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A - 9/7, Kalyani, Nadia

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PIN - 741235

Email: jiaog@iaog.in

website: www.iaog.in

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Dilip Kumar Dutta
Senior Consultant, Obs & Gyn, Gice Hospital, Kalyani, West Bengal
email: editor.jiaog@iaog.in

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Editorial office

A – 9/7, Kalyani, Nadia, West Bengal, India, PIN - 741235
E-mail – jiaog@iaog.in, Website: www.iaog.in



Hope during pandemic this period, all of my esteem medical fraternity are in good health.

As editor of JIAOG I am happy to inform you that VOLUME 3 issue 1 of JIAOG is going to release on 30th July 2021.

Like previous publication we are mainly focussed on evidence based scientific papers covering editorial, original articles and report of short cases etc.

Scientific research showed that covid19 cannot affects the baby in utero. But various scientific reports showed that there is high incidence of abortion, IUGR and pre-term labour etc.

We are working in a multicenter study on macro and microscopic of placenta, amniotic fluid and cervical swab etc. to see presence of any Corona virus or not. This comparative study is done on both covid19 vs non covid19 pregnancy cases and have any effect on baby or not.

Vaccination of covid19 during pregnancy and lactating period showed no impact on mother and neonates. Hence it is safely given during this period.

I am extremely thankful to Dr Ranita Roy Chowdhury, Executive Editor along with our journal team for releasing this volume in time.

With regards.

Dilip Kumar Dutta

Chief Editor

Journal of Indian Academy of Obstetrics and Gynaecology

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Editorial

PREVENTION OF GENITAL AND BREAST CANCER

Dilip Kumar Dutta

Senior consultant, Obs & Gyn, Gice Hospital, Kalyani, West Bengal

INTRODUCTION

The major task faced by a gynecologist, made a diagnosis of genital and breast cancers to determine the most effective therapy and formulate a prognosis for the patient.

Out of genital cancer, Ovarian cancer is the commonest gynecological cancer. The incidence is increasing with around the globe. Unlike cervical cancer, there is no premalignant stage and most cases present with advanced disease (stage III or IV).

Cervical cancer is the most common cancer among women in many developing countries. Incidence is high in early marriage, high number of sexual partners and smoking etc.

Endometrial cancer usually seen in post-menopausal women, is the third common gynecological cancer after the cancer of ovary and cervix. It does not have a long premalignant phase; hence it is not suitable for a screening programme.

Approximately, one in nine elderly women, will eventually be diagnosed as having a breast cancer.

Risk factors for breast cancer, apart from heredity factors include obesity, advancing age, early menarche, late menopause, null parity, delayed age of first birth and alcohol consumption. A woman with sister or mother with bilateral breast cancer would be at a fourfold risk of breast cancer and should undertake breast self-examination and mammography.

PREVENTION AND EARLY DIAGNOSIS

Therefore, early screening (pap smear, biopsy, colposcopy) along with improved socio-economic status, avoid early marriage and multiple sex partners and proper hygiene is very much significant to diagnose and prevent cervical cancer.

As regards, endometrial cancer in addition to endometrial biopsy (D&C, PAP SMEAR, HYSTEROSCOPY, PUNCH BIOPSY) monitoring, prevention and early treatment of irregular menstrual cycle, diabetic, hypertension, obesity, prolonged intake of OC PILLS, Oestrogen & Tamoxifen tab. etc are found to be very significant.

Patients with ovarian cancer are always came in late with indigestion, malaise & weight loss and pelvic mass. Those considered to be at high risk group (family history, prolonged exposure to estrogen or HRT therapy, nulliparous, or late menopause) should be screened for (1) USG/CT SCAN/MRI (2) CA 125 blood test after 35 years of age whereas those with family history of ovarian cancer should be screened for BRCA I & BRCA II tumour suppressor genes & pelvic USG & CA 125 blood tests from <30 years of age.

Breast cancer can be prevented when a woman at gynae clinic with a breast complaint after exclusion of infection, trauma and other benign disease, CBE, Mammogram, USG, U/S guided core biopsy and open biopsy is to be done, assessment of breast cancer risks may be modified by other factors, including prolonged

exposure to estrogens (Endogenous or Exogenous), family history, and (in 5%-10% of women) specific inherited mutations, such as BRCA I or BRCA II.

Management options for women considered to be at high risk for developing breast cancer includes - Bimanual breast examination, Annual mammogram, Annual breast MRI, Tamoxifen 20mg daily for 5 years (after excluding endometrial cancer) (Reduce breast cancer - 50%), Bilateral prophylactic mastectomy with or

without reconstruction (Reduce breast cancer - 98%)

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Original Article

EMERGENCY OBSTETRIC HYSTERECTOMY: A RETROSPECTIVE STUDY FROM A TERTIARY CARE HOSPITAL IN WEST BENGAL

Mousumi Maji,¹ Gairik Bera,^{1✉} Ranita Roy Chowdhury,² Manidip Pal³

ABSTRACT

BACKGROUND: Emergency obstetric hysterectomy (EOH) is a lifesaving procedure performed when all other measures and interventions have failed and maternal life loss becomes inevitable. It is important to study such events as they provide an insight into the standard of care provided and help to formulate strategy to reduce maternal morbidity and mortality in future.

OBJECTIVE: Our aim was to evaluate the incidence, indications, risk factor and fetomaternal complications associated with obstetric hysterectomy, wherein the procedure itself is associated with significant maternal morbidity and mortality.

METHOD: This is a retrospective, observational study of women requiring EOH. We reviewed the data over a two-and-a-half-year period, from 1st October 2018 to 1st April 2021, available in the Department of Obstetrics and Gynecology, COM & JNM Hospital, Kalyani, India.

RESULTS: Uterine atony leading to postpartum hemorrhage is the commonest cause of obstetric hysterectomy followed by ruptured uterus, morbidly adherent placenta, placenta previa and abruptio placentae. During post-operative period, anemia and disseminated intravascular coagulation are the most commonly encountered complications, with a case fatality index 20%.

CONCLUSION: Even after advancement in uterotonic agents, emergency obstetric hysterectomy still remains a necessary tool for obstetricians. In severe hemorrhage, a multi-disciplinary approach including medical, critical care, surgical and radiology departments may reduce maternal mortality and morbidity.

KEY WORDS: Emergency, Obstetric hysterectomy, Uterine atony.

INTRODUCTION

Emergency obstetric hysterectomy (EOH) is defined as the surgical removal of the uterus either at the time of vaginal or caesarean delivery or within puerperium period and is usually performed due to excessive obstetric hemorrhage. It is a lifesaving procedure performed when all other measures and interventions have failed and maternal life loss becomes inevitable¹.

EOH is classified as a “maternal near miss” event by WHO; the mother barely survives the pregnancy and its complications but loses her uterus². A near miss event is defined as a woman who nearly died but survived a complication that occurred during pregnancy, childbirth, or within 42 days of termination of pregnancy. It is important to study such events as they provide an insight into the standard of care provided and help to formulate strategy to reduce maternal morbidity and mortality in future.

Hemorrhage continues to be the leading individual cause of maternal death worldwide, accounting for 27.1% of deaths, in that analysis, India and Nigeria together accounted for a third of global maternal deaths³. More alarming is the fact that some studies from developing nations are pointing towards an increase in the rate of postpartum haemorrhage⁴. One meta-analysis reported an annual increase of 8% in the incidence of EOH around the world⁵.

We aimed to evaluate the incidence, indications, risk factors and fetal-maternal complications associated with obstetric hysterectomy which procedure itself is associated with significant maternal morbidity and mortality.

MATERIALS NEED METHODS

This is a retrospective, observational study of women requiring EOH. We collected all the available data over a two-and-a-half-year period, from 1st October 2018 to 1st April 2021, in the Department of Obstetrics and Gynaecology, COM & JNM Hospital, Kalyani, India.

Inclusion criteria include:

1. All women who delivered in the hospital or referred after delivery between 1st October 2018 to 1st April 2021
2. Delivered above 24 weeks of gestation
3. Underwent emergency hysterectomy for obstetric indications
4. Hysterectomy done at the time of delivery or within 42 days after delivery.

Women who delivered before 24 weeks of gestation, undergoing hysterectomy for indications other than obstetric, or outside the stipulated time of 42 days post-delivery were excluded from the study.

After collecting relevant data from the operation theatre records, each patient’s case record was scrutinized with regard to incidence, age, parity, antenatal high-risk factors, indications, hysterectomy type, and complications, along with the ultimate feto-maternal outcome.

Statistical Analysis

Microsoft Excel software was used for data entry and analysis.

RESULTS

For the last 2.5 years, total 14,032 deliveries were performed at our institute among them, 20 went for obstetric hysterectomy, incidence 1.42 in 1000 deliveries. The youngest woman who underwent obstetric hysterectomy was 21 years and oldest was 35 years (Mean age 28 years), most women were in the 25 to 30 years age group 13(65%). Among 20 cases 13 patients had pre-existing anemia (65%).

Demographic Characteristics	
Age	
20-25	5 (25%)
25-30	13 (65%)
>30	2 (10%)
Parity	
1	12 (60%)
≥2	8 (40%)
Booking Status	
Yes	9 (45%)

No	11 (55%)
Referred Case	
Yes	13 (65%)
No	7 (35%)

Fig 1: Showing Demographic Characteristics among patients went through Obstetric Hysterectomy

Among 20 obstetric hysterectomies 18 (90 %) delivered by Caesarean section. Most common indication for caesarean section was post caesarean section with scar tenderness.

Mode of Delivery	No of cases
Caesarean Section	18
Vaginal Delivery	2

Fig 2: Diagram showing Mode of Delivery distribution among 20 Obstetric Hysterectomy patients

Uterine atony leading to postpartum hemorrhage is the commonest cause of obstetric hysterectomy (about 40%) followed by ruptured uterus (25%), morbidly adherent placenta (15%), placenta previa (15%), and abruptio placentae (5%). Uterine atony was associated with previous caesarean section in 5 cases, anaemia with obstructed labor, and multiple pregnancies for 1 case each. The ruptured uterus was associated with a history of two previous caesarean sections in 2 cases and one previous caesarean section in 3 cases. Among morbidly adherent placenta all 3 cases went through caesarean section before and 2 had an additional history of curettage before.

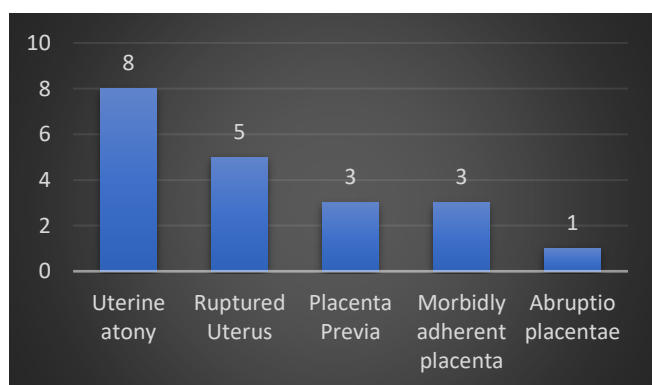


Fig3: Indications for Obstetric Hysterectomy in 20 patients

In most of the cases, total hysterectomy was

performed (17, 85%). Subtotal hysterectomy was done in 3 patients for ruptured uterus patients.

	No of Cases
Total Hysterectomy	17 (85%)
Subtotal Hysterectomy	3 (15%)

Fig4: Type of Hysterectomy done in 20 patients

During postoperative period, anaemia (12, 60%) and disseminated intravascular coagulation, DIC (6, 30%) are the most commonly encountered complications; other complications include hypovolemic shock (4, 20%), sepsis (2, 10%), acute renal failure ARF (2, 10%) and dyselectrolytemia (2, 10%). About 70% of patients received blood products during postoperative care. Seven patients required inotrope support, dopamine being the most commonly used inotropic agent. Two patients required ventilator support among them one survived and one patient received 2 episodes of haemodialysis for anuria due to acute renal failure.

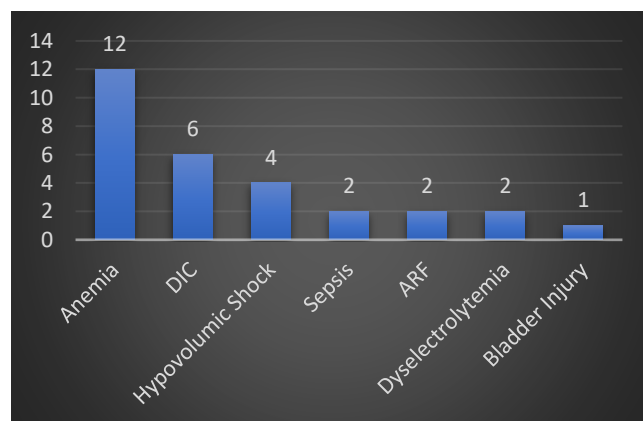


Fig5: Post-operative complications among 20 obstetric hysterectomy patients

	No of Patients
Blood Product	14 (70%)
Inotrope Support	7 (35%)
Ventilator	2 (10%)
Haemodialysis	1 (5%)

Fig6: Interventions required during post-operative care

There were 4 deaths among the study population, a case fatality index of 20%. Hospital stays ranges from six hours to 16 days; the average hospital stay for surviving patients was 8days. Among 4 deaths all had pre-existing anaemia, and we have seen a strong association between pre-existing anaemia and uterine atony (n=6, 75%).

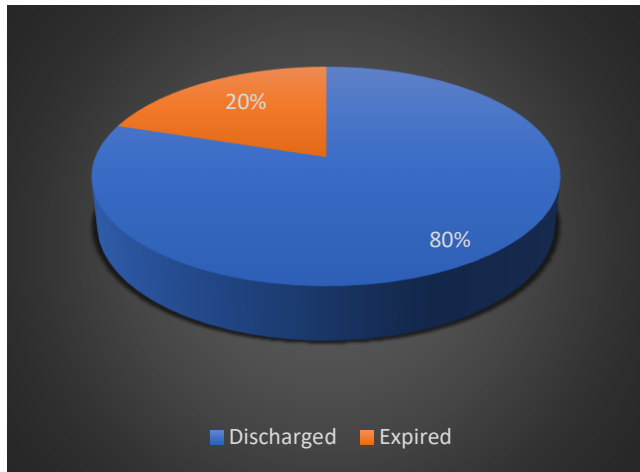


Fig7: Maternal outcome following Obstetric Hysterectomy

There were 6 (30%) fresh stillbirth cases, among them 4 cases were ruptured uterus patients, 1 patient had abruptio placentae. The total preterm baby was 7; among them 2 stillbirths (28%) were among 13 term baby 4 (31%) was stillbirth.

	Live Birth	Still Birth	Total
Pre-term Birth	5 (25%)	2 (10%)	7 (35%)
Term Birth	9 (45%)	4 (20%)	13 (65%)
Total	14 (70%)	6 (30%)	n = 20

Fig8: Foetal Outcome associated with Obstetric Hysterectomy

DISCUSSION

In our institute, the incidence of obstetric hysterectomy is 1.42 in 1000 deliveries for the last 2.5 years compared to 0.8 in Columbia⁶, 2.2 in China⁷, 5.1 in Nigeria⁸, 2.7 in Pakistan⁹, and 0.6 in USA¹⁰.

In a very crucial observation, previous caesarean section was significantly associated with 3 major indications of Obstetric Hysterectomy. In our study previous caesarean section was associated with uterine atony in 60% cases and morbidly adherent placenta in 100%, and uterine rupture in 100% cases. Bateman et al, done a similar study in the USA over 14 years found that the rate of Obstetric Hysterectomy for uterine atony increased four-fold following repeat caesarean section, 2.5-fold following primary caesarean section, and 1.5-fold following primary vaginal delivery¹¹.

The most common cause of obstetric hysterectomy in our study is uterine atony (40%) followed by uterine rupture (25%) and morbidly adherent placenta (15%). This result resembles most developing countries where uterine atony is responsible for most of the obstetric hysterectomy, but there is also a rising no of placental causes like developed countries. Studies from UK¹², Turkey¹³ also show atonic postpartum hemorrhage as the most common indication for obstetric hysterectomy. In our hospital, most uterine atony cases are managed conservatively by timely intervention with uterotonic agents, prevention plays a very important role by identifying high risk factors and active management of labor.

In our study uterine rupture accounts for 25% of obstetric hysterectomy compared to 8% in UK¹⁴ and 17% in Turkey. Unlike our study morbidly adherent placenta being second most common cause for obstetric hysterectomy in Turkey¹⁵ and UK¹⁶, about 38% and 40% respectively, whereas in our study it is 3rd most common cause and accounts for 15% cases. Surprisingly a recent study done in Pakistan by Korejo et al reported that 47.1% of cases were the result of uterine rupture, 28.9% from atony, and 17.4% from placental causes¹⁷.

Obstetric Hysterectomy is a lifesaving procedure that itself has its morbidity and mortality. Juneja SK, et al found febrile morbidity as most common complication in the post-operative period¹⁸, but in our study anaemia is the most common complication; probably early use of broad-

spectrum antibiotics in our institute has reduced the incidence of febrile morbidity. In our study, 30% of patients developed DIC where a study done by Chawla¹⁹ found 12.5%

Urinary tract injury is one of the commonest intraoperative complications encountered during emergency obstetric hysterectomy operation. There is a single case of bladder injury in our study contributing 5% of cases compared to 12.2% at UK²⁰, 3.6% at Nigeria²¹, 4.1% at China²², and 7.93% at another tertiary care centre of India²³. Our bladder injury patient was a post caesarean section ruptured uterus case, where the bladder densely adhered to the posterior surface of anterior abdominal wall, a 3cm incised injury occurred at the dome of the bladder which was repaired in 2 layers by polyglactin 2-0 suture. Foley's catheter was kept for 2 weeks with antibiotics. There was no case that required re-exploration in our study compared to 12.5 % in a study done at Hong Kong²⁴.

Some authors prefer subtotal hysterectomy over total hysterectomy as it offers the advantage of fewer chances of urinary tract injury, and takes less time to complete the operation in the face of a hemodynamic compromise state. But, in our institute, about 85% of patients went through total hysterectomy as some studies show subtotal hysterectomy was not allowing safe conclusion due to the intact cervical branch of the uterine artery²⁵.

Two patients required ventilator support, first patient had a hypovolemic shock with severe anemia that required ventilator support for 2 days with 8 units of blood product (4 units PRBC, 2 units FFP, 2 units Platelet) and inotrope support, the patient was discharged on 8th day after full recovery. Another patient was referred from an outside hospital for uterine atony leading to severe post-partum hemorrhage went through an emergency obstetric hysterectomy, developed severe anaemia, DIC, ARF and even with best of our effort patient expired on 3rd post-operative day. Both patients on the ventilator were treated at HDU. One patient with severe anemia and DIC received 18 units of blood product (8 units FFP, 6

units Platelet, 3 units PRBC and 1 Unit WB) in postoperative period.

Maternal mortality after EOH in our hospital is quite high 20% (n=4), lower rates 12.2% were cited by Najma et al.²⁶ and higher rate 23.8% were found by Umezurike et al.²⁷ The first maternal mortality case in our study was a 26 years old post caesarean section with placenta accreta. Due to intraoperative blood loss superimposed to her pre-existing anemia patient developed severe anemia, hypovolemic shock, and ARF. Even with blood transfusion, inotrope supports the patient expired within 10 hours of postoperative period. The second case was also a post caesarean section case with placenta previa. The patient went through total EOH for uncontrolled PPH after delivering a healthy-term baby. The patient developed severe anemia, DIC, and hypovolemic shock. Resuscitation was done with blood products and inotropes but patient expired within 24 hours of post-operative period. Our third maternal mortality case was an unbooked multipara case that was referred from a peripheral hospital for retained placenta with uterine atony. On admission, the patient was already in hypovolemic shock with severe anemia. As all other measures were failed, total EOH was done with the placenta in situ after ligation of uterine arteries of both sides. The patient was postoperatively immediately shifted to the ICU intubated put on inotrope support and blood products. However, she succumbed on the 3rd postoperative day due to severe sepsis and DIC. The fourth case was a 28 years old patient in term pregnancy with 2 previous two caesarean sections. The patient was admitted in comatose condition with severe anemia. An emergency operation revealed massive hemoperitoneum noted and 3.2kg fresh still born delivered from the peritoneal cavity. Total EOH with bilateral internal iliac artery ligation was done and the patient was shifted to ICU. The patient expired within 2 hours post-operative period due to hypovolemic shock and severe anemia.

Preterm birth as a result of obstetric hysterectomy is seen mostly for patients with placenta previa and placenta accrete cases. However, term delivery leading to obstetric hysterectomy due to

uterine atony, ruptured uterus was observed in most cases. Preterm and term live births are seen in 25% and 45% patients respectively compared to 16 % and 31% was observed by Uma Pandey²⁸.

Our study has few limitations; data collection was done from a single center, options like balloon tamponade, uterine artery embolization, and internal iliac ligation may in some cases remove the need for hysterectomy.

Source of funding – none

Conflicts of interest – none

Acknowledgement- We are thankful to our department of obstetrics and gynecology and OT and HDU staff for their support.

CONCLUSION

Even after advancement in uterotonic agents, emergency obstetric hysterectomy still remains a necessary tool for obstetricians. Uterine atony, placenta previa, primary or repeat caesarean section, pre-existing anaemia, grand multiparity, advanced maternal age all are associated with increased risk of obstetric hysterectomy. In most of cases severe hemorrhage being a leading cause of maternal mortality and morbidity, a multi-disciplinary approach including medical, mechanical, surgical, and radiological is necessary.

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<p>1. Postgraduate Trainee 2. Associate Professor 3. Professor Dept of Gynecology & Obstetrics, COMJNM & Hospital, Kalyani, Nadia. ✉ Email: gairikbera10@gmail.com</p>
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Original Article

MATERNAL PROTEINURIA IN TWIN COMPARED WITH SINGLETON PREGNANCIES

Mallick A¹✉, Shirsath S¹, Jana D²

ABSTRACT

BACKGROUND: The exact amount of albumin filtered each day by kidneys is controversial. Normal rate of albumin excretion is less than 20 mg/day. The upper limit of the urinary protein excretion is 150 mg/d in normal non-pregnant women. Total protein excretion, however, increases to 150-250 mg daily in normal pregnancy due to increase in blood volume and, therefore, the glomerular filtration rate. This study was conducted to compare 24-hour urinary protein excretion in twin and singleton pregnancies, not complicated by hypertension.

MATERIALS AND METHODS: This is a prospective study done in the department of Obstetrics and Gynecology in R.G. Kar Medical College and Hospital, Kolkata from June, 2015 to May, 2016. A total of 86 women (43 twin and 43 singleton pregnancies) participated in this study. Six collections were inadequate based on creatinine excretion and were excluded. So, 80 women (40 twin and 40 singleton pregnancies) comprised the total cohort.

RESULT: In our study four twin pregnancies (10%) were found to have proteinuria ≥ 300 mg/day at the time of the specimen collection but no singleton pregnancy had this level of proteinuria. Of this 4 twin pregnancies, 3 twin pregnancies were normotensive, yet they showed proteinuria ≥ 300 mg/day. Only one of this 4 twin pregnancies (who had proteinuria ≥ 300 mg/day) subsequently developed hypertensive disorder in pregnancy though statistically not significant ($p 0.1238$).

CONCLUSION: Twin pregnancy has more proteinuria as measured by 24-hour urine protein, than singleton pregnancy. And they are more likely to have proteinuria without hypertension and this value can exceed 300 mg/day.

KEY WORDS: Proteinuria, Singleton pregnancy, Albumin, Twin.

INTRODUCTION

The concept of maternal proteinuria and its diagnosis in pregnancy is utmost important. The exact amount of albumin filtered each day by kidneys is controversial. Normal rate of albumin excretion is less than 20 mg/day. The upper limit

of the urinary protein excretion is 150 mg/d in normal non-pregnant women¹. Total protein excretion, however, increases to 150-250 mg daily in normal pregnancy due to increase in blood volume and glomerular filtration rate too. The cut-off value for pathologic proteinuria in pregnancy (accepted as 300 mg of total protein

per 24 hours) was established using samples from pregnancies without preexisting medical conditions and prior to the onset of labor². Proteinuria is an important criterion in diagnosing pre-eclampsia in pregnancy³. Pre-eclampsia is best described as a pregnancy-specific syndrome that can affect virtually every organ system. And, although pre-eclampsia is much more than simply gestational hypertension with proteinuria, appearance of proteinuria remains an important diagnostic criterion. Thus, proteinuria is an objective marker and reflects the systemwide endothelial leak, which characterizes the pre-eclampsia syndrome.

Presence of 30mg of protein in 100 ml of urine results in a positive reaction (1+) on a urinary dipstick. This is not very accurate since the severity of proteinuria is a function of quantity of protein as well as urine volume. Quantitative method for urine protein estimation are 24 hour urine protein estimation and Urine protein/creatinine ratio. Despite recent updates, urinary protein excretion remains an important parameter in evaluation of pre-eclampsia and differentiate preeclampsia from gestational hypertension. Twin pregnancy experience a 2-3 times increase risk of pre-eclampsia⁴ and likely to be affected more by all hypertensive disorders⁵. Hypertensive disorders due to pregnancy are more likely to develop with multiple fetuses. The exact incidence attributable to twin gestation is difficult to determine because twin pregnancies are more likely to deliver preterm before pre-eclampsia can develop and because women with twin pregnancies are often older and multiparous. The incidence of pregnancy-related hypertension in women with twins is 20 percent at Parkland Hospital. Case-control analyses suggest that pre pregnancy body mass index (BMI) ≥ 30 kg/m² and egg donation are additional independent risk factors for pre-eclampsia. The risk for pregnancy associated hypertension was significantly increased for triplets and quadruplets (11 and 12 percent, respectively) compared with that for twins (8%)⁶. These data suggest that fetal number and placental mass are involved in pre-eclampsia pathogenesis. Although one study suggests that urinary protein excretion, as measured by urinary protein -to-creatinine

ratio, is higher in twin pregnancy during third trimester⁷, the same cut off value for proteinuria for diagnosis of pre-eclampsia is used for both twin and singleton pregnancy. No clear cut off value of proteinuria for diagnosis of pre-eclampsia in twin is mentioned in the literature. In a recent study done by Somerson et al ⁸ shows that mean 24-hour urinary protein excretion in twin pregnancies is greater than in singletons. These data suggest a reevaluation of the diagnostic criteria for pre-eclampsia in twin pregnancies. Hence more study is needed to address this issue. The objective of this study will be to determine 24 hour urinary protein excretion and the prevalence of proteinuria in twin and singleton pregnancies, which is not complicated by hypertension and this will give a clue whether urinary protein excretion value(in 24 hours) for the diagnosis of preeclampsia to be re-evaluated differently or not, in singleton and twin pregnancy.

MATERIALS AND METHODS

This is a prospective study done in the department of Obstetrics and Gynecology in R.G. Kar Medical College and Hospital, Kolkata from June, 2015 to May, 2016 with the aim of comparing 24-hour urinary protein excretion in twin and singleton pregnancies not complicated by hypertension. Pregnant women in between 18–45 years attending antenatal clinic in R.G. Kar Medical College and Hospital and carrying either twin or singleton pregnancies of 24-36 weeks gestation were included in the study. Women with urinary tract infections, any hypertension at initial checkup, presentational diabetes, autoimmune disorders, known renal disease, vaginal bleeding, and higher-order multiple gestations were excluded. Following ethical clearance and informed consent from the participants, the study began. Blood pressure was measured and normotensive participants between 24 weeks to 36 weeks were asked to submit 24 hour urine. Blood samples were drawn at the time of urine collection, for serum creatinine estimation. Participants with blood pressure $\geq 140/90$ mm of Hg or urine suggestive of infection were discarded. To ensure adequate follow up to

observe for the development of hypertension, participants who delivered within 2 weeks of submitting the 24-hour urine, were excluded. Participants were advised to discard the first morning urine sample and collect all urine in dark container for 24 hour period ending with the next morning's void. They were instructed to avoid strenuous exercise and intercourse during the time of urine collection. Adequacy of collection were assessed using creatinine excretion as described by Clark et al¹⁵ with a range of 11-25 mg/kg was considered adequate at the time of specimen collection. Women admitted in antenatal ward were eligible only during the first 3 days of admission. Total urinary protein excretion was measured by the Biochemistry department of R.G. Kar Medical College and Hospital. All urine specimens were processed within 1 hour of arrival to the laboratory. To determine the total protein concentrations in the 24-hour urine specimens, the total urine volume (dL) was multiplied by the total urine protein concentration (mg/dL). 24-hour urine protein estimation was done by Eshbach's illuminometer. Demographic and clinical characteristics were noted. Participants were followed for up to 6 weeks postpartum to monitor for the development of hypertension, which was defined as new-onset blood pressure ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic. The primary outcome was to calculate mean 24-hour urinary protein excretion. Secondary outcomes were proteinuria ≥ 300 mg in 24 hours and the incidence of hypertensive disorder during pregnancy.

In a study by Osmundson et al⁸ proteinuria (300mg /day protein excretion or greater) occurred in 38% of twin and 8.2% of singleton pregnancies. Keeping in alpha error of 0.05 and 80% power, and attrition of 50% total sample size was calculated, which came to be 86 with 43 in each arm. So ultimately a total of 86 women (43 twin and 43 singleton pregnancies) were included in this study.

Results: Out of the 86 participants, 6 participants collections were inadequate based on creatinine excretion and were excluded. So, 80 women (40 twin and 40 singleton pregnancies) comprised the final cohort. The two groups were similar in most baseline demographic and

clinical characteristics. Twin pregnancies delivered at an earlier gestational age compared to singleton pregnancies. Mean 24-hour urinary protein excretion was higher in twin than singleton pregnancies (196.30 mg compared with 145.45 mg, $P < 0.0001$). The upper limit of the 95% confidence interval (CI) for the mean urinary protein excretion was 216.2 mg in twin and 157.14 mg in singleton pregnancies. Four twin pregnancies (ten percent) were found to have proteinuria ≥ 300 mg/day at the time of the specimen collection but no singleton pregnancy had this level of proteinuria. Ten percent of singleton (four participants) and fifteen percent of twin pregnancy (six participants) subsequently developed hypertensive disorder in pregnancy (total 10 participants). When the data were reanalyzed excluding these 10 participants ($n = 70$), the findings were consistent with the overall analysis i.e. mean 24-hour urinary protein excretion was higher in twin than singleton pregnancies (193.11765 mg compared with 141.33333 mg, $P < 0.0001$) and 75% of twin who had 24 hour proteinuria ≥ 300 mg were normotensive. This study demonstrates that women with twin pregnancies excrete more protein as measured by a 24 hour urine collection.

Characteristic	Singleton Pregnancies	Twin Pregnancies	P value
AGE	24.45 ± 3.741	24.85 ± 3.325	0.6147
RELIGION HINDU	16 (40)	12 (30)	0.4819
RELIGION MUSLIM	24 (60)	28 (70)	0.4819
NULLIPARITY	20 (50)	22 (55)	0.8228
MULTIPARITY	20 (50)	18 (45)	0.8228
GESTATIONAL AGE AT DATA COLLECTION	28.98 ± 2.516	28.48 ± 2.230	0.3498
BMI	23.5625 ± 1.5561	23.7850 ± 1.1153	0.4689
SBP	119.15 ± 10.953	120.75 ± 10.961	0.5156
DBP	75.95 ± 6.118	77.40 ± 5.995	0.2876
URINE	17.25 ±	18 ±	0.232

CREATININE	2.90667	2.6602	3
SERUM CREATININE	0.72 ± 0.156	0.7 ± 0.165	±0.5791
24 HOUR URINE PROTEIN	145.45 ± 38.276	196.30 ± 62.223	<0.0001
TOTAL PROTEIN ≥300mg	00	4(10)	0.1238
GESTATIONAL AGE AT DELIVERY	38.1 ± 2.318	35.43 ± 1.752	<0.0001
HYPERTENSIVE DISORDER IN PREGNANCY	4(10)	6(15)	0.7353
24 HOUR URINE PROTEIN EXCLUDING THOSE WHO DEVELOP HYPERTENSION LATER	141.33333 ± 37.47761	193.11765 ± 59.76356	<0.0001

Table: Difference of mean of various Characteristics vs Pregnancies

Discussion

This study supports the hypothesis that baseline urinary protein excretion is greater in twin pregnancies. In this study mean 24-hour urinary protein excretion was higher in twin than singleton pregnancies (196.30 mg compared with 145.45mg P<0.0001). The upper limit of the 95% confidence interval (CI) for the mean urinary protein excretion was 216.2 mg in twin and 157.69 mg in singleton pregnancies. And even after excluding the subjects who subsequently develop hypertension mean 24- hour urinary protein excretion was still higher in twin than singleton pregnancies (193.12mg compared with 141.33 mg, P <0.0001). Previously Osmund son et al⁸ compared 24-hour urinary protein excretion in twin and singleton pregnancies not complicated by hypertension. They evaluated mean 24-hour urinary protein excretion in twin and singleton pregnancies between 24 weeks and 36 weeks of gestation. Mean urinary

protein excretion was higher in twin compared with singleton pregnancies (269.36124.1 mg compared with 204.3692.5 mg, P 0.004). Published studies comparing urinary protein excretion in twin and singleton pregnancies are limited. Smith et al compared urine protein-to-creatinine ratios in 51 twin and 51 singleton pregnancies at three time points across gestation. They found that the urine protein-to-creatinine ratio increased significantly over gestation in all pregnancies. Additionally, they found that the odds of an elevated urine protein-to-creatinine ratio—defined as greater than 0.19—was significantly higher in twin compared with singleton pregnancies but only in the late third trimester (34–38 weeks of gestation). Despite the lack of published studies comparing twin and singleton renal physiology, it is biologically plausible that urine protein excretion is higher in twin pregnancies. Pregnancy increases filtration of urinary proteins resulting in increased urine protein excretion compared with the nonpregnant state⁹. This is thought to occur as a result of progesterone-induced permeability of the glomerular basement membrane and a 50% increase in the glomerular filtration rate established as early as the first trimester¹⁰. In twin pregnancies, cardiac output increases by an additional 20% and blood volume increases by an additional 10% compared with singleton pregnancies¹¹. Theoretically, increased cardiac output could lead to an increased glomerular filtration rate resulting in more filtration of protein and more protein excretion. Alternatively, greater proteinuria in twin pregnancy might represent slightly greater accumulation of placental derived vasoactive factors such as sFlt-1, which has been associated with albuminuria in normal pregnancies¹². So our study strengthen the hypothesis that baseline urinary protein excretion is greater in twin pregnancies. Although 300 mg/day of urinary protein excretion is considered as abnormal in pregnancy, it is not clear how this threshold originated¹⁰. In a study by Higbee K¹³ on

normal values of urinary albumin and total protein excretion during pregnancy, 270 healthy pregnant women ≤ 35 years without a history of diabetes, hypertension, pyelonephritis, preeclampsia, or renal or connective tissue disease were evaluated. They found a mean urinary protein excretion of 117 mg and an upper 95% CI limit of 260 mg. Kuo and colleagues¹⁴ reported an upper limit of the 95% CI of less than 150 mg among their population of 205 women with singleton pregnancies. But mean 24-hour urine protein excretion was not reported in this study. So our study also adds to the current literature regarding normal values for urinary protein excretion in pregnancy.

In our study four twin pregnancies (10%) were found to have proteinuria ≥ 300 mg/day at the time of the specimen collection but no singleton pregnancy had this level of proteinuria. And only one of these twin pregnancies (who had proteinuria ≥ 300 mg/day) subsequently developed hypertensive disorder in pregnancy. Rest three twin pregnancies were normotensive, yet they showed proteinuria ≥ 300 mg/day. Though statistical analysis of 24-hour urine protein ≥ 300 mg in singleton and twin pregnancies was not significant ($P=0.1238$) in our study, in the study by Osmundson et al⁸ proteinuria ≥ 300 mg/day occurred in 38.0% of twin and 8.2% of singleton pregnancies and statistical analysis of their study showed significant proteinuria (≥ 300 mg/day) in twin pregnancies compared with singleton pregnancies ($P<0.001$). Proteinuria ≥ 300 mg/day is the cut off value for the diagnosis of hypertensive disorder in pregnancy and currently this value stands for all pregnancies – singleton/ twin/ higher order multiple gestations. Our study showed three normotensive twin pregnancies had proteinuria ≥ 300 mg/day. And similar finding was noted in the study by Osmundson et al⁸. Hypertensive disorder in pregnancy is an important cause of maternal morbidity and mortality in pregnancy. So, an appropriate criterion for its diagnosis is

utmost important. These data suggest a re-evaluation of the diagnostic criteria for preeclampsia in twin pregnancies. Hence more study is needed to address this issue.

In our study four singleton and six twin pregnancies developed hypertensive disorder in pregnancy later in study period. So a total of 10 pregnancies out of 80 participants developed hypertensive disorder in pregnancy. Incidence of hypertensive disorder in pregnancy in our study is 8% which correlated with the reported incidence of preeclampsia (2 - 8% of pregnancies worldwide).

So in conclusion, twin pregnancy had significantly more proteinuria as measured by 24 hour urine protein, than singleton pregnancy. And they are more likely to have proteinuria without hypertension and this value can exceed 300 mg/day. So, a reevaluation of the diagnostic criteria for preeclampsia in twin pregnancies is needed.

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| <ol style="list-style-type: none">1. Department of Obstetrics and Gynaecology, College of Medicine and JNM Hospital, WBUHS, Kalyani, Nadia, West Bengal2. Department of Gynecology and Obstetrics Institute of Post-graduate Medical Education and Research, A.J.C. Bose Road, Kolkata-700020, West Bengal, India. <p>✉ Email: arumallick88@gmail.com</p> |
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Original Article

CLINICAL SIGNIFICANCE OF ACANTHOSIS NIGRICANS (AN) IN ADOLESCENT GIRLS WITH POLYCYSTIC OVARY SYNDROME (PCOS)

NUPUR NANDI^{1✉}, SAHELI KAPAT², ANINDITA JANA³

ABSTRACT

OBJECTIVE: To compare the clinical and biochemical parameters of Indian adolescent girls with PCOS with and without acanthosis nigricans (AN).

MATERIALS AND METHODS: Total 59 adolescent girls (14-19 years) with PCOS (Rotterdam 2003 criteria) were selected for study after considering inclusion and exclusion criteria. Clinical parameters studied are body mass index (BMI), abdominal circumference (AC), waist hip ratio (WHR), blood pressure (BP), hirsutism (modified Ferriman- Galway score; mFG \geq 6), presence of acne and AN. Transabdominal ultrasonography done to record PCO. Biochemical tests included-Serum total testosterone (TT) level, sex hormone binding globulin (SHBG), post prandial plasma insulin (PPI) and post prandial plasma glucose (PPG) (2 hours after 75gm glucose intake). PP insulin (\geq 150 mcu / ml) and PP glucose \geq 140 mg / dl were considered as indicatives of insulin resistance (IR) and glucose intolerance respectively. The subjects were divided into two groups based on the presence or absence of AN. Group A Without AN - 19 cases; Group B With AN - 40 cases.

RESULTS: Significant differences between the two groups were noted in BMI (p=0.0001), AC (p=0.0001), WHR (0.0001), SBP (p=0.03), DBP (p= 0.01), TT (p= 0.002), but no significant difference in the prevalence rates of abnormal glucose tolerance PPG (p=0.92) and IR (p=0.09). Logistic regression modeling with AN (response variable of interest) and BMI, AC, WHR, SBP, DBP, testosterone level, PP insulin and PP glucose levels (as predictors) yields BMI, testosterone, SHBG, PP sugar, PP insulin, as the statistically main determinants. The model signifies positive impacts of BMI, testosterone level, and negative influence of PP sugar, PP insulin level with AN. The overall model is statistically significant with a p value of < 0.000 and is also indicative of a strong relation between BMI and AN.

CONCLUSION: Presence of AN in adolescent girls with PCOS is a clinical marker of obesity and is not just an indicator of underlying IR or glucose intolerance. Follow up studies will detect how many of them ultimately develop IR or diabetes in future.

KEY WORDS: Acanthosis nigricans, Polycystic ovary syndrome, Adolescent girls.

INTRODUCTION

Acanthosis Nigricans (AN) typically affects armpits, groin and neck, is a readily recognizable dermatological manifestation characterized by velvety, papillomatous, brownish-black plaques¹. Hyperkeratosis and papillomatosis are histological characteristics of AN. It is a manifestation of an underlying metabolic defect like insulin resistance (IR) or obesity (BMI) ^{1, 2}. Kahn et al noted AN is a frequent occurrence in hyperandrogenism and IR³.

Polycystic ovary syndrome (PCOS) is a common hormonal condition in women of all ages starting from adolescent period with reproductive, metabolic, and psychological sequelae⁴. Affecting 8 to 13% of all women of reproductive age and 21% in high risk groups, polycystic ovary syndrome (PCOS) is the most prevalent reproductive disorder causing significant health consequences for women impairing quality of life and increasing morbidity⁵. Under diagnosis or delayed diagnosis frequently happens in women with PCOS. The complexity of the disorder, and the impact on quality of life, requires timely diagnosis, screening for complications and management strategies⁴.

PCOS according to the Rotterdam 2003 criteria is a condition of reproductive age group females with at least two of the following features: 1) oligo-ovulation or anovulation, 2) clinical and/or biochemical hyperandrogenism, and 3) ultrasound appearance of polycystic ovaries⁶. Ovulatory dysfunction is assessed after 1-year post-menarche. The Rotterdam Criteria are now internationally accepted, with different phenotypes recognized with varying clinical presentations of PCOS cases like oligo-anovulation (OA), hyperandrogenism (HA), polycystic ovary morphology (PCOM) and varied risk profiles. In Rotterdam revised criteria of 2018 phenotypes of PCOS are classified as A (OA+HA+PCOM), B (OA+HA), C (HA+PCOM), D (OA+PCOM) ⁷.

PCOS in adolescent girls is a Common occurrence⁸. These girls are more prone for development of metabolic syndrome in their future life with unopposed action of excessive estrogen, androgen and insulin.

AN might be present in patients with polycystic ovary syndrome (PCOS) due to their association

with insulin resistance (IR), hyperinsulinemia, and hyperandrogenism (HA)⁸. But AN is not considered in the diagnostic criteria of PCOS³. Hyperandrogenism in PCOS may not always have unwanted hair growth ⁹. AN is more common in obese PCOS patients¹⁰. Presence of AN appears to be more of a sign of IR. Other pathological conditions rarely associated with AN are insulin coma and malignant diseases, especially adenocarcinoma of stomach¹¹.

Need for the study

There are very few studies which have reported the clinical, hormonal and metabolic parameters in adolescent girls of PCOS with AN. In the present study various clinical and biochemical parameters (hormonal and metabolic) of Indian adolescent girls having PCOS with and without AN are compared with an aim to know the significance of the presence of AN.

MATERIALS AND METHODS

This comparative analytical study was done in College of Medicine & JNM Hospital, WBUHS, Kalyani, Nadia and Sambhunath Pandit Hospital. Both are tertiary care hospital with a study period from November 2020 to April 2021. All studied girls and their at least one accompanied parent agreed to the clinical evaluation and investigation protocol.

59 adolescents' girls (age group of 14-19 years) with the complaints of oligomenorrhoea (\leq six menses per year) with clinical evidences of hyperandrogenism (hirsutism and/ or acne) were studied. These girls had detailed clinical and hormones and USG evaluations for the diagnosis of PCOS according to the Rotterdam 2003 criteria with at least two of the following features: 1) oligo-ovulation or anovulation, 2) clinical and/or biochemical hyperandrogenism, and 3) ultrasound appearance of polycystic ovaries.

Secondary causes of hyperandrogenism, as per Rotterdam criteria, were excluded by appropriate clinical and laboratory tests.

Exclusion criteria

- a) Adolescent girls within 1 year of menarche.
- b) Patients with history of steroid or oral contraceptive drug intake in the preceding 3 months

c) Diabetes Melitus-type 1 & 2.

Oligo-ovulation and /or anovulation was characterised by oligomenorrhoea (intermenstrual intervals of >35 days) and amenorrhoea (intervals>3 months). Clinical hyperandrogenism was defined as presence of alopecia, or hirsutism (modified Ferriman - Gallwey score of >=6) and /or acne. Biochemical hyperandrogenism was considered if total testosterone level was more than 0.82ng/ml (normal laboratory range 0.06-0.82 ng/ml) or calculated free androgen index was more than 2.06. Polycystic ovary on ultrasound (transabdominal) was defined as the presence of at least one ovary 10cc or more in volume.

A standard questionnaire was used to document length of menstrual cycles, personal, medical and family history of diabetes, hypertension, obesity. Signs of androgen excess (hirsutism, acne, and alopecia), were noted in the physical examination. Alopecia was assessed using the Ludwig visual score. Acanthosis is counted only for its presence in the neck, not in terms of severity. Anthropometric measurement included abdominal circumference in centimetre as per internationally accepted guidelines (using a 1 cm wide measuring tape). Body mass index (BMI) (Kg / m²) was calculated in each case from height and weight measurement. Blood pressure was measured using a mercury sphygmomanometer in semi recumbent posture in dominant arm (mostly right arm). Both systolic (SBP) and diastolic (DBP) BP was measured in mm of Hg. Trans-abdominal ultrasound was performed to study the morphology of ovaries in all subjects (as transvaginal ultrasound is not permitted for unmarried girls in India). Ovarian volume were measured by three perpendicular dimensions (volume of a prolate ellipsoid= 0.523 x length x thickness x height). Volume of more than 10cc

taken for study groups.

Post prandial plusma glucose (PPG) and post prandial plusma insulin (PPI) levels were estimated 2 hours after 75 grams of glucose intake for all subjects. Plasma glucose was measured by Glucose oxidaseperoxidase method (Roche Diagnostics GmbH,Mannheim, Germany) and was expressed in mg% and plasma insulin level in mcu/ml. PPI more than 150 mcu / ml were considered as indicative of IR., PPG more than 140 mg / dl was considered as indicative of glucose intolerance.

Serum total testosterone level (TT) was measured by using Electrochemiluminescence immunoassay, in ng/ml. Sex hormone binding globulin (SHBG) Level was also measured (nmol/l) on the second or third day of progesterone induced bleeding. Free androgen index (FAI) was calculated by method (TT X 100 X 3.47) / SHBG.

Other causes of secondary hyperandrogenism like 21-hydroxylase deficiency, Cushing's syndrome, hyperthyroidism, hyperprolactinoma and androgen secreting tumours were excluded by appropriate clinical and / or laboratory tests.

RESULTS

Total 59 cases fulfilled all study criterias in the said period of study.The studied adolescents were divided into two groups.

Group A - Without acanthosis nigricans - 19 cases (32.2%).

Group B -With acanthosis nigricans -40 cases (67.7%).

Table 1: Clinical parameters in the two groups.

Datas are plotted as mean (Standard deviation)

Table 1			
Parameters	AN absent (n=19)	AN present (n=40)	p value
BMI (kg/m ²)	22.8 (2.4)	28.1(4.4)	0.0001
AC (cm)	72.3 (5.3)	85.6 (8.8)	0.0001

Table 1			
WHR	0.76 (0.03)	0.84 (0.05)	0.0001
SBP (mm of Hg)	117.7 (11.03)	125.0 (14.5)	0.03
DBP (mm of Hg)	72.9 (7.5)	78.3 (8.1)	0.01

There were significant differences in mean BMI ($p=0.0001$), AC (0.0001), WHR (0.0001), SBP (0.03), DBP (0.01) values between the two groups.

Table 2 : Hormonal and metabolic parameters
 Datas are plotted as mean (Standard deviation) / or number (%)

Parameters	AN absent(n=19)	AN present(n=40)	P value
Testosterone(ng/ml)	0.39(0.13)	0.62(0.43)	0.002
SHBG	35.8(28.1)	31.8(25.4)	0.60
FAI	4.91(2.2)	10.1(8.2)	0.002
Number of cases with PPI ≥ 150 mcu/ml (%)	3 (15.8)	15(37.5)	0.09
Number of cases with PPG ≥ 140 mgm (%)	4 (21.0)	8(20.0)	0.92

Table 2. shows the hormonal and metabolic parameters of the two groups. Testosterone ($p=0.002$) and FAI ($p=0.002$) values showed significant difference whereas SHBG ($p=0.60$), PPI ($p=0.09$) and PPG ($p=0.92$) showed no significant differences.

In Statistical analysis, Logistic regression modeling is used and AN as the response variable of interest. All the studied parameters as predictors such as BMI, testosterone, PP sugar, PP insulin, SHBG as the statistically main determinants. By Analysis it was found that there were positive impacts of BMI, testosterone level on AN. PP insulin, PP sugar, SHBG levels have negative influence on AN.

DISCUSSION

We have found highly significant association of increased BMI ($p=0.0001$) with AN in adolescent girls with PCOS. According to Cassar S et al BMI exacerbated insulin resistance by 15% in women with PCOS and had a greater impact on insulin resistance in PCOS than in controls¹².

Present study has demonstrated higher mean postprandial insulin values although not statistically significant ($p=0.09$) among subjects with AN. Study done by Menon et al have reported statistically significant insulin resistance

only in obese patients having AN¹³. PCOS is associated with impaired glucose tolerance (IGT) in up to 30% and type 2 diabetes in up to 10% of women with PCOS as observed in the study of Legro RS et al¹⁴.

As PPI level is not significantly high ($p=0.09$) in the AN group of our study, we can infer AN is not always an indicator of insulin resistance. In a study on PCOS patients, Panidis D et al also mentioned that insulin resistance is not the only factor which leads to development of AN¹⁵.

Central obesity plays an important role for

association of AN as revealed in our study result which showed very, very significant p value ($p=0.0001$) of abdominal circumference in PCOS adolescent girls having AN. Obesity is an important clinical parameter associated with AN- is also found in the study of Araujo L. M. et al¹⁶. Maitra S.K et al reported that AN is a common finding in obesity syndrome¹⁷. We have noted statistically very significant higher values of WHR ($p=0.0001$) in adolescent PCOS girls having AN. To study the Metabolic risk assessment of Indian women with polycystic ovarian syndrome Tripathy P et al found significant predictors for metabolic syndrome within the PCOS cohort are waist circumference $>80\text{cm}$, hypertension ($p<0.001$)¹⁸.

In current study both DBP ($p=0.01$) and SBP ($p=0.03$) are significantly higher in AN group of PCOS girls. A case-control study of 1,550 women with PCOS by Pinola P reported both systolic and diastolic blood pressure is higher compared with controls, independent of BMI¹⁹.

Biochemical hyperandrogenism as depicted by testosterone level and FAI values are significantly higher ($p=0.002$) in AN group of our study. Tripathy P et al grouped PCOS women into 4 phenotype divisions as per Rotterdam 2018 criteria. They have noted highest level of androgen in phenotype A (OA+HA+PCOM) which is the commonest group (55.8%), and prevalence of metabolic syndrome is more common in phenotype A and B (OA+HA)¹⁸.

The clinical Importance of AN has been claimed to be due to its association with various hormonal and metabolic abnormalities such as obesity, diabetes, PCOS, dyslipidemia, thyroid dysfunction etc. In a systemic review meta-analysis done by Lim SS et al considered the implications of obesity on reproductive, metabolic, and psychosocial health of PCOS women²⁰. To check obesity and its ill effect, lifestyle interventions, including incorporating a healthy diet, increasing physical activity, and implementing behavioral strategies, are the first-line treatment for PCOS²¹.

CONCLUSION

Present study signifies that AN in adolescent girl with PCOS is another clinical marker of central obesity. This study shows presence of AN is not always an indicator of glucose intolerance, rather

obesity and metabolic syndrome are frequently associated with AN in PCOS adolescent girls. While dealing with PCOS and AN at the tender age of adolescent period, Clinicians should focus on lifestyle adjustments by weight management and physical exercise as the first-line intervention to improve reproductive, metabolic, cardiovascular, and psychosocial outcomes.

Prospective follow up studies are needed to detect how many of them ultimately develop Insulin resistance or diabetes in future. Current study points both the clinician and the public's attention to the importance of a high -quality lifestyle to control obesity and so as to reduce chances of developing metabolic syndrome in adolescent girls with PCOS and AN.

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1. Professor, Dept of Obstetrics and Gynaecology, COMJNMH, WBUHS, Kalyani,
 2. DNB Post-graduate Trainee, Dept. of Obstetrics and Gynaecology, Sambhunath Pandit Hospital, Kolkata
 3. MS Post-graduate Trainee, Dept of Obstetrics and Gynaecology, COMJNMH, WBUHS, Kalyani, Nadia
 ✉ Email: nupurnandi2002@gmail.com

Original Article

SCREENING OF CERVICAL CANCER BY PAP SMEAR- A CROSS-SECTIONAL STUDY

Dilip Kumar Dutta¹, Indranil Dutta², Ranita Roy Chowdhury³, Gairik Bera⁴✉

ABSTRACT

BACKGROUND: Cancer of uterine cervix is a leading cause of mortality and morbidity among women worldwide. In developing countries this is the most common gynaecological cancer. The simplicity, effectiveness and versatility of Pap test have made it an integral part of routine clinical practice. Pap smear is a simple, safe, non-invasive and cost-effective method for the detection of pre-cancerous, cancerous and benign lesions of cervix. The use of Pap smear as a screening tool has reduced morbidity and mortality of cancer cervix patients.

OBJECTIVE: Timely detection of cervical cancer by clinical examination and Pap smear is one of the most important steps to prevent mortality and morbidity at low resource set up.

METHOD: This is a cross-sectional study of women attending GICE nursing home Gynaecology OPD, Kalyani, India from 1st January 2018 to 1st December 2020.

RESULTS: Pap smear result shows about 61% women have nonspecific cervicitis, hyperplasia and dysplasia was found in 18% and 14% women respectively. Our study found LSIL in 11 women, HSIL in 16 and carcinoma in situ in 8 women.

CONCLUSION: Cervical carcinoma is a preventable disease, but there is no perfect screening test that has 100% sensitivity and specificity. Pap smear test can help early detection of cervical pathology.

KEY WORDS: Pap smear, HSIL, Cervical cancer

INTRODUCTION

Cancer of uterine cervix is a leading cause of mortality and morbidity among women worldwide. In developing countries this is the most common gynaecological cancer. According to National Cancer Registry Program of India, cancers of uterine cervix and breast are leading malignancies seen in Indian women¹. According

to WHO 80% deaths from cervical cancer were from developing countries and India accounts for 1/5th of the burden of cervical cancer². As per the GLOBOCAN 2018, there are 96,922 new cervical cancer cases in India, this year with an age-standardized incidence rate of 14.7/10⁵ and 60,078 cervical cancer deaths with a mortality rate of 9.2/10⁵.³

Unlike most other malignancies, cancer of cervix

is readily preventable as it is easy to detect and treat its precursor lesions. Cervical cancers in their early stage of development are treatable as the cancer cells are confined to the surface of the cervix and have not spread into the deeper tissues. Screening programmes have reduced the incidence and mortality due to cervical cancer significantly, for which sensitization of women is required through community-based approach.

The test was first suggested by Papanicolaou in 1928 but it took almost 15 years before it was generally accepted by the medical community. The Papanicolaou (Pap) smear was introduced in 1941 and became the standard screening test for cervical cancer and premalignant lesions⁴. This is because the Pap test detects cervical epithelial cell abnormalities which represent a spectrum of intraepithelial lesions, from mild-to-severe dysplasia to invasive cancer and facilitates early diagnosis.⁵ Pap test not only plays a crucial role in detection of cervical cancer and its precursor lesions, but also aids in the diagnosis of infective and inflammatory conditions including the identification of causative organism, hormone related benign epithelial changes and changes due to therapeutic agents.⁶

The simplicity, effectiveness and versatility of Pap test have made it an integral part of routine clinical examination and large chunk of workload in gynaecological and pathological practice is due to this test. Pap smear is a simple, safe, non-invasive and cost-effective method for the detection of pre-cancerous, cancerous and benign lesions of cervix. Pap smear screening has sensitivity of 50-75% and specificity of 98-99%.^{2,6} With the use of Pap smear as a screening tool for the detection of abnormal epithelial lesions in cervix, more cases can be diagnosed early and thus the morbidity and mortality of patients can be decreased.

MATERIALS AND METHODS

In this study Pap smears were obtained from women examined and analysed at GICE NH cytology section from January'18 to December'20. Informed consent was obtained.

Inclusion criteria:

- Age between 25 to 70 years
- Sexually active women

Exclusion criteria:

- Known case of cancer cervix
- Pregnancy

Procedure: Detailed history including menstrual history, sexual history, obstetric history, marital history and educational history was taken. It was ensured that no local douche, antiseptic cream and no local internal examination was done on day of test. Pap smears are taken by using Ayres Spatula in dorsal lithotomy position.

- The broad end of spatula was placed on the Cervix and rotated through 360° and the collected material was spread over a glass slide.
- The oblong relabelled narrow end of spatula was used to take smear from posterior vaginal fornix and spread over a second glass slide.
- The Endo cervical sample was collected using a Cytobrush and was spread over labelled third glass slide.

All the slides were labelled and immediately transferred to 95% Ethyl alcohol (Transport Medium) and sent to Pathology Department for Cytological study.

Statistical Analysis

Microsoft Excel software was used for data entry and analysis.

RESULTS

Total 500 cases were analysed, age of women ranged from 25 to 70 with average age of 48.6 Years. Most of the women were less than 40 Years age group (Table 1). Women with Para >4 (n = 266) and poor socioeconomic status (n = 300) had maximum participation. About 60% of the women were from Muslim community.

Socio demographic Characteristics		Number	Percentage
Age	< 40 Years	200	40
	41-50 ears	195	39
	> 50 Years	105	21
Parity	<2	54	10.8
	2-4	180	36
	>4	266	53.2
Socioeconomic Status	Good	80	16
	Average	120	24
	Poor	300	60
Age of Marriage	< 18 Years	226	52
	19-25 Years	180	36
	>25 Years	60	12
Religion	Hindu	180	36
	Muslim	300	60
	Christian	10	2
	Others	10	2

Table 1: Socio demographic characteristics among women

Among 500 women, 394 women had menarche at age more than 14years. Most of the women have regular menstruation cycle (n = 335) and 65 post-menopausal women participated in this study.

Menstrual History		Number	Percentage
Age of Menarche	<14 Years	106	21.2
	>14 Years	394	78.8
Menstrual History	Regular	335	67
	Irregular	100	20
	Menopause	65	13

Table 2: Distribution of women according to menstrual history

In our study 1% (n = 5) of women have positive history of cervical cancer in first degree relatives (Mother of 4 women and sister of 1 woman have history of Cervical carcinoma).

Family History		Number	Percentage
History of Carcinoma Cervix	Mother	4	0.8
	Sister	1	0.2
	Other	0	0
	Relatives		

Table 3: Distribution according to family history of cervical carcinoma

About 79.2 % women gave history of continuous OC pill intake for 5 years or more.

Contraception History		Number	Percentage
OC Pill	Yes	396	79.2
	No	104	20.8

Table 4: Distribution according to OC Pill intake history

Among 500 women, 65 women (13%) had multiple sexual partners.

Sexual History			Number	Percentage
H/O Partner	Multiple	Yes	65	13%
		No	435	87%

Table 5: Distribution according to H/O multiple partners

Distribution of Pap smear result shows about 61% (n = 305) women have nonspecific cervicitis, NILM and ASCUS was found in 79% (n = 395) and 14% (n = 70) women respectively. Our study found LSIL in 11(2.1%) women, HSIL in 24(4.9%) and carcinoma in situ in 8 (1.6%) women.

PAP Smear Test Result	Number	Percentage
NILM	395	79
ASCUS	70	14
LSIL	11	2.1
HSIL	24	4.9

Table 6: Distribution of Pap smear analysis report

DISCUSSION

The incidence of cervical cancer is quite high because prevention programs are either non-existent or poorly implemented. It is a well-known fact that the burden of cervical cancer has been reduced dramatically after the introduction of screening programmes, but awareness within the community about the Pap smear test is very low. According to the American Cancer Society (2012), the Pap smear test is a routine cancer screening method that should be done every 3 years, and a Pap smear with an HPV DNA test is recommended as a screening method every 5 years.⁷

In our study most, women are below 40 years age group, similar result was found by Sachan PL et al⁸ and Shashidhar M R et al⁹, may be younger women are more aware of cervical cancer. In our

study 60% women was from Muslim community contrary to Sachan PL⁸, they had 70% Hindu in the study. About 60% of women were from poor socioeconomic status as government runs the cervical cancer screening awareness program mostly in rural areas.

In our study 13% women were post-menopausal, Kannan A¹⁰ done a study on 978 women where 41% women were postmenopausal. In our hospital number of postmenopausal women were less may be due to their shyness, or they were unaware of the cervical cancer screening program.

We found 13% women had multiple sexual partners but a study done by Pragati Sharma et al¹¹ and L N Biswas et al¹² found 4.5% and 17% respectively.

Our study showed that there were 79% benign and inflammatory and 21% were premalignant

and malignant lesion whereas Mandakini M Patel¹³ et al found 94.5% and 5.5% respectively. Our analysed 61% smear was nonspecific cervicitis similar to P.R Kulkarni et al¹⁴ study 73.7% but Lawley et al¹⁵ found significantly lower rate of 14.3%. In the new Bethesda systems, CIN I is known as LSIL, and CIN II and III known as HSIL. We found LSIL 2.1%, HSIL 4.9 % and Z.S Nayani¹⁶ in her study found CIN I 8.6%, CIN II 3.8% and CIS 0.9% another study by C.P Padmini¹⁷ shows CIN I 5%, CIN II 3%, and CIS 1%.

CONCLUSION

Cervical carcinoma is a preventable disease, but there is no perfect screening test that has 100% sensitivity and specificity. Pap smear testing is a very useful, simple, economical, and safe tool to detect pre-invasive cervical epithelial lesion. Pap test has been regarded as the gold standard for cervical screening programs. All medical professionals such as doctors, nurses, anganwadi workers, midwives, and other health-care workers should be trained to reach out to these women so as to improve their knowledge and awareness regarding Pap smear examination.

Conflicts of interest - none

Funding- self

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|---|
| <ol style="list-style-type: none">1. Consultant Gynaecologist & Obstetrician, Gice Hospital, Kalyani2. Professor, Dept. of G & O, IQ City Medical College, Durgapur3. Associate Professor, Dept. of G & O, COMJNMH, Kalyani4. Post graduate Trainee, Dept. of G & O, COMJNMH, Kalyani <p>✉ Email: gairikbera10@gmail.com</p> |
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Original Article

LAPAROSCOPY IN EVALUATION OF CHRONIC PELVIC PAIN

Dilip Kr Dutta¹, Indranil Dutta², Ranita Roy Chowdhury³, Rahul Chaudhuri⁴✉

ABSTRACT

BACKGROUND: Chronic pelvic pain is a noncyclical pain of duration more than 6 months and is the most common presentation in gynaecological outpatient department.

OBJECTIVES: To evaluate the role of laparoscopy in chronic pelvic pain and to correlate laparoscopic findings with preoperative pelvic findings, to determine the type of pathology existing and to re-evaluate the treatment strategy.

RESULT: Diagnostic laparoscopy could accurately identify the role of chronic pelvic pain in those cases that were normal by detailed clinical evaluation. In laparoscopy only 5(16.7%) patients had normal finding contrary to clinical findings where 20(66.7%) patients were detected normal. Endometriosis was seen in 9 (30%) patients in laparoscopy followed by uterine fibroid in 3 (10%) patients and chronic PID also 3 (10%) patients.

CONCLUSION: laparoscopy proved promising in accurately diagnosing endometriosis and PID.

KEY WORDS: Chronic, Laparoscopy, Pelvic pain.

INTRODUCTION

Chronic pelvic pain is a noncyclic pain of duration of 6 or more months that localises to the anatomical pelvis, anterior abdominal wall at or below the umbilicus and the lumbosacral area. It should be sufficiently severe to cause functional disability.¹ The prevalence varies from 12 to 39 percent in reproductive age women.² CPP may be related to a variety of gynaecological causes along with gastrointestinal or urological pathologies.³ In 25-50% cases more than one anomaly can be found. So, a full medical history along with complete medical examination is key to correct

diagnosis and management. A multidisciplinary approach is preferred for diagnosis.^{4,5}

Laparoscopy is a valuable tool in the evaluation of undiagnosed CPP. It can establish a definitive diagnosis and modify the treatment without resorting to exploratory laparotomy. It is also an extremely valuable aide in gynaecologist's armamentarium especially in validating minimal disease and adhesions, which cannot be revealed sonographically. The following study is an attempt in understanding the aetiology of such a complex and confusing problem in day-to-day gynaecological practice.

MATERIALS AND METHODS

It is descriptive observational study conducted in a private nursing home in Kalyani. The presentation of symptoms, pelvic examination findings at the admission, operative findings were recorded.

Study type - Cross sectional study

Period of study – 6 months

Inclusion criteria: Women presenting to the GOPD with pain in lower abdomen and pelvic region for more than 6months, above the age of 20 years; after proper consent were included in the study.

Exclusion criteria: Patients with chronic pelvic pain due to nongynecological causes.

Outcome was evaluated on the basis of preoperative abdominal and bimanual findings which were categorised as clinical findings as against laparoscopic diagnosis.

Statistical analysis -Done in Microsoft excel.

RESULTS & ANALYSIS

We conducted this study on 30 patients presenting with chronic pelvic pain.

It was found that 50% of the patients were in 30 - 40 years age group.

Age in years	Number	percentage
20	1	3.3
20-30	4	13.3
30-40	15	50
40	10	33.4
Total	30	100

Fig 1 age distribution

Parity	Number	Percentage
Nulliparous	5	16,7
1-2	13	43.3
3-4	10	33.4
4	2	6.6

Fig 2 parity distribution

So, majority 43.3% of women were parous with 1-2 child followed by 3-4 children.

	Number	Percentage
Low	15	50
Medium	5	16.7
High	10	33.4

Fig 3 socioeconomic distribution

Clinical findings in these 30 patients presenting with chronic pelvic pain were as follows; 20 patients were normal on detailed clinical evaluation, 5 patients had inflammatory mass, 3 patients had tubo-ovarian mass, ovarian cyst was present in 1 patient and fibroid was seen in 1 patient.

	Number	Percentage
Normal	20	66.7
PID	5	16,7
T.O mass	3	10
Fibroid	1	3.3
Ovarian cyst	1	3.3
	30	100

Fig 4 clinical diagnosis

All these 30 patients underwent diagnostic laparoscopy both with normal and abnormal clinical findings

The laparoscopic findings are tabulated below (fig 5)

	Number	Percentage
Normal	5	16.7
Endometriosis	9	30
Uterine fibroid	3	10
Broad ligament cyst	1	3.3
Ovarian cyst	2	6.7
Chronic PID	3	10
Chronic tubercular salpingitis	4	13.3
Omental adhesion	3	10
Total	30	100

Fig 5 laparoscopic findings

In laparoscopy only 5 patients had normal finding contrary to clinical findings where 20 patients were detected normal. Endometriosis was seen in 9 patients in laparoscopy followed by uterine fibroid in 3 patients, chronic tubercular salpingitis in 4 patients, omental adhesion in 3 patients and ovarian cyst in 2 patients broad ligament cyst in 1 and chronic PID in 3 patients.

DISCUSSION

This study confirms the previous observations that laparoscopy is an effective tool in the evaluation of women with CPP. There is error in diagnosis at preoperative pelvic examination in this study. We conducted a study with 30 patients presenting with chronic pelvic pain in the OPD of a private medical centre. The most common presentation was lower abdominal pain bearing no relation to the menstrual cycles. There was better correlation between abnormal preoperative pelvic examination and abnormal laparoscopic findings.^{9,10}

Among them majority 50% were in age group 30 - 40 years followed by 33.4% in age group above 40 followed by those between 20-30. So, in our study majority of patients were above 30 who presented with chronic pelvic pain contrary to the study done P. Bhatia where majority of the patient in age group 28.⁶

In our study majority of the patient with chronic pelvic pain had a parity between 1-2(43.3%) and 3-4(3-4%) and very minority of them were nulliparous (16.7%). This is similar to the study done by P Bhatia where the incidence of chronic pelvic was in para 2.⁶

In our study majority of the patients presenting with chronic pelvic pain belonged to lower socioeconomic status followed by high and middle socioeconomic group, Contrary to the study done P. Bhatia et al where majority belonged to middle socioeconomic group.⁶

Clinically majority of the patients were normal 20 (66.3%) in detailed clinical evaluation. A 16.7% presented with PID, 10% had tuboovarian mass and 1(3.3%) patient has ovarian cyst. Antibiotic was given for adequate duration in those who had questionable evidence of PID and were considered for laparoscopy only after they failed to respond for medical therapy to confirm the diagnosis. In a similar study, only 33 (38%) had significant findings on preoperative pelvic examination in contrast 57 (66%) had abnormal findings on laparoscopy. Conversely 53 (62%) had normal preoperative pelvic findings and 29 (33%) were negative for pathology on laparoscopy.⁸

At exploratory laparoscopy, endometriosis was found in 9 patients (30%), chronic tubercular salpingitis was found in 4 case (13.3%), uterine fibroid in 3 patients (10%), chronic pelvic

inflammatory disease was found in 3 cases and omental adhesion in 3 cases (3%) and 5 cases were found normal. Tubercular salpingitis was diagnosed by from the washing and biopsy specimen by subjecting them to Gene expert and HPE AFB culture. Similar to the study done by Geraldine Brichant et al where 46% cases had endometriotic lesions 12% uterine anomalies, 17% adnexal abnormalities and 31% abdominoperitoneal adhesion.⁷

Drawback of the study is too less a sample to come to an inference regarding the causation of CPP coming to GOPD in this area.

Source of funding: none

CONCLUSION:

One of the most confusing problems facing the gynaecologist is the patient who has CPP. When there are objective physical signs and symptoms, the accuracy for diagnosis of origin of pain is increased. Diagnostic laparoscopy had a great advantage in finding out the actual cause of chronic pelvic pain and help the gynaecologist to treat the disease correctly. Besides it might also help treat the cause in the same sitting. In the present study laparoscopy proved promising in accurately diagnosing endometriosis and PID in the study participants.

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|---|
| <ol style="list-style-type: none">1. Consultant Gynaecologist & Obstetrician, Gice Hospital, Kalyani2. Professor, Dept. of G & O, IQ City Medical College, Durgapur3. Associate Professor, Dept. of G & O, COMJNMH, Kalyani4. Senior Resident, Dept. of G & O, COMJNMH, Kalyani <p>✉ Email: rahulchaudhuri101089@gmail.com</p> |
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Case Report

HERLYN-WERNER-WUNDERLICH (HWW) SYNDROME AND ITS SURGICAL MANAGEMENT- A CASE REPORT

Arunasis Mallick¹, Swarna Nandi², Arijit Debnath³, Sumit Verma⁴

ABSTRACT

Herlyn- Werner-Wunderlich is a rare congenital anomaly which is generally detected just after menarche. In this case report a 11year old girl presented with cyclical lower abdominal pain and complaints of hypomenorrhea. After radiological imaging it was found that she was having uterine didelphys and unilateral obstruction and blind hemivagina. She was relieved of her symptoms by surgically opening the blind hemivagina and the dilatation of the strictured cervix.

KEY WORDS: Mullerian anomaly, Renal agenesis, Hematocolpos, Hematometra, Blind hemivagina

INTRODUCTION

Approximately 10% of infants are born with some abnormalities of the genitourinary system¹. The Herlyn-Werner-Wunderlich syndrome is a rare congenital anomaly characterised by uterus didelphys with blind hemivagina and ipsilateral renal agenesis². This syndrome was suspected for the first time in a young woman with regular menstruation and gradually increasing pelvic pain and a pelvic mass after menarche in 1922 and it was described in literatures. The true incidence of this anomaly is still unknown, but it has been reported between 0.1% and 3.8%³. Renal agenesis with an ipsilateral blind hemivagina was initially described in 1971 by Herlyn and Werner as Herlyn-Werner syndrome⁴. Wunderlich found an association of right renal aplasia with a bicornuate uterus and a single vagina in the presence of an isolated hematocervix In 1976⁵. In this case report we describe about a 11year old girl with complaints of hypomenorrhea and progressive

cyclical lower abdominal pain since menarche and her surgical management.

CASE REPORT

A 11-year-old girl presented in a Gynaecological OPD of a tertiary care medical college of West Bengal with cyclical lower abdominal pain during menstruation since her menarche and complaints of scanty menstruation. She had an average built, adequate nutrition, and of good intelligence quotient. Her general survey was within normal limits. On abdominal examination there was no tenderness or rebound tenderness in any quadrant. Tanner stage for breast was stage 2 and tanner stage for pubic hair was stage 3, without any axillary hair. On external vaginal examination no visible abnormality was identified.

Radiological investigations were done where ultrasonography of whole abdomen revealed she is having two separate uterine body and cervix

with two complete separate endometrial echo. Localised echogenic collection (62*29mm) seen in left sided lower endometrial cavity and cervical canal; suggestive of hematometra and haematocolpos on left side. Right endometrial cavity and cervix appear normal. Vagina could not be visualised properly. Right kidney normal and left kidney not visualised in its normal location or in any ectopic position.

MRI revealed two separate uterine horns having separate endometrium and myometrium. Complete thin septa noted in between two cervical canals. Left cervical canal is hugely distended with collection having blood products within. Right cervical canal is compressed, showing thin T2 hyperintense fluid. The two cervical canal is opening into the vagina with narrowing at cervico-vaginal junction suggesting stenosis. Left ovary is not visible; right ovary identified with tiny follicles. Left kidney is not visible. Right kidney enlarged with compensatory hypertrophy. Features are suggestive of uterine didelphys with cervicovaginal stenosis and left sided hematometra and congenital absence of left kidney.

After proper blood investigations, decision for examination and dilatation of cervix under anaesthesia was taken to relieve her symptoms. On 09/04/2021; exploration and dilatation was attempted and intra operatively it was found that only right cervical canal is visible and left cervix was not at all visualised. Right cervix was also having stenosis and after mild dilatation foul smelling blood came out; suggesting old menstrual blood. Per rectally a boggy mass was being felt even after evacuation of blood but the left cervix remained unapproached in this sitting. Post operatively her pain was reduced and she had no other complaints. Before discharge another ultrasonography was done in order to evaluate the patient on later stages. This ultrasound revealed 50*15 mm localised collection in left sided lower endometrial cavity. Right sided cervix appeared normal. But on her next menstrual cycle she again started having dysmenorrhea and scanty menstruation.

She was planned for another setting of evaluation under anaesthesia during her menstrual period. After proper asepsis and in lithotomy position, with the help of two Sims speculum, one cervix is identified at right side. A vaginal bulge with

bluish hue was identified on left side. Incision made over the bulge, foul smelling brownish fluid; suggesting old menstrual blood came out. Incision extended and it is identified that there is a longitudinal vaginal septum. Left sided external os identified and it is dilated with dilator. The incision line is oversewn with 3-0 vicryl to secure hemostasis. The two vaginas are intercommunicating in the lower third of the vaginal canals. The girl was discharged after 2 days with advice of local oestrogen cream application and oral oestrogens.

On follow up scans it was found that there is no stricture and no hematocolpos or hematometra is being formed. On the next menstrual cycle there was no complaints of dysmenorrhea and hypomenorrhea.



FIG 1: Intra-operative photo showing bluish hue and a bulge on left side of the vaginal canal.



FIG 2: on giving a sharp nick at the most prominent area; evacuation of altered blood noted.



FIG 3: opening of the blind vaginal canal



FIG 4: Image showing healthy right cervix and the newly created left hemivagina.

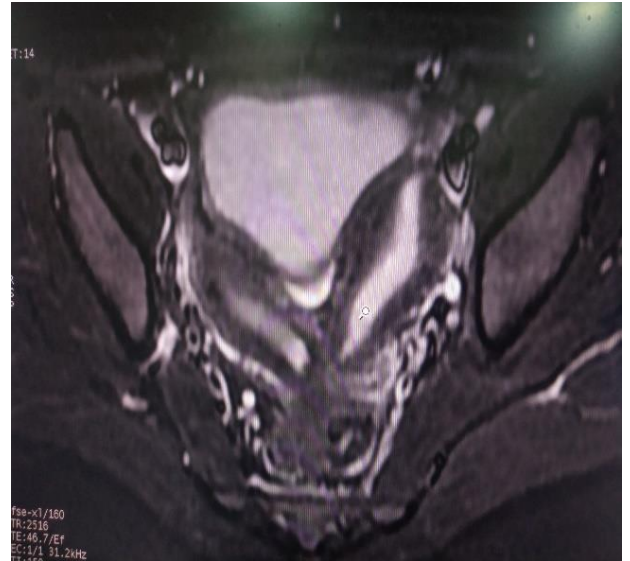
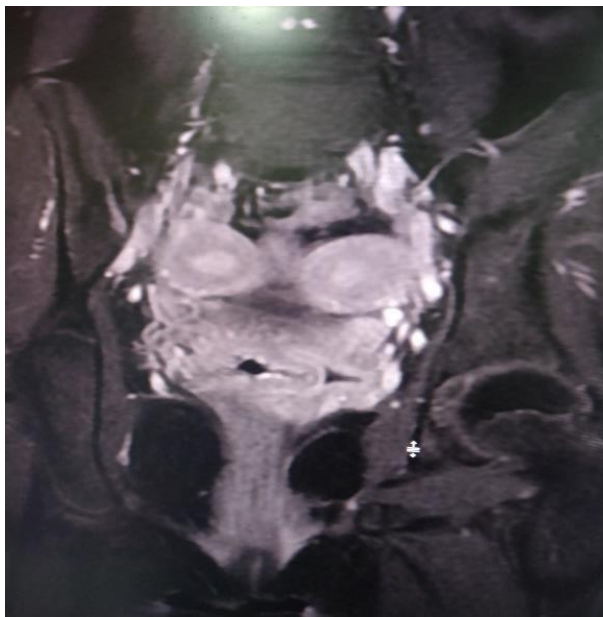


FIG 5: Post operative MRI showing didelphys uterus without any gross distension.

DISCUSSION

The urogenital system is derived from Intermediate mesoderm and the primitive urogenital sinus; which is a part of the cloaca. The uterine tubes are derivative of Paramesonephric duct; mesodermal origin. The uterus is formed by fusion of right and left paramesonephric ducts (uterovaginal canal). As the thickness of the myometrium increases, the unfused horizontal parts of the two paramesonephric ducts come. External genitalia formed from swellings that appear around the urogenital membranes. The two paramesonephric ducts get fused and give rise to uterine body and cervix. Vagina on the other hand has double origin; upper one third is derived from uterine canal and lower two thirds from urogenital sinus.

Lack of fusion of paramesonephric ducts in a localised area or throughout the length of the ducts may explain all possible uterine congenital anomalies. Our case comes under the classification where there is complete obstruction of hemivagina; uterus behind the septum is completely isolated from the contralateral uterus. There is no communication between the two uterus and vagina. Hematocolpos might occur after few months of menarche⁶.



FIG 6: Schematic diagram showing complete obstruction of a hemivagina with isolated uterus and formation of hematocolpos and hematometra. [according to the new classification system of Herlyn Werner Wunderlich syndrome]

Wolfian Duct is responsible for giving rise to ipsilateral ureter and kidney. On failure of formation of Wolfian duct (Left side for the present case scenario), the ipsilateral Mullerian duct gets displaced laterally and a blind sac and hemivagina is created from the Mullerian duct system; which fails to fuse with the other side and gives rise to a blind uterine sac leading to formation of hematocolpos and hematometra after menarche. The distal portion of vagina remains unaffected as it has a different origin⁷.

CONCLUSIONS

The Herlyn-Werner-Wunderlich (HWW) syndrome being extremely rare there needs to be a high amount of suspicion and clinical eye to isolate it from other mullerian anomalies. It is very commonly mistaken with other mullerian anomalies and the complaints of hypomenorrhea and dysmenorrhea are not taken into consideration. The diagnosis done via ultrasonography and MRI is of utmost help as it is noninvasive and do not cause any additional radiation.

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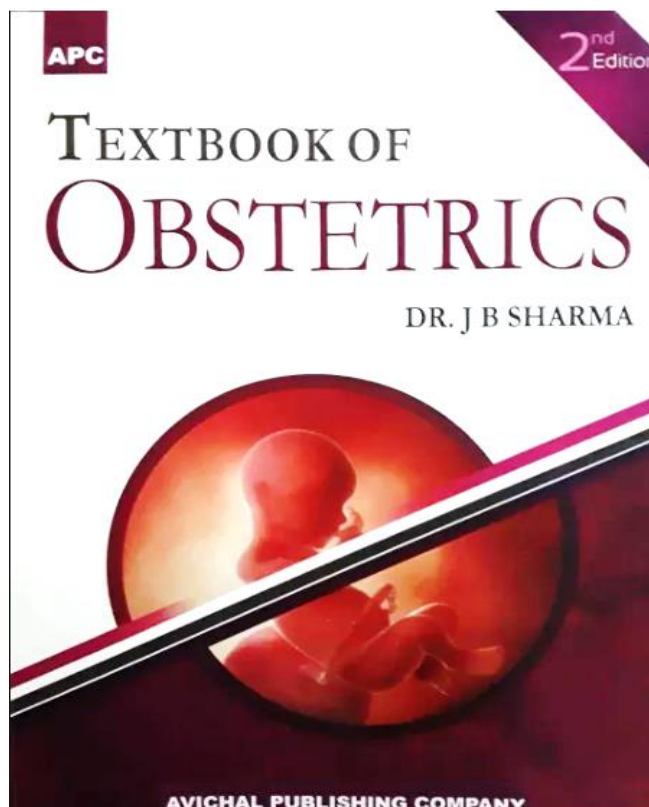
1. Senior Resident, Dept. of G & O, COMJNMH, Kalyani
2. Corresponding author- Post Graduate Trainee, Dept. of G & O, COMJNMH, Kalyani
3. Assistant Professor, Dept. of G & O, COMJNMH, Kalyani
4. Senior Resident, Dept. of G & O, COMJNMH, Kalyani

✉ Email: swarnandi25@gmail.com

Book Review

TEXTBOOK OF OBSTETRICS BY DR J B SHARMA

Manidip Pal



Textbook of Obstetrics, 2nd Edition, by Dr J B Sharma, Professor of Obstetrics and Gynecology from All India Institute of Medical Sciences, New Delhi is published by Avichal Publishing Company, New Delhi in 2019. The book is very lucid and illustrative over 824 pages. It is systematically divided into 21 sections. Section 1 deal with 10 chapters on Maternal Anatomy, Physiology, Fetal Growth and Development while section 2 deals with Antenatal Care including Prenatal Diagnosis and Therapy and has 5 chapters including early gestational hemorrhage. Section 3 is on Normal Labor with 4 chapters while section 4 deals with Abnormal Labor with 7 chapters covering all aspects of

labor including malpresentations, malpositions and complications of third stage of labor. Section 5 is on Neonatology by Prof Ramesh Kumar, Department of Neonatology, AIIMS, New Delhi. Section 6 is on two chapters on Normal and Abnormal Puerperium. Antepartum complications are discussed in section 7 with 4 chapters including antepartum hemorrhage. Section 8 has detailed medical, surgical complications including infection while section 9 has special conditions like Rh negative pregnancy. Section 10 deals with Operative Obstetrics with details of all operations like cesarean section, instrumental deliveries etc while section 11 is on Contraception. Miscellaneous chapters are discussed in section 12 including chapters on National Programs, Imaging, Obstetric Instruments, Specimens, Drugs, Spots etc. There is a separate chapter on Theory and Practical Examinations for different types of examination of MBBS, MD, DGO and DNB. The chapters on practical tips are very useful for students appearing in practical examinations.

The book uses evidence-based medicine with guidelines from the WHO and Various Colleges like American College and Royal College. The book is easy to understand and is up-to-date. It is very useful to PGs and UGs for their examination's preparations and to the clinicians for their day to day practice.

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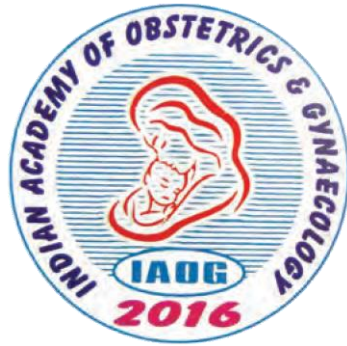
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