA and causing a build-up of double-stranded DNA breaks, which exacerbates genetic instability. Additionally contributing to cellular stress and genetic instability, adipokine-mediated inflammation and the production of mitochondrial reactive oxygen species in obesity further encourage mutagenesis[11].

For patients with gynecologic cancer, treatment modalities that are adversely affected by obesity include radiation, chemotherapy, and surgery. Due to variables including body weight and comorbidities that may reduce surgical tolerance or feasibility, obese patients may have difficulty obtaining standard care. The fact that obesity is commonly linked to other comorbid conditions like diabetes mellitus, cardiovascular disease, and obstructive sleep apnea complicates the safe administration of surgical procedures even more[12]. Regardless of whether the surgery was done via laparotomy or laparoscopy, the rate of pelvic lymph node dissection in the current study was similar across the BMI groups. However, patients who had a BMI of ≥ 30 kg/m^2 and underwent surgical staging by laparotomy had a significantly lower rate of paraaortic lymph node sampling. This finding implies that, in comparison to patients with a BMI of < 30 kg/m^2, patients who are obese may have inadequate lymph node assessment due to the technical difficulties in exposing and accessing the deep surgical fields. This kind of data is crucial for directing adjuvant treatments. In patients with a BMI of ≥ 30 kg/m^2, we also observed a trend toward shorter operative times, shorter hospital stays, and lower estimated blood loss volumes. This trend may be related to the lower rate of complete surgical staging

in this population. Between the two BMI groups, there were no appreciable variations in intraoperative or postoperative complications, though. In contrast, a comprehensive analysis found that women with a BMI below 30 kg/m^2 had considerably reduced estimated blood loss, shorter operational times, shorter hospital stays, and decreased incidence of perioperative problems compared to women with a BMI of 30 kg/m^2 or above[13]. In the present study, the higher rate of no adjuvant treatment in the obesity group can be attributed to the higher percentages of younger patients, FIGO stage I disease, and low-grade histology. This finding contrasted with another study in which the need for adjuvant treatment was similar between obese and non-obese patients[14].

Obesity's effect on PFS and OS in EC patients is still debatable[15, 16]. A prospective cohort study with > 900,000 participants revealed that a BMI of > 40 kg/m^2 was linked to a 60% increased risk of dying from any cancer. For patients with a BMI of 30-34 and > 40 kg/m^2, the relative risk of dying from EC ranged from 2.53 to 6.25, respectively[17]. In our study, we found a higher overall OS rate in patients with a BMI of ≥ 30 kg/m^2, despite the low rate of complete surgical staging in this population. The lower FIGO stage and the greater frequency of low-grade histology may explain this finding. This result remained significant even after stratifying patients in the early-stage group. However, in advanced-stage disease, the survival advantage was no longer apparent. This suggests that the potential protective effect of obesity may be limited to early-stage disease, whereas in advanced-stage cases, other factors such as tumor burden, treatment resistance, and comorbidities may play a more significant role in survival outcomes. We also discovered a higher incidence of type I EC in obese patients, which was consistent with other studies[9, 18]. Furthermore, the univariate analysis significantly linked aspirin use to a lower risk of death and recurrence; however, the multivariate analysis did not support this association. Arem along with others15 examined 12 researches on the prognosis for EC and obesity. In 7 of these 12 studies, the BMI and specific mortality did not consistently correlate, according to the authors; however, some studies suggested that obesity patients had lower grades and stages as well as higher all-cause mortality[15]. Güzel and associates compared to patients with a BMI of < 40 kg/m^2, there was a non-statistically significant trend toward lower PFS and OS in patients with morbid obesity[19]. In an ancillary data analysis from the Gynecologic Oncology Group LAP2 study, obesity was associated with death from all causes but not from cancer[7]. An independent study conducted by Gaballa and colleagues revealed no connection between survival and obesity. The correlation between obesity and enhanced OS raises intriguing questions about the underlying mechanisms[9]. More research is needed to understand the complex interactions between obesity, tumor biology, and treatment response in patients with EC.

The retrospective cohort study design, along with its performance at a single academic cancer center recognized for its aggressive surgical management, is a noteworthy strength. Nevertheless, it's critical to acknowledge the study's three main limitations. To begin with, the retrospective design of the study has built-in limitations, including biases and a reliance on easily accessible medical records. Second, the study cohort comprised only a small number of laparoscopic surgeries. It's possible that the small sample size had an impact on the actual surgical results, particularly in terms of the estimated blood loss and operating time. Third, the survival analysis did not account for cause-specific mortality, which may affect the interpretation of overall survival outcomes. It is therefore important to use caution when extrapolating the results of this study to broaden demographics or different surgical contexts.

Conclusion

Our findings suggested that patients with EC who had a BMI of ≥ 30 kg/m^2 exhibited no significant difference in PFS but had significantly longer OS than those with a BMI of < 30 kg/m^2. Adjuvant radiation therapy and an ECOG performance status of 1 were found to be independent predictors of PFS. Older age

(> 60 years), advanced FIGO stage (III/IV), non-endometrioid histology, and non-optimal surgery were significantly poor prognostic factors for OS.

Potential conflicts of interest

The authors declare no conflicts of interest.

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OBSTETRICS

The Effectiveness of Telemedicine for Pregnant Women with Gestational Diabetes Mellitus at Nong Khai Hospital

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ABSTRACT

Objectives: To evaluate the effectiveness of telemedicine in managing and controlling gestational diabetes mellitus (GDM) among pregnant women.

Materials and Methods: This study was a randomized controlled trial, in which the experimental group received telemedicine care, while the control group received standard care. The effectiveness was assessed based on maternal blood sugar control, weight gain during pregnancy, delivery outcomes, and neonatal outcomes. A total of 40 participants were enrolled, with 20 in each group.

Results: The group using telemedicine had exhibited better blood sugar control than the control group, with 95% of the experimental group managing their blood sugar effectively compared to 50% in the control group. Additionally, the experimental group showed less weight gain during pregnancy. There were no statistically significant differences in neonatal outcomes between the two groups.

Conclusion: This study demonstrated that telemedicine could be effective in helping pregnant women with GDM control their blood sugar levels without adverse effects on neonatal outcomes. Moreover, telemedicine had enabled the pregnant women to manage their diabetes mellitus more effectively through continuous monitoring by remote healthcare providers.

Keywords: telemedicine, gestational diabetes mellitus, blood sugar control.

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ประสิทธิภาพของการแพทย์ทางไกลสำหรับหญิงที่เป็นเบาหวานขณะตั้งครรภ์ที่โรงพยาบาลหนองคาย

รัฐวิชญ์ สุนทร

บทคัดย่อ

วัตถุประสงค์*: เพื่อประเมินประสิทธิภาพของการแพทย์ทางไกล (telemedicine) ในการดูแลและควบคุมโรคเบาหวานในหญิงตั้งครรภ์ที่เป็นเบาหวานขณะตั้งครรภ์*

วัสดุและวิธีการ*: การศึกษานี้เป็นการสุ่มแบ่งกลุ่มแบบควบคุม (randomized controlled trial) โดยกลุ่มทดลองได้รับการดูแลผ่านระบบการแพทย์ทางไกล (telemedicine) และกลุ่มควบคุมได้รับการดูแลตามปกติ มีการประเมินประสิทธิภาพโดยวัดจากการควบคุมระดับน้ำตาลในเลือดของมารดา น้ำหนักตัวที่เพิ่มขึ้นระหว่างตั้งครรภ์ การคลอด และผลลัพธ์ของทารก จำนวนอาสาสมัครทั้งหมด 40 คน แบ่งเป็นกลุ่มละ 20 คน*

ผลการศึกษา*: กลุ่มที่ใช้การแพทย์ทางไกล (telemedicine) สามารถควบคุมระดับน้ำตาลในเลือดได้ดีกว่ากลุ่มควบคุม โดยพบว่ามีการควบคุมระดับน้ำตาลในเลือดมีประสิทธิภาพถึงร้อยละ 95 เมื่อเทียบกับกลุ่มควบคุมที่ร้อยละ 50 นอกจากนี้ กลุ่มทดลองยังมีน้ำหนักตัวที่เพิ่มขึ้นระหว่างตั้งครรภ์น้อยกว่า ผลลัพธ์ของทารกในทั้งสองกลุ่มไม่มีความแตกต่างที่มีนัยสำคัญทางสถิติ*

สรุป*: การศึกษานี้ชี้ให้เห็นว่าการแพทย์ทางไกล (telemedicine) มีประสิทธิภาพในการช่วยควบคุมระดับน้ำตาลในเลือดของหญิงตั้งครรภ์ที่เป็นเบาหวานขณะตั้งครรภ์ โดยไม่ส่งผลเสียต่อผลลัพธ์ของทารก นอกจากนี้ ยังช่วยให้หญิงตั้งครรภ์สามารถจัดการโรคเบาหวานได้ดีขึ้น ด้วยการติดตามจากแพทย์ทางไกลอย่างต่อเนื่อง*

คำสำคัญ*: การแพทย์ทางไกล,เบาหวาน,ควบคุมระดับน้ำตาลในเลือด*

Introduction

Gestational diabetes mellitus (GDM) affects 15% of pregnancies and is the most common metabolic complication during pregnancy[1]. In the past, perinatal mortality rates have been significantly high, but with advancements in understanding the pathophysiology, insulin therapy, fetal monitoring, and appropriate delivery planning, perinatal mortality has now decreased to rates close to those of non-diabetic pregnancies[2]. GDM can be classified into two types. Firstly, GDM, which is diagnosed during pregnancy and accounts for 90% of diabetes mellitus cases in pregnant women, often emerges between 24-28 weeks of gestation (late second to third trimester). This condition can lead to macrosomia, shoulder dystocia, and preterm labor[3]. Secondly, pregestational diabetes mellitus (overt DM), which is diagnosed before pregnancy and includes both type 1 and type 2 diabetes mellitus, carries a higher risk of complications, such as miscarriage and fetal anomalies[4].

Inadequate glycemic control during pregnancy can have detrimental effects on both maternal and fetal health. Maternal complications include a fourfold increased risk of preeclampsia[5], polyhydramnios due to fetal hyperglycemia, and an increased susceptibility to infections, such as pyelonephritis and respiratory or urinary tract infections[6]. Furthermore, during pregnancy, poorly controlled diabetes mellitus can lead to postpartum hemorrhage and an elevated maternal mortality rate, which is often due to diabetic ketoacidosis, hypertensive disorders, or superimposed cardiac conditions[7]. Neonatal complications include an increased risk of neonatal hypoglycemia, with rates ranging from 8-30%[8], and birth asphyxia, which affects approximately 2-23% of infants that are born to mothers with diabetes mellitus[9].

Given its capacity for continuous and real-time monitoring, telemedicine has emerged as a critical tool that can be used to manage chronic diseases, particularly among those pregnant women who have been diagnosed with diabetes mellitus. This approach provides patients with immediate access to healthcare professionals without the need for frequent in-person clinic visits and thereby reduces travel burdens and enhances convenience. In high-risk populations, such as GDM, telemedicine has been especially beneficial because frequent monitoring and timely therapeutic adjustments are pivotal in order to achieve optimal glycemic control and minimize adverse outcomes[10].

The COVID-19 pandemic further accelerated the adoption of digital health technologies, including telemedicine, in obstetrics and gynecology practices around the world. In Thailand, for instance, telemedicine was rapidly integrated into the healthcare services to reduce direct patient-provider contact, consequently mitigating the risk of viral transmission[11]. This “new normal” in healthcare delivery has underscored the value of telemedicine as a sustainable means of preserving the continuity of care while alleviating clinical congestion and exposure risks, particularly among members of vulnerable groups.

In prenatal care, not only does telemedicine support routine glucose monitoring, dietary counseling, and timely insulin adjustments via digital platforms, but it also offers real-time feedback from healthcare providers. Its efficacy in improving glycemic control has been documented in patients with poorly controlled type 2 diabetes mellitus, while it similarly reduces hospital visits and enables early interventions for pregnant women with GDM[12-14]. Notably, Ebtisam et al (2019) demonstrated that using a telemonitoring system had significantly improved postprandial glucose levels and had reduced excessive maternal weight gain among pregnant women with GDM, which reinforced the effectiveness of telemedicine in promoting adherence to healthier lifestyles and in providing better clinical outcomes[15].

Given its ability to provide continuous monitoring, immediate interventions, and real-time consultations, telemedicine represents a powerful strategy for maintaining optimal glycemic control during pregnancy, which is an essential factor in preventing complications for both mothers and infants.

Nonetheless, further research is warranted to elucidate the specific impacts that telemedicine can have on clinical outcomes across various settings. Building on these promising findings, the present study aimed at evaluating the effectiveness of telemedicine for pregnant women with GDM at Nong Khai hospital.

Materials and Methods

This study was conducted at Nong Khai Hospital from 14 May 2023 to 31 August 2024 as a randomized controlled trial. The experimental group received care via telemedicine, while the control group received standard care. The study was approved by the Ethics Committee of Nong Khai Hospital (Ethics No.08/2566dated 12 May 2023) and was registered with the Thai Clinical Trials Registry (TCTR) (Registration no. 20230913001).

The inclusion criteria consisted of women aged 18-45 years, carrying a singleton pregnancy, had been diagnosed with GDM using the 100 g oral glucose tolerance test (OGTT) test in accordance with the National Diabetes Data Group (NDDA) criteria, and were able to record their blood glucose levels. The exclusion criteria were as follows: 1) patients who did not own a smartphone, and 2) those who were unable to attend all the scheduled follow-up appointments.

After obtaining written informed consent, the participants were randomized using block randomization with a block size of 5 and a 1:1 ratio. (Fig. 1) The telemedicine consultations involved adjusting the dosages of insulin and/or metformin according to blood glucose measurements. Consultations occurred regularly (1–2 times per week) and were scheduled every week, with each session lasting approximately 10-15 minutes during working hours (between 9:00 AM and 4:00 PM). The telemedicine group was monitored for blood glucose levels and reported their glucose levels via video calls or Line application. They received dietary guidance, medication adjustments, and instructions on how to lower their blood sugar levels. While the control group received standard care with outpatient visits every 1-3 weeks until delivery.

Between 24 and 28 weeks of gestation, the GDM diagnoses were confirmed using the 100 g OGTT with of glucose in women without pre-existing diabetes mellitus. Both groups were provided with glucose monitors to check their levels 4 times daily (fasting and 2-hour postprandial glucose levels). The participants were instructed to measure their blood glucose levels four times per day: 1) a fasting blood sugar measurement (FBS) in the morning (between 6:00 AM and 8:00 AM), 2) a 2-hour postprandial glucose measurement after breakfast (between 8:00 AM and 10:00 AM), 3) a 2-hour postprandial glucose measurement after lunch (between 1:00 PM and 3:00 PM), and 4) a 2-hour postprandial glucose measurement after dinner (between 7:00 PM and 9:00 PM). All blood glucose measurements were performed using the "Accu-Chek Performa glucometer" (Roche Diagnostics, Mannheim, Germany) The control group recorded their data on paper and brought it to the physician at each visit, while the telemedicine group submitted their reports via the Line application. The same obstetrician reviewed the telemedicine group's data on a daily basis, as well as issued alerts and provided consultations when any abnormal values were detected. Good blood glucose control was defined as having an FBS of less than 95 mg/dL and 2-hour postprandial glucose of less than 120 mg/dL in accordance with the guidelines of the American Diabetes Association (ADA) 2025[16].

Sample size was calculated based on a previous study by Ebtisam et al (2019)[15]. The study reported a mean 2-hour postprandial glucose level of 8.8 [standard deviation (SD) 1.5] in the telemonitoring system group and 10.4 [SD 2] in the standard care group. With an alpha (α) = 0.05, Z (0.95) = 1.96, beta (β) = 0.20, and Z (0.800) = 0.84, ratio = 1.0, the sample size was determined to be 20 participants in each group, which resulted in 20 in the experimental group and 20 in the control group. This is the formula used for sample size calculation. Sample size for comparing continuous outcome in randomized controlled trial (RCT) was from n4Studies[17-19].

$$n_{trt} = \frac{(z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2 \left[\sigma_{trt}^2 + \frac{\sigma_{con}^2}{r}\right]}{\Delta^2}$$
$$r = \frac{n_{con}}{n_{trt}}, \quad \Delta = \mu_{trt} - \mu_{con}$$

Statistical analyses were performed using the chi square test or Fisher's exact test for categorical variables and independent t test or the Mann-Whitney U test for continuous variables. Regarding the within-group comparisons before and after the intervention, McNemar's chi square test or exact methods were used for the categorical data, and the paired t test or Wilcoxon signed-rank test were utilized for the continuous variables.

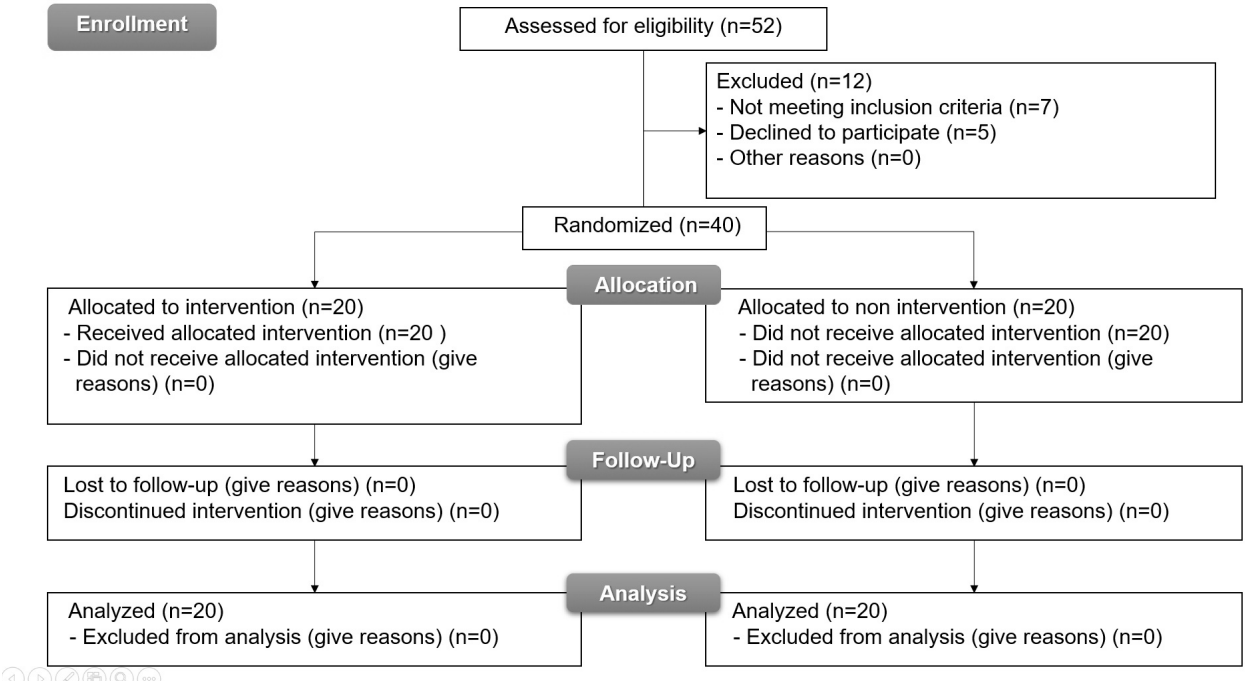

Fig. 1. The CONSORT flow diagram showing the recruitment and selection process.

Results

The baseline characteristics of the participants in both the control and experimental groups (20 participants in each group) showed that the median age was 32 years in both groups, with no statistically significant difference (p = 0.97). Similarly, prepregnancy body mass index (BMI) had a median of 27.41 in the control group and 27.75 in the experimental group, with no significant difference (p = 0.46). Additionally, the proportion of participants with family histories of diabetes mellitus was comparable between the control group (10%) and the experimental group (15%). The history of cesarean section also showed no significant difference (p = 0.72). However, regarding a history of GDM, three participants in the control group (15%) had received a previous GDM diagnosis, whereas none in the experimental group had shown such a history (p = 0.07). In terms of the type of GDM diagnosis, there had been a slight increase in GDMA1 cases in the experimental group, though this difference was not statistically significant (Table 1).

This study found that the participants in the experimental group, who had used the telemedicine services, had an average of 6-10 sessions, each lasting around 15 minutes. All participants had successfully reported their blood glucose levels, and their satisfaction with the service was high, with an average score of 9 out of 10 (Table 2).

According to the results shown in Table 3, the experimental group, which received the telemedicine care, had demonstrated significantly better blood glucose control compared to the control group across all measured time points, except for the FBS measurement at T1 for which there was no statistically significant difference.

Table 1. The baseline characteristics.

Variables	Control group (n = 20)	Telemedicine group (n = 20)	p value
Age (years) (median, IQR)	32 (28 - 36)	32 (29 - 36)	0.97
Prepregnancy BMI (kg/m^2) (median, IQR)	27.41 (24.55 - 30.63)	27.75 (25.96 - 32.03)	0.46
First degree relative with DM	2 (10.0)	3 (15.0)	0.63
Previous GDM	3 (15.0)	0 (0)	0.07
Previous cesarean delivery	5 (25.0)	6 (30.0)	0.72
Diagnoses			0.20
GDMA1	6 (30.0)	11 (55.0)	
GDMA1 -> GDMA2	10 (50.0)	5 (25.0)	
GDMA2	4 (20.0)	4 (20.0)	

IQR: interquartile range, BMI: body mass index, DM: diabetes mellitus, GDM: gestational diabetes mellitus

Table 2. The baseline telemedicine group.

Variables	Telemedicine group (n = 20)
Use of the telemedicine services	
6	6 (30.0)
7	6 (30.0)
8	7 (35.0)
10	1 (10.0)
Average duration of the telemedicine sessions	15 minutes
Complete glucose reporting	20 (100.0)
Patients satisfaction score	9 (9 - 10)

Table 3. Glycemic control.

Times	Control group (n = 20)	Telemedicine group (n = 20)	p value
T1 (28-30 weeks)			
FBS	95.26 (36.15-109.36)	81.70 (0-93.36)	0.06
Mean 2-hr PP morning	124.93 (59.26-130.25)	199.20 (0-122.67)	0.04
Mean 2-hr PP afternoon	122.29 (58.76-129.41)	99.74 (0-114.95)	0.04
Mean 2-hr PP dinner	124.51 (59-132.26)	108.4 (0-116.03)	0.01
T2 (30-32 weeks)			
FBS	97.01 (94.83-109.26)	81.5 (76.65-95.2)	0.01
Mean 2-hr PP morning	122.52 (118.29-129.14)	97.12 (86.92-119.88)	< 0.01
Mean 2-hr PP afternoon	125.64 (121.44-130.88)	104.17 (89.20-114.75)	< 0.01
Mean 2-hr PP dinner	122.96 (118.0-133.48)	105.27 (91-113.80)	< 0.01
T3 (32-34 weeks)			
FBS	101.03 (95.85-109.55)	82.53 (78.11-93.78)	< 0.01
Mean 2-hr PP morning	124.36 (119.86-129.41)	100.45 (95.70-116.9)	0.02
Mean 2-hr PP afternoon	125.49 (120.33-130.29)	102.54 (90.99-114.3)	< 0.01
Mean 2-hr PP dinner	125.65 (121.25-130.54)	101.90 (93.04-115.27)	< 0.01
T4 (34-36 weeks)			
FBS	97.37 (95.40-102.44)	82.47 (80.8 – 92.02)	< 0.01
Mean 2-hr PP morning	122.46 (118.39-127.29)	100.77 (94.91-114.74)	< 0.01
Mean 2-hr PP afternoon	122.92 (120.30-129.38)	102.55 (95.74-112.52)	< 0.01
Mean 2-hr PP dinner	122.9 (118.92-125.93)	104.52 (95.37-114.30)	< 0.01
T5 (36-38 weeks)			
FBS	96.35 (94.38-99.92)	85.24 (74.03 – 92.02)	< 0.01
Mean 2-hr PP morning	122.35 (118.94-125.55)	97.30 (87.84 – 111.74)	< 0.01
Mean 2-hr PP afternoon	122.93 (119.1 – 127.76)	101.49 (90.54 – 110.38)	< 0.01
Mean 2-hr PP dinner	125.31 (120.01-128.57)	102.17 (91.49-110.81)	< 0.01

FBS: fasting blood sugar measurement, PP: postprandial

From the maternal outcome data, there were significant differences between the control and the experimental groups, particularly in maternal weight gain. The control group had an average weight gain of 4.5 kilograms, while the experimental group gained an average of 2.35 kilograms. Moreover, blood

glucose control was significantly better in the experimental group, with 95% of the participants able to control their glucose levels compared to 50% in the control group (Table 4).

Regarding neonatal outcomes, no significant differences were found between the control and the experimental groups in variables, such as birth weight, incidences of neonatal hypoglycemia, or length of hospital stays. However, there was a statistically significant difference in the gender of the newborns, with the experimental group having a higher proportion of male infants (80% in the experimental group compared to 50% in the control group) (Table 5).

Table 4. Maternal outcomes.

Variables	Control group (n = 20)	Telemedicine group (n = 20)	p value
Hospital admissions	4 (20.0)	3 (15.0)	0.67
Weight gain (kg)	4.5 (1.5-8.5)	2.35 (1.5-5.0)	0.15
Mode of delivery			0.08
Vaginal	12 (60.0)	5 (25.0)	
Caesarean elective	4 (20.0)	8 (40.0)	
Caesarean emergency	4 (20.0)	7 (35.0)	
Maternal blood sugar before delivery	106 (94-131)	94.5 (84-110.5)	0.06
Blood sugar control	10 (50.0)	19 (95.0)	< 0.01
Hypoglycemic medication at delivery	14 (70.0)	9 (45.0)	0.11

Table 5. Neonatal outcomes.

Variables	Control group (n = 20)	Telemedicine group (n = 20)	p value
Preterm labor	1 (5.0)	2 (10.0)	0.54
Birth weight (grams)	3,295 (3,060-3,555)	3,190 (2,930-3,410)	0.24
Sex			0.04
Male	10 (50.0)	16 (80.0)	
Female	10 (50.0)	4 (20.0)	
Shoulder dystocia	0	0	NA
Neonatal hypoglycemia	5 (25.0)	2 (10.0)	0.21
Blood sugar			
- At birth	67.5 (48-80.5)	59.5 (53.5-74.0)	0.89
- At 1 hour	70 (53.5-78.8)	65.5 (57-79)	0.84
- At 2 hours	76 (70-81)	73.5 (70-86.5)	0.60
Neonatal jaundice	5 (25.0)	2 (10.0)	0.21
Transient tachypnea of the newborn	2 (10.0)	0 (0)	0.14
Respiratory distress syndrome	-	-	
Neonatal intensive care unit	1 (5.0)	0	1.00
Lengths of hospital stays	3 (2-3)	3 (2-3)	0.44

Discussion

Pregnant women with GDM are often scheduled for multiple appointments and daily blood glucose (BG) monitoring so that the effectiveness of treatment can be assessed. Typically, the patients would record their BG values in logbooks and present them to their healthcare providers during each visit. However, the frequency of monitoring may negatively affect maternal compliance and psychological well-being[20,21]. Telemedicine, which helps to reduce the number of clinic visits, can enhance the quality of life for pregnant women without increasing the risk of adverse outcomes for both the mother and the baby. Additionally, it improves the availability of healthcare providers and promotes patient satisfaction with treatment[22].

This study found that the use of telemedicine for monitoring and managing pregnant women with GDM had been more effective than standard care in controlling BG levels. The experimental group successfully managed their blood sugar levels in 95% of cases, compared to only 50% in the control group. These results were consistent with findings by Ying Tian et al[23]. The blood glucose control rate in the experimental group had been higher than that of the control group at nearly every point in time in groups 1 to 3, with three time points showing statistical significance: group 1 at T3 (54.8% vs 83.3%), group 2 at T3 (62.5% vs 80.0%), and T7 (75.0% vs 100%). This suggested that the continuous monitoring provided by telemedicine had allowed for more consistent follow-up, which was in contrast to the standard care, in which the patients typically visit the hospital every 1-3 weeks[24]. Close monitoring enables physicians to promptly adjust treatment plans when BG levels are found to be outside the optimal range. Additionally, telemedicine allows patients to reach out to physicians or healthcare teams immediately whenever they are in need of consultation or are facing difficulties in managing their blood glucose levels, which can result in the swift and effective resolution of problems. Due to continuous communication, patients using telemedicine are more likely to adhere to medical recommendations, such as dietary modifications, medication adjustments, and appropriate exercise regimens. This promotes greater self-awareness and proper adherence to health management protocols[25].

Recent evidence confirms telemedicine's effectiveness in GDM management, with a meta-analysis by El Seifi et al (2024)[26] demonstrating improved two-hour postprandial glucose control and reduced cesarean rates. Similarly, Wang et al (2025)[27] introduced a WeChat-based model that lowered two-hour postprandial glucose, boosted self-management, and decreased neonatal complications. These findings underscore the usability of mobile health (mHealth) applications, highlighting telemedicine's convenience, reduced healthcare visits, and better patient engagement. Collectively, they emphasize telemedicine's potential as a beneficial and practical option for GDM care.

Additionally, the study found that the experimental group had gained less weight during pregnancy compared to the control group, although the difference was not found to be statistically significant. This finding was consistent with a study by Sara Montori et al[28], who also reported that the experimental group had gained less weight than the control group without reaching statistical significance. This could have been attributed to the continuous nutritional advice and dietary counseling that had been provided through telemedicine, enabling the experimental group to enhance the modification of their eating behaviors more effectively.

The neonatal outcomes in both the experimental and control groups were not significantly different, aligning with the findings of Sara Montori et al[28], who also reported no significant differences in neonatal outcomes. This indicated that the use of telemedicine had not adversely affected the health of newborns. However, the experimental group had exhibited a higher proportion of male infants compared to the

control group. This may have likely been a coincidence since there is no causal link between the use of telemedicine and the sex of the newborn.

The level of satisfaction among the participants using the telemedicine system was determined to be high, reflecting the convenience and accessibility of providing medical services in a timely and efficient manner without the need for frequent hospital visits. Additionally, the participants were able to consistently report their BG levels and receive continuous guidance from physicians, both of which had further enhanced their experiences with the telemedicine system. In addition to clinical outcomes, the acceptance of the system by the physicians is crucial for the successful integration of telemedicine into routine practice. In this study, the physicians expressed a high degree of satisfaction, noting the convenience and ease of integrating telemedicine consultations into their daily workflow. The short duration for consultations (approximately 15 minutes per session on average) minimized disruptions and enhanced acceptance. This finding aligned with recent studies, which indicated that telemedicine interventions are, in general, being well-received by healthcare providers, particularly when the technology being used is user-friendly and does not significantly alter the existing clinical routines. However, in order to ensure sustained physician engagement and optimal telemedicine utilization, continuous education, clear guidelines, and technical support still remain essential[28, 29].

This study's limitations include a small sample size, recruitment from a single center, and a brief follow-up period, all of which may reduce the generalizability of the findings. Telemedicine-specific challenges comprised limited digital literacy among some participants, dependence on reliable internet and equipment, and the need for periodic in-person evaluations (e.g., ultrasounds). Delays in data transmission or physician responses can also be problematic in conditions like GDM, where rapid intervention is crucial. Moreover, entrusting telemedicine-based care to a single physician constrained scheduling, clinical perspectives, and overall applicability. This reliance on one provider additionally limited the study's capacity to assess physician satisfaction; involving multiple physicians or a multidisciplinary team could yield more comprehensive insights into provider acceptance and engagement with telemedicine. Future telemedicine initiatives should focus on improved user-friendliness, broader access to technology, and robust communication systems to ensure consistent, high-quality care for women with GDM. Larger, multicenter studies with extended follow-up durations are recommended to validate the long-term benefits and address postpartum outcomes such as maternal glucose control and infant development. By strengthening telemedicine's infrastructure and expanding training opportunities for both providers and patients, researchers and practitioners can help establish a more sustainable, inclusive model of GDM management.

Conclusion

This study demonstrated that telemedicine was effective in helping pregnant women with GDM to control their blood sugar levels without adverse effects on neonatal outcomes. Moreover, it was found that telemedicine had enabled pregnant women to manage their diabetes mellitus more effectively through continuous monitoring by remote healthcare providers.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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CASE REPORT

Spontaneous Uterine Perforation Presenting with Acute Abdominal Pain is a Rare Gynecologic Emergency Condition: Three cases report

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ABSTRACT

Uterine perforation is a rare but serious gynecologic condition, most commonly associated with induced procedures. However, spontaneous uterine perforation due to infection and pyometra has been reported, though data is limited. Severe complications, including purulent peritonitis and sepsis, can lead to high morbidity and mortality rates.

This case report presents three patients admitted to Lerdsin Hospital with generalized peritonitis, requiring emergency surgery, and diagnosed with spontaneous uterine perforation. The patients had distinct clinical courses and final diagnoses, including necrotizing endometritis, advanced cervical cancer, and endometrial carcinoma. Despite varying clinical courses, all patients had favorable outcomes with timely intervention.

Spontaneous uterine perforation is a life-threatening condition with high morbidity and mortality, requiring consideration in acute peritonitis diagnosis. In order to avoid lethal consequences, optimal management is essential, which includes early detection and timely surgery.

Keywords: pyometra, spontaneous uterine perforation, acute abdominal pain, generalized peritonitis, septic shock.

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อาการปวดท้องฉุกเฉินจากมดลูกทะลุ ภาวะที่พบได้น้อยในทางนรีเวช

นิธิสา ตะพานวงศ์

บทคัดย่อ

ภาวะมดลูกทะลุเป็นภาวะฉุกเฉินทางนรีเวชที่พบการรายงานได้น้อย โดยปกติมดลูกทะลุมักเกิดจากการทำหัตถการทางการแพทย์ เช่น การขูดมดลูก การส่องกล้องโพรงมดลูก การใส่ห่วงอนามัย หรือการฝังแร่ในช่องคลอดเพื่อรักษามะเร็ง เป็นต้น ภาวะมดลูกทะลุจากปัจจัยอื่น มักมีสาเหตุนำจากการตีบตันของปากมดลูก เกิดมดลูกอักเสบติดเชื้อและเกิดของเหลวร่วมกับหนองสะสมขึ้นภายในโพรงมดลูก จนกระทั่งมีการทะลุของชั้นกล้ามเนื้อมดลูกตามมา

จากการทบทวนวรรณกรรมที่มีการรายงานภาษาอังกฤษ ย้อนหลังพบการรายงานผู้ป่วยมดลูกทะลุจากมดลูกติดเชื้อเพียงส่วนน้อย เพื่อที่จะเพิ่มความระมัดระวังในการวินิจฉัยและรักษา ทางผู้วิจัยจึงนำเสนอรายงานผู้ป่วย 3 ราย ที่เข้ารับการรักษาในโรงพยาบาลเลิดสิน และได้รับการวินิจฉัยมดลูกทะลุ ผู้ป่วยทั้ง 3 รายนำมาด้วยอาการปวดท้องเฉียบพลัน โดยรายงานผู้ป่วย นำเสนออาการแสดง ภาวะแทรกซ้อน การรักษา และผลพยาธิวิทยา ที่แตกต่างกันในผู้ป่วยแต่ละราย ได้แก่ เยื่อบุโพรงมดลูกอักเสบอย่างรุนแรง มะเร็งปากมดลูก และมะเร็งเยื่อบุโพรงมดลูก โดยผู้ป่วยทั้งสามรายได้รับการรักษาอย่างเร่งด่วนและผู้ป่วยสามารถรอดชีวิตจากภาวะวิกฤต

โดยสรุป ภาวะมดลูกทะลุ เป็นภาวะฉุกเฉินที่เกิดภาวะแทรกซ้อนอื่นๆตามมาสูง ไปจนถึงมีอัตราการเสียชีวิตสูง อาการแสดงอาจคล้ายอาการทะลุของระบบทางเดินอาหาร ดังนั้นการวินิจฉัยแยกโรคก่อนผ่าตัดควรพึงระลึกถึงภาวะนี้ในสตรีที่มาด้วยอาการปวดท้องเฉียบพลัน

คำสำคัญ*: หนองในโพรงมดลูก, มดลูกทะลุ, อาการปวดท้องฉุกเฉิน, เยื่อบุช่องท้องอักเสบ, ภาวะติดเชื้อในกระแสเลือด*

Introduction

Uterine perforation is a rare gynecologic condition, most frequently associated with obstetrical and gynecological procedures, including uterine curettage, hysteroscopy, intrauterine device insertion, and brachytherapy for cervical cancer treatment. However, spontaneous uterine perforation has been reported in association with uterine infection, followed by pyometra. Pyometra is the persistent collection of purulent material within the uterine cavity resulting from impaired natural drainage due to cervical stenosis[1]. The reported incidence of pyometra ranges from 0.13-0.4% among gynecological patients, with a notably higher prevalence of 13.6% in older women. This condition may arise secondary to malignancy and their associated treatment or as a consequence of benign pathologies such as cervical polyp and age-related cervical stenosis[2, 3]. The classical clinical manifestations of pyometra include uterine bleeding, especially in the postmenopausal age group, vaginal discharge, uterine enlargement, and cramping pain. However, asymptomatic cases have been reported in approximately 50% of patients[4]. Rare but serious complications include purulent peritonitis and sepsis, both of which are associated with significantly high morbidity and mortality[2, 5].

To date, fewer than 50 cases of spontaneous uterine perforation of pyometra have been reported in the English literature, and a limited number of cases have been documented in Thailand[6, 7]. Here, presenting a case series of three patients diagnosed with spontaneous uterine perforation complicated by generalized peritonitis who were admitted to Lerdsin Hospital.

Case 1

A 52-year-old nulliparous woman presented with acute abdominal pain and fever persisting for three days, and her pain worsened in the preceding two hours. She reported no abnormal uterine bleeding, abnormal vaginal discharge, or history of prior pelvic examinations. Upon arrival at the emergency department, she exhibited signs of septic shock, including fever (38°C), hypotension (76/48 mmHg), and pulse rate of 64 beats/min. Immediate fluid resuscitation and broad-spectrum antibiotics were initiated. Physical examination revealed generalized abdominal tenderness with peritonitis, while pelvic examination identified a cervical mass with minimal bleeding and thickening parametrium bilaterally.

Transvaginal ultrasonography demonstrated a normal-sized uterus without intrauterine fluid collection or an adnexal mass, but the free fluid was detected in the pelvic cavity. Acute abdomen series imaging showed no evidence of pneumoperitoneum or hollow viscus organ perforation. A computed tomography (CT) scan was performed, but an official report was pending. The initial gynecologic assessment raised suspicion of primary peritonitis due to hollow viscus organ perforation, with the exophytic cervical mass deemed unrelated to the acute presentation. A general surgeon consultation was obtained, and an emergency diagnostic laparoscopy was performed after informed consent.

The intraoperative findings revealed an intact bowel loop, uterine fundal perforation with purulent discharge, and foul-smelling pus in the cul de sac. The peritoneal cavity was irrigated, and a closed-suction drain was placed in the cul de sac. Postoperative CT imaging officially confirmed a 3-cm cervical mass causing uterine obstruction, secondary pyometra, and rupture of the uterine fundus with intraperitoneal free air. (Fig. 1)

The patient underwent pus drainage and received a 14-day course of intravenous ceftriaxone and metronidazole. Hemoculture and pus cultures were negative for pathogens. She demonstrated clinical improvement and was discharged on postoperative day 15.

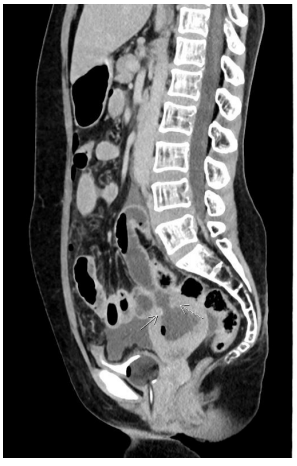

Fig. 1. Computed tomography in the sagittal view presented a ruptured fundal wall of the uterus (arrow).

Management was guided by the cervical punch biopsy, which revealed metastatic low-grade serous carcinoma favoring a tubo-ovarian origin, with imaging confirmed bone metastases at T11-12. The patient underwent neoadjuvant platinum-based chemotherapy (four cycles), followed by cytoreductive surgery, including abdominal hysterectomy with bilateral salpingo-oophorectomy. The primary goal of surgery was optimal tumor debulking, aiming for no residual disease, as in the management of advanced ovarian cancer. Pelvic lymphadenectomy was omitted due to its lack of survival benefit and associated surgical risks. Intraoperatively, cervical malignancy was suspected due to left parametrium involvement. However, radical hysterectomy was contraindicated due to the high risk of left ureteric injury. Final pathology confirmed adenocarcinoma of the cervix (p16 positive), leading to a revised diagnosis of advanced cervical malignancy with bone metastases. After completing six cycles of chemotherapy, the patient was referred for adjuvant radiotherapy.

The patient remained in good clinical condition, with stable bone disease and no evidence of local recurrence or new metastases on follow-up imaging. The progression-free interval was 11 months post-treatment.

Case 2

A 47-year-old nulliparous Thai woman presented with a palpable abdominal mass persisting for one month and sought emergency care due to acute severe abdominal pain. Her vital signs were stable, and she was afebrile on her first hospital visit. Abdominal examination revealed generalized tenderness with peritonitis and a palpable pelvic mass. Bedside transabdominal and transvaginal ultrasonography identified a heterogeneous echogenic mass within the myometrium, measuring 13 × 10 cm, with no identifiable endometrial lining. Additionally, free fluid and a collapsed inferior vena cava were detected in the hepatorenal space, raising concerns about hemodynamic instability. Initial management included fluid resuscitation and further investigation through CT. The patient was admitted under the care of a general gynecologist.

During observation in the gynecologic unit, the patient developed respiratory failure, necessitating intubation and transfer to the intensive care unit. A computer tomography pulmonary angiography (CTPA) ruled out pulmonary embolism but revealed significant

free intraperitoneal fluid and pneumoperitoneum. While awaiting the official CT report, she developed a high-grade fever (39-40°C) and exhibited clinical signs of septic shock with respiratory and hepatorenal failure. An urgent consultation with the gynecologic oncology team was obtained, and emergency exploration surgery was performed.

Intraoperative findings revealed purulent fluid in the abdominal cavity. The uterus was markedly enlarged, measuring 18 x12 x 8 cm, with an infected necrotic tumor (7 x 8 cm) at the fundus (Fig. 2). The uterine cavity contained friable tissue and foul-smelling pus. The tumor was adhered to bowel loops, and the omentum densely covered the pelvic organs. Additional friable tissue was identified at the mesentery and bowel loops. The procedure involved a total abdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy, small bowel resection with end-to-end anastomosis, adhesiolysis, abdominal lavage, and delayed primary suture performed in collaboration with the gynecologic oncologists and general surgeon team. The procedure lasted 3 hours and 35 minutes, with an estimated blood loss of 1,000 mL. Intraoperative disseminated intravascular coagulation (DIC) was detected, necessitating blood component transfusion.

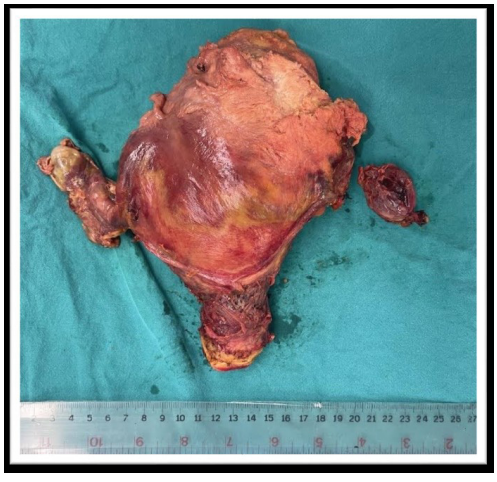

Fig. 2. Gross specimen of the uterus with infected tumor size 7x8 cm at the fundus.

Postoperatively, the patient remained in the intensive care unit for one week to manage sepsis and multi-organ dysfunction. Blood cultures identified Clostridium perfringens. Histopathology reported grade 3 endometrioid carcinoma of the endometrium with metastatic involvement of the omentum and small bowel, free of tumor at surgical margins. She received intensive intravenous meropenem and later switched to piperacillin/tazobactam following consultation with the infectious disease team.

On postoperative day 14, the patient developed wound infection and wound evisceration, necessitating vacuum-assisted closure therapy. These complications prolonged hospitalization and delayed the initiation of adjuvant chemotherapy. The total hospital stay was 79 days. The final diagnosis was endometrial carcinoma, FIGO stage IVB, with omental and small bowel metastases. Once the infection resolved, she received platinum-based chemotherapy, achieving a favorable response. Following the completion of chemotherapy, she was referred for adjuvant radiotherapy.

The patient completed adjuvant chemotherapy and radiotherapy. She regained full functional status without activity restrictions. Follow-up CT imaging of the chest and abdomen confirmed a complete

response, with no evidence of recurrence or distant metastases. As of the latest follow-up, the disease-free interval is eight months.

Case 3

A 63-year-old postmenopausal Thai woman presented to the emergency department with acute abdominal pain, persisting for eight hours. Her medical history included diabetes mellitus and hypertension. She had three previous vaginal deliveries and underwent natural menopause at age 50 without hormonal treatment. She had a known diagnosis of pelvic organ prolapse treated with a pessary and was scheduled for routine follow-up at another hospital. She denied any history of sexually transmitted disease, history of postmenopausal bleeding, or abnormal vaginal discharge.

On physical examination, her vital signs were stable, with a body temperature of 37.6°C, pulse rate of 70 beats/min, and blood pressure of 130/80 mmHg. Abdominal examination revealed generalized tenderness with muscular guarding and rebound tenderness, suggesting peritonitis.

Laboratory investigations demonstrated leukocytosis with a white blood cell count of 18,700/mL (78% neutrophil, 17% lymphocyte), while other parameters were within normal limits. CT with intravenous contrast revealed intra-abdominal free air, leading to a presumptive diagnosis of diffuse peritonitis secondary to a hollow viscus organ perforation. A general surgeon was consulted, and an emergency laparotomy was performed after obtaining informed consent.

The laparotomy revealed 600 mL of pus and ascitic fluid. No abnormalities were detected in the alimentary tract, liver, or gallbladder. A 1 cm perforation with necrosis was identified in the anterior uterine wall. (Fig. 3). Intraoperative consultation with a gynecologist led to a multidisciplinary surgical approach. The general surgery team performed an appendectomy, omental biopsy, and adhesiolysis of bowel loops, and the gynecologic oncologist performed a total hysterectomy with bilateral salpingo-oophorectomy, bilateral pelvic lymph node sampling, and peritoneal lavage. The total estimated blood loss was 700 mL.

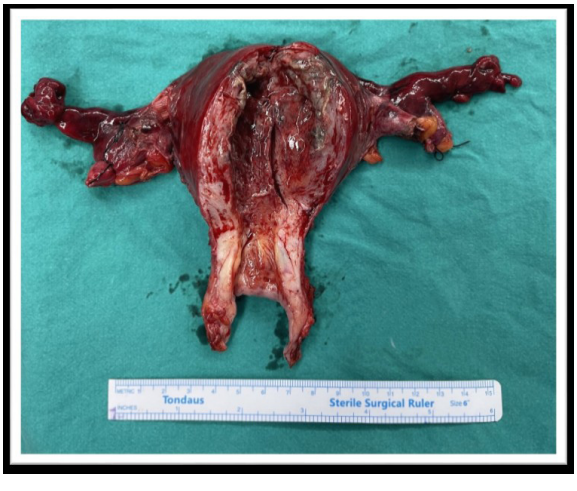

Fig. 3. Gross specimen of the uterus with necrosis of myometrium.

Intraoperatively, the patient developed oliguria and hypotension, leading to the diagnosis of septic shock. Inotropic agents were administered, and she was transferred to the intensive care unit (ICU) postoperatively with intubation and ongoing vasopressor support. Intensive broad-spectrum

antibiotics and strict respiratory and circulatory management were maintained for the first three postoperative days.

After clinical improvement, the patient was transferred to the gynecologic department for further care. The initial antibiotic regimen of ceftriaxone and metronidazole was escalated to meropenem postoperatively. After an infectious disease consultation, the regimen was further adjusted to piperacillin/tazobactam for a total antibiotic course of 14 days. However, an extended septic workup was performed due to persistent low-grade fever, leading to an additional seven days of meropenem, resulting in a total antibiotic duration of 21 days.

Pus and blood cultures yielded negative results. Histopathological examination confirmed active and chronic endometritis with diffuse necrosis, transmural myometrial necrosis, and perforation of the myometrium, along with acute peri-appendicitis. No malignancy was identified. The final diagnosis was necrotizing endometritis.

On postoperative day 14, the patient developed acute pulmonary embolism, necessitating prolonged hospitalization for anticoagulant therapy. Upon complete recovery, she was discharged on the postoperative day 21.

At the two-month follow-up, the patient fully recovered. Her pulmonary embolism remained well controlled with oral warfarin. However, she was noted to have grade 1–2 vaginal vault prolapse.

Discussion

The correlation between pyometra and spontaneous uterine perforation emphasizes how crucial it is, making caution when handling gynecologic problems, particularly in elderly females. The preoperative diagnosis was challenged by timely recognition and intervention. Life-threatening complications can result from a delayed or missing diagnosis; as illustrated in case 2 of this study, the patient experienced multiple organ failure and septic shock.

The preoperative diagnosis of uterine perforation in pyometra cases is seldom established due to its nonspecific presentation, often mimicking acute complications of gastrointestinal tract disease. Retrospective studies have reported that preoperative diagnoses in such cases were gastrointestinal tract perforation in 50% of cases and generalized peritonitis in 18.4%, with only 21% having an accurate preoperative diagnosis[8, 9]. Furthermore, classic gynecologic symptoms such as abnormal vaginal bleeding or discharge are frequently absent. Ruptured pyometra has a median onset age of 73.8 years, with a high mortality rate of up to 25-40%[10]. The studies also indicate that 22% of cases are associated with malignancy, 4% with genital tract abnormalities, and 74% are idiopathic[3]. Notably, in most case reports, uterine perforation in gynecologic malignancy is linked to radiotherapy treatment[11].

The high proportion of asymptomatic pyometra cases reported in up to 50% of patients emphasizes the necessity for routine screenings and thorough examinations, especially in elderly females or those with risk factors such as cervical stenosis.

Cervical stenosis was a common underlying risk factor in all three cases presented in this report. The first case involved cervical obstruction due to cervical malignancy, the second case was advanced endometrial carcinoma without vaginal bleeding due to nulliparous cervix, and the third case involved cervical stenosis in a postmenopausal woman using a pessary. Notably, two cases were associated with advanced gynecologic malignancy: endometrial carcinoma and cervical malignancy. As illustrated by cases 1 and 3, it suggests that spontaneous uterine perforation could be a rare but severe manifestation of advanced gynecologic malignancies and complicated treatment.

The high mortality rate of uterine rupture highlights the urgency for prompt surgical intervention. The cornerstones of management are hysterectomy, bilateral salpingo-oophorectomy, abdominal lavage, and broad-spectrum antibiotics[12, 13]. The decision to perform surgical staging in cases suspicious of malignancy must be carefully weighed in the context

of the emergency setting, patient condition, stage of malignancy, and the surgeon's experience.

This report is valuable because it is a resource for healthcare professionals on the rare conditions of spontaneous uterine perforation with different benign and malignancy conditions. It offers detailed management and treatment protocols for better patient outcomes.

Conclusion

Spontaneous uterine perforation is a life-threatening gynecologic condition. It is essential to differentiate this condition from gastrointestinal tract perforation in women with clinical abdominal peritonitis. Identifying key risk factors, particularly cervical stenosis, and utilizing preoperative imaging are crucial for accurate diagnosis.

A comprehensive approach involving a multidisciplinary team, emergency laparotomy with peritoneal drainage, and broad-spectrum antibiotics therapy are essential for optimizing patient outcomes. Early recognition and prompt surgical intervention remain the mainstay of management in preventing fatal complications.

Acknowledgment

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Potential conflicts of interest

The author declares no conflicts of interest.

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