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Editorial Board

Journal Contact

Mailing Address

Nepal Society of Obstetricians and Gynaecologists (NESOG)
Paropakar Maternity and Women's Hospital
Thapathali,
GPO : 23700,
Kathmandu,
Nepal

Principal Contact

Prof Gehanath Baral
Editor-in-Chief

Nepal Society of Obstetricians and Gynaecologists (NESOG)
Paropakar Maternity and Women's Hospital
Thapathali,
GPO : 23700,
Kathmandu,
Nepal

Phone: +977 1 4252315
Fax: +977-1-4215175
Email: njogeditor@gmail.com

Support Contact

Office of the Editorial Board

Phone: +977 1 4252315
Email: nesog2011@gmail.com

Design and Layout
Mr Milan Chandra Khanal, Assistant Editor (9841426101)
E-mail: milanchandra2002@gmail.com

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Research tool

Baral G
Chief Editor, NJOG

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ABSTRACT

Background: Research usually uses a representative sample to draw an inference, thus it requires a methodologically strong research process that is ascertained by its research tool or instrument.

Conclusion: A good research uses a validated research tool.

Keywords: reliability, research, tool, validation, validity

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INTRODUCTION

Research tool or instrument denotes a means of collecting information or data.[1] Without this tool it is not possible to collect information in a desirable form. Therefore, the researchers use research tools of any kind and form during their research work and evaluation projects. Some of the tools will be devised then and there to address the specific issue or research question. Some tools are already in practice somewhere that has been used as such or used after their validation at research site. Use of validated tools in a study assures strength of the research methodology and the result would have external validity as well. Tools could be structured most of the time and some are unstructured like in qualitative study. Research project has a pre-defined time frame and the tools would have been structured but an unstructured tool may invite unpredictable result in terms of content or time duration.[2] Research (re-search) means a systematic investigation (search) or activity to gain new knowledge of the already existing (re-) facts. The purpose of research is to find out a solution or answer to the question through the application of scientific procedure and the solution carries validity if the tool used in this process is validated and established.[1]

Research tools could be open or copy righted and every researcher should respect it appropriately. A gray line appears if it is used entirely for academic purpose as the scientific knowledge is conveyed for the further scientific act but if not then it is considered as violation of ethical norms. A common understanding is that the scientific activities are not legally binding but by the professional and ethical norms in the scientific world.[3] Research tool becomes robust if it has both internal and external validity as well as with the reliability of reasonable degree. That's why there is a need to validate every research and practice tool.[4]

CONCLUSIONS

A good research tool should have validity, reliability and validated status for the generation of a generalizable scientific message.

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CORRESPONDENCE

Gehanath Baral,
Chief-Editor, NJOG
Paropakar Maternity and Women's Hospital, Kathmandu
Phone: +977-9841228829
Email: gehanath@gmail.com; njogeditor@gmail.com

Hepatitis B infection among indigenous people in Nepal: looking through an equity lens

Shedain PR[1], Baral G[2], Maharjan B[3]
[1]National Center for AIDS and SDT Control, Teku, Kathmandu, [2]Paropakar Maternity and Women's Hospital, Thapthali, Kathmandu, [3]Community Health Development Program, Public Health Concern Trust -NEPAL

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Aims: Disparity in health care service and disease prevalence are global issues. Hepatitis B infection is a global public health problem; its prevalence is ubiquitous and heterogeneous.

This article reviews the situation and an impact of hepatitis B infection in the indigenous people in Nepal through the lens of equity perspective.

Methods: Literature search and collection of information from different sources.

Results: Hepatitis B prevalence is low (0.9%) at the country level in Nepal but higher, up to 38%, among the indigenous population compared to the national prevalence. Those who live in the high endemic areas are at risk of getting the infection from both vertical and horizontal mode of transmission. The unvaccinated cohort of infant (0-11 months) between 2003 and 2016 has swollen, 2764362 in number or 29 % of the total cohort. The National Immunization Program (NIP) administered hepatitis B vaccination at 6 weeks of birth, considering the low prevalence at the national level. The NIP does not prevent perinatal transmission of the infection. The mother to child transmission of the infection often leads to chronic liver diseases and about 20–30% of adults who are chronically infected will develop cirrhosis and/or liver cancer. The indigenous populations are thus disproportionately affected by the infection.

Conclusions: The policy update is required to implement the hepatitis B vaccination at birth or within 24 hours in high endemic setting along with a comprehensive package to reduce the disparity, prevent the transmission, risk of chronic infection and its sequelae to achieve the national goal and international commitment on the sustainable development goal by 2030.

Keywords: equity; hepatitis b; indigenous people; mountain; Nepal

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INTRODUCTION

Hepatitis B infection is a global public health problem. An estimated 257 million people are living with chronic hepatitis B infection that is 3.5% of the global population, and mortality caused by viral hepatitis on the rise.[1] The hepatitis B surface antigen (HBsAg) seroprevalence of ≥8% defines high endemic areas, prevalence of 5%–7% defines high intermediate, 2%–4% low intermediate, and < 2% defines low endemic areas.[2,3] Hepatitis B was also used to be known as the "Australian Antigen" as it was discovered in Australian aboriginal people in 1960s. An universal infant hepatitis B immunization program was introduced nationally in 2000.[4] Still, a significant health disparity persists between indigenous and non-indigenous population in Australians,[5] the acute infection rates per 100000 populations for all ages were 3.6 and 1.1 for indigenous and non-indigenous people respectively between 2005 and 2015.[4] Likewise, the infection is widely prevalent among racial and ethnic minorities in the United States.[6,7] Similarly, pockets of higher endemicity are also found in tribal areas of India.[8] The infection varies considerably among the WHO Regions, with the highest in the African (6.1%) and Western Pacific Regions (6.2%), and among countries ranged from 0.20% (Mexico) to 22.38% (South Sudan).[9] All these facts conclude that the prevalence of the infection is ubiquitous and heterogeneous, it appears as a global phenomenon and indigenous ethnic populations are disproportionately infected. Thus, WHO has also considered indigenous population as a special community for the management of hepatitis B infection.[3]

In Nepal, the prevalence of the hepatitis B infection is considered low (0.9%).[10] A national survey conducted in pre and post vaccinated-children has revealed that the prevalence of the infection among the children is

CORRESPONDENCE

Dr Purusotam Raj Shedain
National Center for AIDS and SDT Control,
Teku, Kathmandu
Phone: +977-9841323924;
Email: shedaindr@gmail.com

0.3 and 0.1 percentage, respectively.[11] An estimate with a systemic review of the published data between 1965 and 2013 estimated 218943 HBsAg-positive population in Nepal, and country prevalence is low, 0.82% (0.80-0.84).[9] Other key population have low to high intermediate prevalence, i.e., the sero-prevalence is a low among HBV in Blood donors (0.35%-1.2%) and ante-natal mothers (0.5%);[12] and an intermediate among Injecting Drug Users (5.5%),[13] and people living with HIV/AIDS (4.4%).[14]

In contrast, a various contextual studies have shown that the prevalence of hepatitis B infection is high among the indigenous people. This article reviews the situation and future impact of hepatitis B infection and its sequelae in the indigenous peoples in Nepal through the lens of equity perspective.

METHODS

The literature searches were carried out in PubMed, Google scholar and search, and other relevant websites using the words; “hepatitis b”, “indigenous people”, “ethnic community”, and Nepal”. Relevant references were compiled in the EndNote X7.0.1 [Bld 7212] software, @ 1988-2013 Thomson Reuters. Due to the paucity of data and information related in the subject matter, the review has to be relied on various sources such as the Google search, and grey articles. The ethical approval was not required as this study is based on publicly available secondary data and information that already have taken consent or based on de-identify and aggregated population based information.

RESULTS

The prevalence of the infection and risk factors

The search was done with PubMed using the key words “hepatitis b and indigenous”, 193 articles were found, then the search was done with the words “hepatitis B" and indigenous and Nepal”, only one article was found,[15] which has suggested high prevalence of hepatitis B infection among mother (17%) and children living with hepatitis B infected mothers (48%%). The search with the words “hepatitis B and ethnic group”, 1138 articles were found; again search with the words "hepatitis B and ethnic group and Nepal”, one article was found that suggested some ethnic groups and geographic areas have higher prevalence (3.5-7.5%) rate of hepatitis B infection.[16,20,21] The literature searches were also carried out in Google scholar with the words: “hepatitis B and indigenous”, 10 results were found. Then search with the words; "hepatitis B" and indigenous in Nepal; one article was found that suggested high prevalence of the infection.[15] The gray literatures were also searched.

A study among mothers and under 5-year children has revealed the high prevalence of the infection among indigenous peoples in upper mountain region, i.e., 17% (95% CI, 11.01–22.99%) mothers and 48% children (95%CI, 28.42–67.58%) living with hepatitis B positive mother were infected. Among the infected mothers, 40% were hepatitis B envelope antigen (HBeAg) positive, higher prevalence of HBsAg among the children living with HBeAg positive mothers compared to HBeAg negative one (60% vs. 40%), and male children compare to female (60 % vs. 33%). Furthermore, only 36% of children were vaccinated with the third dose vaccination, among the vaccinated children 56 % were HBsAg positive.[15]

Likewise, a study conducted among seasonal migrants from indigenous community during the winter season from upper part of the Dolpa to Kathmandu, in 2006, had shown high prevalence of the infection, i.e., about 38%. A risk behavior were highly prevalent among the migrants; only 45% heard about the condom, overwhelming did not use condom (92%) , only few people (1.5%) used condom to protect STI. The consistence use of condom was absolutely non-exisistent, and early marriage at the age of 9 to 19 was rampant (82%). About 97% males and 50% female used alcohol either daily or at least once a week.[17]

Some other reports have also mimicked the previous findings; reports of winter clinic conducted by the Dolpa Tulku Charitable Foundation, among migrant from upper part of the Dolpa to Boudha Kathmandu, showed that about 18% migrants in 2012 and 14% in 2014 were HBsAg positive.[18,19] Other studies among the ethnic groups have also suggested the high prevalence of the infection as compare to the general population (0.9%), such as Gurung from Manang (7.3%) and Sherpa from Solukhumbu area (3.5%) in Nepal.[20,21]

A study conducted among pregnant women (N=16400) in Paropakar Maternity and Women Hospital revealed that the hospital prevalence of the infection among the pregnant was low (0.32 %). The prevalence of the infection among the Janajati was 0.5% and other than Janajati was 0.2%. The infection rate was significantly high among the Janajati (Pearson

Chi-Square 11.788, p=.001). The unadjusted odds of the infection among the Janajati with reference to other than Janajati was 2.596 (1.475-4.569), p=.001. The overwhelming number of participants were unaware of the infection (84.4%), less than one- fifths had heard of the infection (15.6%), and a very few were informed about their status (3.1%) (unpublished study).

The indigenous people who live in the areas were deprived of adequate modern health care services and compounded by a poor universal precaution.[22] Alcohol consumption in the indigenous communities is at epidemic rates.[15,17,23] They have their own health care system such as local doctors (Amchi) are providing various surgical procedures without proper sterilization, cultural practices of polyandry or polygamy, making lukewarm food into the mouth or premastication of food and feeding the baby, lack of awareness, unavailability of condoms, and other unsafe practices such as tattooing, piercing without sterilization and using common razors are putting the people at risk of the infection.[15,17,24] With these findings, we can conclude that the risk factors and prevalence of the infection are clustered in some ethnic indigenous population in Nepal.

Hepatitis B infection and sequaelae

The persons with chronic hepatitis B infection are at risk for serious illness and death, about 20–30% of adults who are chronically infected will develop cirrhosis and/or liver cancer.[2,3] These facts indicate the gravity of the problem among the indigenous community. A various studies have shown that jaundice and liver cancer is increasing in the indigenous community; the Nepal Living Standards Survey (NLSS), a national representative survey conducted by the Central Bureau of Statistics (CBS), has revealed the burdens of illness (liver) are disproportionately high among indigenous peoples, and hindering their economic advancement.[25] However, there is no hepatitis B specific surveillance, notification, and registration system in Nepal.

Table-1: WHO vaccine-preventable diseases: monitoring system. 2017 global summary, WHO UNICEF estimates time series for Nepal (Last updated 28-Feb-2018)

Year	2003 to 2016	2016	2015	2014	2013	2012	2011	2010	2009	2008	2007	2006	2005	2004	2003
Targeted (0-11 months)*	9,687,188	623,919	660,629	608,802	630,249	630,249	659,016	656,339	754,987	751,620	748,074	742,164	735,339	728,858	756,943
HepB3 coverage (%)	-	87	91	92	92	90	92	82	89	82	82	69	41	27	2
Vaccinated (n)	6,922,826	542,810	601,172	560,098	579,829	567,224	606,295	538,198	671,938	616,328	613,421	512,093	301,489	196,792	15,139
Unvaccinated (n)	2,764,362	81,109	59,457	48,704	50,420	63,025	52,721	118,141	83,049	135,292	134,653	230,071	433,850	532,066	741,804
Cumulative unvaccinated cohort	2,764,362	2,764,362	2,683,253	2,623,796	2,575,092	2,524,672	2,461,647	2,408,926	2,290,785	2,207,736	2,072,445	1,937,791	1,707,720	1,273,870	-
Cumulative unvaccinated cohort (%)	29	-	-	-	-	-	-	-	-	-	-	-	-	-	-

*MOHP/DoHS targeted (0-11 months) population, Nepal

Program perspective

In 2002, Nepal introduced single antigen hepatitis B vaccine in a phased manner, since 2004 the single antigen vaccine was replaced with a tetravalent vaccine (DPT-HepB). From 2009, hepatitis B vaccine has been administered as a pentavalent (DPT-HepB-Hib) vaccine to all infant at 6 weeks, 10 weeks and 14 weeks.[26] In 1016, national coverage with the third dose of hepatitis B vaccine reached 87%, but there are coverage gaps between the provinces [Province-1 (85.6%), Province-2 (76.1 %), Province-3 (90.4 %), Province-4 (94.7 %), Province-5 (89.1%), Province-6 (83.3%), and Province-7 (92.7%)]. However, a context specific study has shown that a very low coverage (36%) of third dose hepatitis B vaccine among indigenous children under 5-year in a mountain region.[15] The birth dose of infant hepatitis B vaccine has not surveyed in the National Demographic Health Surveys as at birth dose vaccine not yet administered in Nepal,[26] whereas, the global coverage with birth dose of hepatitis B vaccine was 39% in 2015 (baseline), and it has targets to reach 50% in 2020, and 90% in 2030.[27]

Furthermore, in Nepal, the unvaccinated cohort of infant (0-11 months) between 2003 and 2016 has swollen, 2764362 in number, which is 29 % of the total cohort [Table-1]. Obviously, those who live in the high endemic areas are at risk of getting the infection from both vertical and horizontal mode of transmission, as the policy is silence about the catch-up vaccination program for the risk population. Categorically, the unimmunized children and adolescents in the endemic areas are at high risk. However, those who are susceptible to the infection, the vaccination could avert future morbidity and deaths.

The birth dose of hepatitis B vaccine remains the cornerstone of prevention for mother-to-child transmission of the virus, especially for high endemic areas.[2,28] The first dose of hepatitis B vaccine (timely birth dose) prevents the establishment of the infection to newborn that already exposed, as a post-exposure prophylaxis, and the efficacy in preventing mother-to-child transmission ranges from 80 to 95% with sustained high coverage three dose vaccines.[29] However, the efficacy declines with increasing intervals between birth and the administration of the vaccine.[30] In Nepal, the proportion of women with a postnatal check within 2 days increased from 45% in 2011 to 57 % in 2016.[31] The birth dose could be administered with maternal health care services, and proceed to easy to difficult-from institution to home delivery as a recommended pragmatic strategy.[30]

Infants can acquire the infection from their untreated HBV infected mothers mostly during the birth. The mother to child transmission of the infection often leads to chronic liver diseases.[3] Use of hepatitis B immunoglobulin (HBIG) in infants born to mothers with active infection is also helpful to prevent the transmission.[32,33] An appropriate prophylaxis consists of HBIG and or hepatitis B vaccine at birth.[29,33,34] At birth vaccination with HBIG could reduce the mother-to-child transmission of the infection (overt), though, occult hepatitis B infection could be higher due to the immune pressure of HBIG and suggested administration of antiviral and HBIG during pregnancy to prevent mother-to-child transmission.[35]

The intervention's efficacy is determined by the concentration of the HBV in the mothers' blood. Infected mothers with HBeAg-negative have a near 0% risk of the transmission to their children vaccinated at birth, however, HBeAg-positive mothers have a 20 % risk of the transmission despite the vaccination at birth.[27,32] Treatment of pregnant with antiviral further reduces the risk of transmission to infants from the mothers with a high viral load, though standard guideline on this is awaited.[32]

National Immunization Program (NIP) has provided the vaccine at the 6 weeks of birth with the consideration of the low prevalence of the infection, low rate of facility delivery and cost of the program.[36] The introduction of at birth dose hepatitis B vaccine is still under consideration.[32,37] Furthermore, there is no specific hepatitis B control program in Nepal, though a various activities have been contributing to prevent the infection that include; infection prevention activities through safe motherhood program, harm reduction program through HIV/AIDS control program, infant vaccination program through the NIP, and condom promotion.

Vaccination against hepatitis B has become part of national immunization schedules in 179 countries.[38] WHO has recommended the birth dose vaccination within the 24 hours of birth, the vaccine is under used, reaching 39 % globally in 2015.[27] The prevalence of hepatitis B infection is a global in nature and disproportionately prevalent among the indigenous peoples and WHO considered the indigenous people

as special population for the management of hepatitis B infection that need to be further geared up with an effort.

CONCLUSIONS

Despite the low prevalence of the infection at the country level, the infection prevalence is disproportionately high among the indigenous people. The global momentum has been initiated for the prevention and control of viral hepatitis infection, a various initiation and policy and program document have been prepared.[2, 3, 27, 32, 37-41] These policies and initiations are supportive to formulate the national and contextual policy and program focusing on equity health care service to combat the infection among the indigenous people.

A national strategy or plan for the prevention, treatment and control of viral hepatitis including hepatitis B infection is required addressing the need of the indigenous populations that include: focused information system and response, intervention with continuum services ensuring outcome and impact, services based on equity, minimizing the risk of financial hardship providing cost effective and efficient services near to their community and context specific response with a innovation that globally accepted and suggested.[40] A triple elimination strategy (HIV, Syphilis and HBV) could be cost effective intervention combating hepatitis B mother-to-child transmission.[42,43] In Nepal, the national HIV Strategy Plan (2016-21) targets to eliminate vertical transmission of HIV and congenital Syphilis for fast-tracking response by 2021, there are possibilities of an integration or coordination between the programs such as National HIV/AIDS and STD control, National Tuberculosis, National Immunization, Safe motherhood and so on.[26,44,45]

To achieve the greatest impact, intervention should be tailored for the indigenous population such as a comprehensive hepatitis B virus immunization program: universal childhood vaccination with birth-dose, catch-up vaccination for children or adolescents where vaccination coverage is low and drop out high, and offering the vaccine to people who are at risk of infection or transmitting the virus.[27,46,47]

This is the high time to start interventions against the disparity issue, as nation has international commitment on SDG to eliminate viral hepatitis; national constitution has firmly stated that every citizen shall have the right to free basic and equity health care services from the State (article-35 and others).[48] Thus, to protect the health right of the indigenous people as per the constitution requires an update in the existing policy and implementing the program and activities that could address the needs of the people.

Finally, hepatitis B prevalence is low at the country level in Nepal but higher among the indigenous people. Given the high prevalence of the infection among the indigenous people; the national policy update along with a comprehensive package is needed to reduce the disparity, prevent the transmission, risk of chronic infection and its sequelae to achieve the national goal and international commitment on the SDG, a 90% reduction in new chronic infections and a 65% reduction in mortality, by 2030, which can benefit the indigenous people, nation and global community.

Disclosure

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Serum β-hCG Levels between 13-20 Weeks Gestation can Predict Development of Pregnancy Induced Hypertension

Kour G[1], Kour S[2]

[1]Combined Hospital, Sikandrabad, Uttar Pradesh, India [2] Department of Obstetrics and Gynecology Acharaya Sri Chander College of Medical Sciences, Sidhra, Jammu, Jammu & kashmir India,

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Aims: To find out predictive value of serum β human chorionic gonadotropin (β HCG) levels between 13-20 weeks of gestation in predicting the development of pregnancy induced hypertension (PIH) or pre-eclampsia, eclampsia.

Methods: Serum β HCG level was estimated in 200 normotensive patients between 13-20 weeks of gestation. The median value of Serum β HCG was calculated and patients were divided into two groups as per two times multiple of median (2MOM) values of Serum β HCG i.e. those above and below the 2MOM values. The patients were followed up to delivery and were evaluated for the development of PIH, pre-eclampsia and eclampsia.

Results: As per the median score of Serum β HCG in studied patients, the determined value of 2MOM was 30845 mIU/ml. Out of 200 patients, 23 (11.5%) patients were found to have values of Serum β HCG ≥ 2MOM. Twelve (52%) patients in Serum β HCG ≥ 2MOM group developed hypertension on follow up as compared to 13 (7.3%) patients in < 2MOM group ($p < 0.0001$). Also patients in the ≥ 2MOM group had higher prevalence of maternal and fetal complications.

Conclusions: Serum β HCG levels between 13-20 weeks of gestation can predict development of PIH in pregnant females

Keywords: β HCG; maternal complications; pregnancy-induced hypertension.

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INTRODUCTION

Gestational hypertension is one of the most common medical complication of pregnancy. It can lead to complications like preeclampsia, eclampsia, antepartum hemorrhage and is one of the common causes of maternal and fetal mortality and morbidity. How pregnancy incites or aggravates hypertension remains an unanswered question despite huge amount of research in this area.[1]

Placenta is central to the pathogenesis of gestational hypertension. Women with pregnancy induced hypertension (PIH) have hyperplacentosis. Early placental vascular damage in preeclampsia leads to placental hypoxia and increased production of β human chorionic gonadotropin (β hCG) by syncitiotrophoblastic cells.[2] Patients with twin pregnancies and molar pregnancies have increased β hCG levels and carry increased risk of PIH. Thus increased levels of β hCG in late first and early second trimester may be used as a marker of impending PIH.[3-5] We conducted this study to find out the predictive value of raised β hCG levels in predicting the development PIH, preeclampsia, or eclampsia.

CORRESPONDENCE

Sandeep Kour
House No. 141, Vasant Vihar,
Extension Sector 3 Trikuta Nagar Jammu
Jammu & Kashmir- India- 180012
Mobile: +91-94192-26645
E – mail: sandeepkour06@yahoo.com

METHODS

Two hundred patients with a gestational age of 13-24 weeks according to last menstrual period or according to ultrasonography (USG) were enrolled. A single serum β hCG level estimation was done between 13-20 weeks of gestation. Patients with history of hypertension, renal disease, diabetes, heart disease, thyroid disorders, multiple pregnancy, polyhydroamnios, or patients with USG documented congenitally malformed fetus were excluded from the study. After detailed history and clinical examination baseline investigations including complete blood count (CBC), renal and hepatic function tests, routine urine examination, fasting blood glucose, ABO and Rh grouping was done. Quantitative estimation serum β hCG level estimation was done by immunoenzymatic colorimetry method. Serum β hCG level of two times multiple of median (2MOM) for a given population of pregnant females is known to be associated with adverse pregnancy outcomes.

Therefore, the patients were dicotomised as per 2MOM criteria into two groups as high β hCG group i.e. Serum β hCG values ≥2MOM (≥ 30,845mIU/ml) and low β hCG group i.e. Serum β hCG values < 2MOM (< 30,845 mIU/ml). PIH was defined as a blood pressure reading of ≥140/90 mmHg.

Patients were followed in the outpatient department and were evaluated for development of PIH and associated symptoms of edema, puffiness of face, headache, decreased urine output. At the time of delivery maternal complications like eclampsia, abruption placenta, preterm labor, postpartum hemorrhage and fetal complications such as intrauterine growth retardation, prematurity, intrauterine death or stillbirth were noted. All patients provided informed consent. The study was approved by the Institutional Ethics Committee.

RESULTS

The mean age of the patients was 25.8±4.7 years (range = 17-38). Eighty seven patients (43%) were nulliparous and 46 (23%) had a history of one or more abortions in the past. Twenty three patients (11.5%) had Serum β-hCG values ≥2MOM [Table-1]. Patients in as high β-hCG group were found to have significantly more chances of developing PIH (52% vs. 7%) on the follow up. High β-hCG group patients were also significantly more likely to get maternal complications like eclampsia, abruption placenta, preterm labor, postpartum hemorrhage as compared to low β-hCG group (39% vs. 7.9%). Fetal complications like IUGR, prematurity, IUD were also seen significantly more in High β-hCG group (30% vs. 7.9%) [Table-2].

Table-1: Baseline characteristics of the patients (N=200)

Characteristics	Value
Age	25.8±4.7 (17-38) years
Parity	
Nullipara	87 (43%)
Para 1	63 (31%)
Para 2	29(14%)
Para 3 or more	21(10%)
History of Abortions	46 (23%)
Patients with Serum β hCG values ≥2MOM*	23 (11.5%)

*β hCG values ≥2MOM: β human chorionic gonadotropin values ≥ two times multiple of median

Table-2: Comparison of patients between high and low serum β-hCG values

Characteristics	High β-hCG group (n=23)	Low β-hCG group (n=177)
PIH	12 (52%)	13 (7 %)*
Maternal complications	9 (39%)	14 (7.9%) **
Fetal complications	7 (30%)	14 (7.9%) ***

PIH: Pregnancy Induced Hypertension *p<0.0001, **p<0.0005, ***p<0.005 by Fisher's Exact test

DISCUSSION

Gestational hypertension is one of the most common complication of pregnancy and it has an adverse impact on the maternal as well as the fetal outcome.[6,7] The exact cause of gestational hypertension is still not known. At present the termination of pregnancy is the only definitive treatment available to control the gestational hypertension.[8] Though the gestational hypertension manifests in the third trimester the underlying mechanisms start operating early in the pregnancy. It is with this information in background that researchers are trying to look for early markers of gestational hypertension so that patients can be picked up early and given special care.

Studies have shown that serum β-hCG levels are increased in patients with preeclampsia and eclampsia. There appears to be a positive correlation between raised serum β-hCG levels and preeclampsia and eclampsia with severe forms of disease having higher levels of serum β-hCG levels.[3,4,5,9] We decided to look for the serum β-hCG levels at 13-20 weeks of gestation as early pick up of the patients who are likely to get gestational hypertension gives more time to the physician to institute therapy.

In our study, we found out that patients with higher levels of serum β-hCG had significantly higher likelihood of developing gestational hypertension on follow up. This has been seen in previous studies also.[4,5,9] The origin of gestational hypertension lies in the placenta and occurs because of ischemia secondary defective trophoblastic invasion of spiral arteries. The ischemic placenta releases the substances which in turn act on the endothelium leading to gestational hypertension.[10,11] At present only calcium supplements and low dose aspirin have been shown to have preventive effect in gestational hypertension.[12,13]

In our study we also looked for the maternal and fetal outcome in patients. We found that patients with

higher levels of serum β-hCG levels had significantly more maternal and fetal complications as compared to patients who had low levels of serum β-hCG levels. This, however, could be related to the fact that patients with higher levels of serum β-hCG levels were more likely to be having PIH.

CONCLUSIONS

Thus, in our study we found out that higher levels of serum β-hCG levels estimation at 13-20 weeks of gestation was a good predictor of subsequent development of gestational hypertension and can be used in the outpatient setting to identify such patients and give them special care.

Conflict of interest: None

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Profile of Fetal Echocardiography in a Tertiary Cardiac Centre of Nepal

Sharma P[1], Shrestha P[1], Shrestha M[1], Sharma D[1]
[1]Shahid Gangalal National Heart Centre, Nepal

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Aims: To analyze the fetal echocardiographic diagnosis.

Methods: A descriptive study of fetal echocardiographic diagnosis at Shahid Gangalal National Heart Centre between October 2016 to September 2017.

Results: Total of 615 fetal echocardiography was performed in 607 pregnancies. Intrauterine heart disease noted in 79 cases. Echogenic intracardiac foci was the most common abnormality (6%) followed by VSD (1.3%), fetal arrhythmia (1.1%), pericardial effusion (1.6%), cardiomyopathy (0.3%), hypoplastic left ventricle (0.6%), DORV (0.3%) and tricuspid atresia (0.4%). Similarly, the most common referral for fetal echocardiography was for maternal disorder mostly diabetes mellitus.

Conclusions: Fetal echocardiography is an important tool for the antenatal diagnosis of congenital heart defects. Appropriate timing and judicious use increases the sensitivity and improves the perinatal outcome of newborns with congenital heart disease

Keywords: congenital heart disease; fetal echocardiography; Nepal

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INTRODUCTION

Heart defects are the most common congenital malformation in a fetus.[1] The incidence of CHD is 8 per 1000 live births.[2–4] Improvements in the antenatal diagnosis of cardiac anomalies have resulted in a significant reduction in neonatal morbidity and mortality.[5,6] Moreover, early diagnosis provides an appropriate pre and post natal planning, allowing appropriate prenatal counselling and improving parental psychological state. Emergent treatments and procedures, such as initiation of prostaglandin to maintain patency of the ductus arteriosus and balloon atrial septostomy, can be planned ahead of time, thereby avoiding hemodynamic compromise.[7–9] Ultrasound imaging of the fetal heart has been an established modality for detection of cardiac diseases in prenatal period. Fetal echocardiography is an advanced imaging tool requiring sophisticated ultrasound system and highly skilled manpower. Currently available ultrasound technology permits definition of complex fetal cardiac pathology in the hands of experienced clinicians and sonographers much as is done after birth.[10] Its use is not readily available specially in resource limited countries like Nepal. Fetal echocardiography services began in 2007 in Shahid Gangalal National Heart Centre and continues to be one of the few centres in Nepal with ongoing services. Here, we present the one year result of fetal echocardiography performed in the only referral centre of Nepal.

METHODS

All cases who underwent fetal echocardiography from October 2016 to September 2017 were included in the study after taking informed consent from the participants. Demographic profile, gestational age, reason for referral, maternal history and family history was recorded. Fetal echocardiography was performed by two dimensional, pulsed wave and color doppler echocardiac methods using a Philips Affiniti 70G echo machine with a convex array probe with frequencies between 1MHz to 5MHz. The major scanning views obtained were four chamber view, outflow tract view, three vessel view and ductal and arch view. The cardiac situs, ventriculoarterial connections, venous inflow, atrial and ventricular

CORRESPONDENCE

Dr Poonam Sharma
Shahid Gangalal National Heart Centre, Kathmandu Nepal
Phone: +977-9855056256;
Email: medpoonam@gmail.com

chambers, atrioventricular and semilunar valves and cardiac rhythm were assessed.

RESULTS

Total of 615 fetal echocardiography was performed in 607 pregnancies. Among them 536 fetal echocardiography were found to be normal and intrauterine heart disease noted in 79 cases. The most common referral for fetal echocardiography was for maternal disorder mostly diabetes mellitus, screening purpose and significant family history [Table-1].

Table 1: Indication for referral for Fetal Echocardiography

Indication	No.	%
Maternal Disorders	244	40.1
Screening	141	23.2
Family History	139	22.8
Abnormal USG	57	9.3
Fetal abnormality	26	4.2

The most common cardiac finding was echogenic foci followed by structural defects [Table-2].

Table-2: Findings in Fetal echocardiography

Echocardiographic findings	Number (percentage)
Echogenic Foci	37 (6%)
Pericardial effusion	10 (1.6%)
Isolated VSD	8 (1.3%)
Fetal arrhythmia	7 (1.1%)
Hypoplastic left ventricle	4 (0.6%)
Tricuspid atresia	3 (0.4%)
Cardiomyopathy	2 (0.3%)
DORV	2 (0.3%)
One each of TAPVC, TGA, Intra cardiac mass, AVSD, Ebsteins Anomaly, Dextrocardia with common inlet double outlet single ventricle	

Note: VSD: Ventricular Septal Defect, TAPVC: Total Anomalus Pulmonary Venous Return, AVSD: Atrioventricular Septal Defect, DORV: Double Outlet Right Ventricle

DISCUSSION

Routine screening with obstetrical ultrasound may not detect subtle cardiac abnormalities which are the most common congenital malformation in a fetus. Moreover cardiac disease is known to occur more frequently in apparently low risk pregnancies.[11]However, according to the American Society of Echocardiography, the primary indications for fetal echocardiography are fetal heart abnormalities or fetal arrhythmia detected by routine prenatal sonography along with family history of congenital heart disease, maternal diabetes or systemic lupus erythematosus, fetal exposure to a teratogen, fetal karyotype abnormality, and other fetal system abnormalities.[12]

Our study shows a five-fold increase in the volume of fetal echocardiography over a period of two years in the same centre.[13]In our study, most common referral indication for fetal echocardiography was maternal condition, mostly diabetes mellitus, followed by abnormal prenatal sonographic findings and family history. Similar referral patterns are found in various literatures[14,15] Whereas in some studies abnormal cardiac findings in prenatal sonography was major referral indication.[16,17] Postnatal echocardiograms or pathology and autopsy reports, and patient medical records.

RESULTS

Of 6,002 pregnant women who had undergone prenatal sonographic examination during the study period, 275 (4.6% With the incidence of congenital heart disease of 8-10 per 1000 live births, the incidence of fetal echocardiography is estimated to be ten times more.[18]This increased incidence of heart disease in the fetus depends on the systematic screening and definite protocols for fetal cardiac screening within a country. In our study the frequency of intrauterine heart disease is 12.8 % which is concordance with the literatures.[19–21] The most common finding was echogenic focus in the left ventricle which was 6% in our study which is similar to the study done by Shipp et.al.[22] Echogenic foci in the heart has been known to be present in 1.5-4.0% of pregnancies which can reach to up to 10-30% in Asian populations.[22,23] Pericardial effusion which is defined as an accumulation of pericardial fluid in utero of thickness of than 2 mm was found in 2% of low risk pregnancy by Dizon-Townson et al which is similar to our observation.[24] Fetal arrhythmia may be defined as an irregularity of the cardiac rhythm, as an abnormally slow (<100 bpm) or fast (>180 bpm) heart rate, or as a combination of irregular rhythm and abnormal heart rate. Fetal arrhythmias are detected in at least 2% of unselected pregnancies during routine obstetrical scans and are a common reason for referral to the fetal cardiologist.[25] In present study, 7 out of 615 (1.1%) fetuses had arrhythmia, 5 of which were sinus bradycardia without associated structural heart disease and 2 of them were complete heart block.

Limitations: Major limitation of our study was the lack of follow up of the newborns screened and the absence of autopsy report of aborted fetuses.

CONCLUSIONS

The increasing number for fetal echocardiography performed in the centre suggests increasing referral for early detection of cardiac abnormalities.

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Awareness with Recall in General Anesthesia undergoing Cesarean Section

Gurung T,[1] Shrestha S[1], Basnet U[1], Shrestha AB[1]
[1]Paropakar Maternity and Women's Hospital, Thapathali, Kathmandu

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Aims: To determine the incidence of awareness with recall in parturient undergoing cesarean section under general anesthesia in Paropakar Maternity and Women's Hospital.

Methods: Retrospective observational cohort study of the patients who underwent cesarean section under general anesthesia from April mid 2014 to April mid 2017 (Baishakh 2071 to Chaitra 2073 BS). Awareness questionnaires filled up through the modified Brice interview.

Results: A total of 162 patients underwent cesarean section under general anesthesia and 138 were included in the study. None of them had awareness and six patients had a dream.

Conclusions: No awareness with recall found and prospective study is required to determine the condition.

Keywords: awareness with recall; cesarean section; dream; general anesthesia

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INTRODUCTION

Awareness is defined as a recall of events occurring during general anesthesia.[1] This term almost universally accepted by both medical and legal circles, and its meaning is well understood. Patients undergoing cesarean section, cardiothoracic surgery or emergency surgery, patients with a difficult airway and those developing intraoperative hypotension are among those considered to have increased chances of awareness and the incidence in this group may be as high as 1–2%.[2] Additionally, in a survey of 3,000 patients who had general anesthesia for cesarean section, an incidence of about 0.9% for any recall and 7% for dreaming, was reported.[3]

The most commonly used method of monitoring for awareness is measurement of the patients' end tidal volatile agent concentration.[4] Assurance of 0.8-1 MAC of exhaled anesthetic agent is likely to assure lack of awareness.

Awareness with recall (AWR) during anesthesia is important because of the long-term complications that the episode may cause. Post-traumatic stress disorder (PTSD) was found in 14.3%. Characteristic symptoms include anxiety and irritability, insomnia, repetitive nightmares, depression, a preoccupation with death, and a concern with sanity that makes the patients reluctant to discuss their symptoms.[5] They may fear of doctors, hospital and particularly future operation.

The objective of the study was to evaluate the incidence of awareness with recall in general anesthesia during cesarean section patients through a retrospective cohort analysis, and the clinical description, including the psychological outcome, of the detected cases. Secondary objectives were to evaluate the urgency of cesarean section and the types of awareness.

METHODS

The study design was approved by Paropakar Maternity and Women's Hospital, Institution Review Committee. As this was retrospective observational cohort study, only verbal consent was obtained from patient while interviewing them. All the parturient scheduled for lower segment cesarean section under general anesthesia were enrolled in the study from the period Baisakh 2071 to Chaitra 2073 BS (April 2014-April 2017).

CORRESPONDENCE

Dr. Tara Gurung,
Senior Consultant Anesthesiologist
Paropakar Maternity and Women's Hospital,
Thapathali, Kathmandu
Email: grgtara@hotmail.com;
Mobile No: 9841379504

The demographic data of the parturient such as age, parity and ASA grading and indication for general anesthesia were recorded from hospital record book. All these variables were already incorporated in the hospital record book. Those patient's contact details was taken from the record section.

Assessing the Incidence of Awareness

We assessed the presence of awareness with recall via phone calls. Given the number of patients was interviewed; we chose only one interview time point. Interviewer questionnaires conducted through the modified Brice interview-6 which is defined by the following questions:

- What was the last thing you remember before going to sleep?
- What is the first thing you remember after waking up?
- Do you remember anything between going to sleep and waking up?
- Did you dream during your procedure?
- What was the worst thing about your operation?

After above questions was asked, if the patient had awareness we further classified through Michigan awareness classification.

- Michigan Awareness Classification Instrument
- Class 0: No awareness
- Class 1: isolated auditory perceptions
- Class 2: Tactile perceptions (e.g. surgical manipulation or endotracheal tube)
- Class 3: Pain
- Class 4: Paralysis (e.g. feeling one cannot move, speak or breathe)
- Class 5: Paralysis and pain

An additional designation of "**D**" for distress was also included for patient reports of fear, anxiety, suffocation, sense of doom, sense of impending death, etc.

Patients who were mechanically ventilated/died in the postoperative period which resulted in a missed interview were excluded in the final analysis.

The choice of anesthetic agents, muscle relaxants, and perioperative analgesia was left to the discretion of the theater anesthesiologist. Being a tertiary care center, all the cases in our institution are managed by anesthesia residents in training supervised by qualified consultant anesthesiologist. All patients received balanced anesthesia (induction with propofol/sodium thiopentone or ketamine and succinylcholine, maintenance of anesthesia with muscle relaxants and isoflurane (<1 %), opioid after delivery of the baby). Intraoperative monitoring includes continuous electrocardiogram monitoring, pulse oximetery, capnography and noninvasive blood pressure in regular intervals.

Evaluation of awareness was based upon the interview. The primary outcome measure was the incidence of confirmed awareness, which was defined by the patient's recollection of intraoperative events during interview using the structured questionnaire. All patients who were suspected to have awareness as per interview were to be reinterviewed by an independent reviewer to confirm the diagnosis of awareness. Definite awareness was defined as occurring when the patient was certain of having been aware at any time during the operation. Awareness was considered as possible in those cases where the patient thought she had been awake during surgery, but was not completely sure.

All data generated during this study were kept confidential in accordance with institutional policies and that the investigator did not use such data and records for any purpose other than to conducted this study.

Collected data was entered using Microsoft Excel 2010. An awareness endpoint was carried out with the data from patients classified as 'AWR yes' or 'AWR no' as well as 'dreaming yes' or 'dreaming no' in the initial assessment. Results were presented in number (%).

RESULTS

Total delivery in Paropakar Maternity and Women's Hospital during 3 years of periods from 2071 to 2073 BS (April 2014 to April 2017) were 55,642, out of which 41,293 were vaginal delivery and remaining 14,349 were cesarean delivery. Thus the rate of cesarean delivery of was 25.78%. Among total cesarean section in 14,349 cases; only 162 (1.13%) cases had undergone general anesthesia; and 138 of them were included in the final analysis. Twenty four parturient (14.81%) were excluded, three maternal death and 21 parturient could not be reachable.

The demographic data of the parturient were shown in Table 1. One hundred thirteen patients were from age group of 20-35 years which was commonest

reproductive age group. There was 119 ASA I and 19 ASA II parturient. Primigravida were 57 (41.30%), second gravida were 41(30.43%) and multigravidas were 40(28.98%).

Table 1.

	Variables		Number (%)
1	Age in years	<20	14 (10.14%)
		20-35	113 (81.88%)
		>35	11 (7.97%)
2	ASA	II	119 (86.23%)
		III	19 (13.76%)
3	Parity	Primi	57 (41.30%)
		Second	41 (29.71%)
		Multi	40 (28.98%)

Table 2.

Indication for General anesthesia for CS	Number
Cord prolapse	40 (28.98%)
Failed SAB or prolong surgery	36(26.08%)
APH	22 (15.94%)
Eclampsia	12 (8.69%)
Hypertensive disorder	9 (6.52%)
Obstructed & 2nd stage of labor	6 (4.34%)
Anatomy difficulty	5 (3.62%)
Chorioamnionitis	4 (2.89%)
HELLP	4 (2.89%)

The most common indication for general anesthesia was cord prolapse followed by failed spinal or prolongation of surgery. There were 40 (28.98%) cases of cord prolapse and 36(26.08%) cases of failed spinal cases requiring the general anesthesia.

Table 3.

	Total number
Awareness with recall	0
Dream	6 (4.35%)

In the study, none of the parturient has awareness with recall but six parturient (4.35%) had a dreaming as shown in Table 3.

DISCUSSION

Awareness during surgical anesthesia is not a new problem. Incidences were high in the early days. As techniques improved the problem of awareness with recall dwindled into insignifance. The risk of awareness correlates with depth of anesthesia. The patient is paralyzed by a neuromuscular blocking agent, are associated with highest risk of awareness, if the depth of anesthesia was inadequate. Cesarean sections have been defined as a risk factor for the development of awareness under general anesthesia.[7,8]

In a study conducted by Lyon G et al.[3] in 3000 patients who underwent cesarean section under general anesthesia, the frequency rate of remembering anything and the frequency of dreaming were reported to be 0.9 % and 7%, respectively. In this study six (4.35%) patients had dreams; however the relationship between dreams and light anesthesia is not fully established. Bogod DG et al.[9] found higher incidence of dreaming in the emergency group (28% compared with 7%), stated that may be due to greater degree anxiety.

Awareness in the cesarean section in our population has never been studied; we therefore wanted to detect the incidence of awareness in parturient

The rates of awareness with recall and unpleasant dreams during general anesthesia have been reported in many previous studies. In this study, we have collected total 162 cases in three years period from Baishakh 2071 to Chaitra 2073. Twenty one cases that we couldn't reach through their contact number and three cases of maternal mortality were excluded. However, intraoperative death has not been recorded. In rest of the cases nobody has complained of awareness with recall; although six cases said that they had a dream, which they couldn't remember it. One possible explanation for this difference between our study and the published data could be a variation in anesthetic techniques and because of retrospective study of three years period; while we interviewed some parturient may not recall anything.

Ambulkar RP et al[10] conducted prospective observational study of 934 high risk cancer patients. Those patients were interviewed at three points using the modified Brice interview questionnaire, as we did it our study. They concluded none of their patients reported awareness.

Bergman IJ et al[1] reviewed 8372 incidents reported to the anesthetic incident monitoring study, 81 cases had in which perioperative recall was consistent with awareness; 51 cases of definite awareness and 31 cases with a high probability of awareness. Awareness was mainly due to drug error resulting in inadvertent paralysis of an awake patient and failure of delivery of volatile anesthetics. In developed countries, it also has financial, professional and personal consequences for the anesthesiologist. In a recent closed claims analysis from the USA there were 18 claims for awake paralysis, with a median payment of US $9500, suggesting that the financial

implications are not trivial.[11]

Even though central neuraxial blocks are most popular technique for cesarean section; some parturient still undergo the surgery under general anesthesia, because of various reasons like safety of mother (eclampsia, coagulation disorder etc) or safety of baby (cord prolapse, fetal bradycardia etc). In our study cord prolapse is the most common indication for general anesthesia. Besides, hypertensive disorder in 21 cases, almost all the cases had received analgesic dosages of ketamine (20 mg) during induction, which might be the reason patients didn't recall anything. Previous study showed Ketamine more effectively blocked maternal responsiveness to commands and strong stimuli during the first few minutes after anesthetic induction for cesarean section than did thiopental or a combination of thiopental and ketamine, each at a lower dose.[12] Another reason is, in the previous years, we have been using nitrous oxide as analgesia along with other inhalation agent (Isoflurane) during general anesthesia because of institute personal reason we couldn't continue nitrous oxide in our new operation theater. The incidence of awareness appears to vary inversely proportion with the concentration of nitrous oxide. It has been reported to be essentially ablated if a low concentration of a volatile agent is administered with 50% of nitrous oxide in the interval between induction and delivery (e.g. Halothane 0.5%, isoflurane 0.6% etc) and increased concentration of nitrous oxide.[13] In this study one patient had a failed intubation, in which laryngeal mask airway was inserted. Indication for general anesthesia was for prolongation of surgery.

Assessing depth of anesthesia is challenging as clinical signs are unreliable and not specific. The clinical signs signaling development of awareness are mainly signs due to sympathetic stimulation. Intraoperative hypertension, tachycardia, lacrimation, sweating, coughing and patient movements could indicate development of awareness. BIS monitoring has been proven to be effective for monitoring depth of anesthesia and scores <60 had been recommended to prevent the occurrence of awareness.[14] However, its availability and cost[15] limit its routine use.

Cesarean section has more chances of awareness, renders patients at risk of inadequate anesthesia because of avoidance of opioids and benzodiazepine until the delivery of baby, as well as rapid induction and maintained with limited volatile agents concentration to decrease the chances of uterine atony, more the concentration of inhalation anesthetic agent, more the chances of uterine relaxation.[14] Another reason to keep light anesthesia, is the important element in resuscitation management due to hemodynamic instability of the patient. However, a noteworthy result was our patients did not remember the period of anesthesia, or their dreams.

Limitation of this study is as this is a retrospective study, some data were missing and there are chances that patient might forget the moment of operation because of an anxiety or long time. Total cases were very low as compared to cesarean section under spinal anesthesia.

CONCLUSIONS

Our investigation showed that none of the cases had the incidence of awareness with recall, however, dreaming were noticed in six patients. Nitrous oxide and ketamine plays vital role in abolishment of awareness with recall.

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Review of uterine rupture at Paropakar Maternity and Women's Hospital

Uprety I[1], Baral G[2], Shrestha A[3]
[1]Paropakar Maternity and Women's Hospital, Kathmandu, Nepal

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Aims: To determine the case profile of uterine rupture.

Methods: Retrospective descriptive study from in-patient record file during two years period.

Results: Incidence of uterine rupture recorded was 72 per hundred thousand deliveries (1 in 1390), 25% had ruptured uterus antepartum and 60.7% had live baby.

Conclusions: Scarred uterus was the commonest risk factor for rupture uterus and antepartum rupture is not uncommon.

Keywords: cesarean section, scarred uterus uterine rupture

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INTRODUCTION

Ruptured uterus is the obstetric emergency, which accounts for major risk factor for maternal and fetal mortality and morbidity. This catastrophic condition is often seen in women undergoing vaginal birth post cesarean delivery (scarred uterus). But ruptured uterus is even seen in primipara women who has unscarred uterus, which is extremely rare condition, which is estimated to occur in 1 in 8,000 to 1 in 15,000 deliveries.[1,2]

There are many factors reported in different literatures which increases the risk of uterine rupture which may be scarred uterus, grand multiparity, uterine anomaly, fetal malpresentation, fetal macrosomia,, induced labor, obstructed labor or instrumental delivery.[3-5]

Due to unavailability of proper health care facility in every village, lack of education, ignorance, poverty, social taboos and many other reasons, majority of women of our country are not having regular antenatal checkups and proper hospital deliveries. They prefer to deliver at home unattained by skilled birth attendant. They only visit the hospital setting when the situation is grave and in need of emergency intervention threatening the life. Increasing trend of cesarean delivery has also increased the risk of women for uterine rupture in her following delivery.[6,7]

Ruptured uterus may present with abdominal pain in previous scarred uterus, PV bleeding, abnormal fetal heart rate or uterine inertia post severe pain abdomen. Most common fetal heart rate pattern associated with uterine rupture is fetal bradycardia and late deceleration, which accounts for about 87.5% of cases.[3,7]

Uterine rupture is fortunately a preventable condition. And to prevent and reduce the maternal and fetal mortality and morbidity it is important to identify and determine the risk factor for uterine rupture, which is one of the leading causes of maternal death in developing countries like ours.[8]

METHODS

This is the retrospective analysis of 2 years (April 2016 - April 2018) at Paropakar Maternity and Women's Hospital of women attending for care. During the course of time total of 28 patients were diagnosed to have ruptured uterus and were included in the study. The ethical committee of the hospital approved the study. Detail analysis of the charts of the patient was done and data regarding demographic characteristic, clinical presentation, risk factors, operative findings, management, maternal and fetal outcome were studied. Full thickness rupture and scar dehiscence and maternal bleeding that needed immediate operative interventions were included in our study.

CORRESPONDENCE

Dr IcchaUprety
Paropakar Maternity and Women's Hospital, Kathmandu, Nepal
Email: iccha.uprety@gmail.com
Mobile: +977-9851213180

RESULTS

During the study period, 28 cases (72 per 100 thousands) of ruptured uterus were identified out of 38,922 deliveries. Out of 28 cases 15 (53.57%) were unbooked and 13 (46.42%) were booked in our center. The mean age, parity and gestational age were28.6 years (range = 21-39), 2.75 (range = 1-7) and 36.75 weeks (range = 30-40) respectively.

The incidence of uterine rupture was 1 in 1390 deliveries which is 0.071% with 1.5% in scarred uterus and 0.64% in unscarred uterus [Table-1].

Table-1: Risk factors associated with uterine rupture

Risk factor		Number	Percentage (%)
Scarred uterus (75%)	Prior 1 LSCS	17	60.7
	Prior 2 LSCS	4	14.3
Un scarred uterus (25%)	Unexplained	4	14.3
	Fetal malpresentation	2	7.1
	Grand multipara	1	3.5
	Obstructed labor	1	3.5
	Instrumental delivery	1	3.5

Three-forth cases were in spontaneous labor and rest had rupture before going into labor [Table-2].

Table-2: Distribution of case of uterine rupture in terms of labor status

Uterine rupture	Spontaneous labor	Not in labor
Unscarred uterus	9	-
Prior 1 LSCS	9	6
Prior 2 LSCS	3	1

Lower segment uterine rupture were found in 15 cases (53.6%) followed by 6 cases (21.4%) of lower segment rupture extending to upper segment, 1 case of rupture involving bladder rupture and in 2 cases rupture was extending upto broad ligament.

Intra-operatively the estimated blood loss ranged from 300ml to 4 liters and hemoperitoneum was identified in 7 cases (28.6%) [Table-3].

Choice for repair were mainly based on the extent, type and location of rupture, and hemodynamic status of the patient; 24 patients (85.7%) underwent repair of rent with (6, 21.4%) or without (4, 14.3%) tubal ligation and 4 patients (14.3%) underwent subtotal hysterectomy in which repair was not possible.

Despite of grave maternal complication associated with uterine rupture, there was no maternal mortality present during the study period due to ruptured uterus and60% had live baby [Table-4].

Table-3: Intraoperative findings

Findings	Number	Percentage (%)
Hemoperitoneum	8	28.6
Fetus in abdomen	4	14.3
Fetus inside uterus	21	75.0
Broad ligament hematoma	2	7.1

Table-4: Fetal Outcome following uterine rupture

Fetal Outcome	Number	Percentage (%)
Alive	17	60.7
IUFD	9	32.1
Still Birth	2	7.1

DISCUSSION

Rupture of the gravid uterus is the rare, and potentially life threatening and devastating condition. It is still considered to be the one of the serious obstetric emergency.[9] If not detected timely and it cases serous fetal and maternal health consequences even in the presence of advance medical facility.

The incidence in our center was found to be 1 in 1,390, which accounts for 0.071%, which is similar to the reports in previous publications.[10-13] Our study not only confirmed the risk factors for uterine rupture like scarred uterus, fetal malpresentation, instrumental deliveries and multiparity but also demonstrates that these four major risk factors contributed 84.7% of uterine rupture in our series. The single leading risk factor (previous cesarean section) contributed to 75% of uterine rupture, a great deal of caution should be taken while managing and giving trial of labor to the previously scarred uterus.

Different literatures suggested grand multiparity, obstetrical trauma, malpresentation, and fetal macrosomia to be the leading risk factors for uterine rupture.[3-5] But in our study the major risk factor turned out to be prior cesarean delivery. This may be due to continuous rise to cesarean deliveries and women presenting in their next pregnancy in labor leading to increase risk of maternal morbidity including uterine rupture.[15]

The life threatening consequences secondary to uterine rupture depends on the duration between the uterine rupture and the effective management. So, prompt diagnosis and maternal and fetal resuscitation and emergency management should be taken into account to avoid the catastrophic situations like life threatening uterine hemorrhage, maternal shock and mortality.

Surgical intervention would be either repair of rupture or subtotal or total hysterectomy according to clinical and obstetric condition. This also depends upon the type, site and extent of rupture of uterus. Several literatures have suggested subtotal or total hysterectomy as procedure of choice but some suggest that surgical repair is safer and immediate treatment of choice.[16,17] In our series we achieved successful repair in 85.7% cases. However, the risk of recurrence of uterine rupture in subsequent pregnancy is high.[18,19] So, the decision of repeat Cesarean Section and Vaginal Birth After Cesarean (VBAC) should be meticulously judged. Proper counseling and repeated follow up is needed. We performed tubal ligation in 21.4% of cases.

Though we didn't find any maternal mortality after uterine rupture, some studies report maternal mortality rate ranging from 0 to 13%.[20,21] Absence of maternal mortality in our study demonstrates that with prompt diagnosis and timely intervention and management with the patient with high risk can reduce maternal mortality to zero.

Definitive management for the fetus is the prompt delivery to reduce the fetal morbidity including fetal hypoxia, anoxia, acidosis and fetal mortality. Delivery within 30 min of uterine rupture is associated with good neonatal outcome.[22-24] However, majority of the cases in our study were unbooked so we were unable to exactly tell the exact time of the rupture of uterus and the time of management. The time delay between the rupture and delivery were the major contributory factor for the poor fetal outcome in our study (39.3%). Timely detection, proper availability of the transportation and early referral to the equipped center should be emphasized

CONCLUSIONS

Previous cesarean delivery (scarred uterus) was the most common risk factor for uterine rupture. Timely detection and management saves women's life. Prospective study would have determined other potential risk factors like grandmultiparity, fetal malpresentation and obstructed labor.

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Maternal and perinatal outcome of teenage pregnancy in a tertiary care centre

Subedi A[1], Shrestha J[1], Shrestha A[1], Gurung S[1]
[1]Department of Obstetrics and Gynecology, Manipal College of Medical Sciences, Pokhara

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Aims: To evaluate the maternal and perinatal outcome in adolescent pregnancy,

Methods: This was a cross-sectional study conducted in Department of Obstetrics and Gynecology, Manipal Teaching Hospital, Pokhara from October 2017 to March 2018 for duration of 6 months.

Results: There were total 82 cases of teenage pregnancy in the study duration with incidence of 6% among total deliveries. Majority of cases were of age 19 and were primigravida. Fifty five percent of the cases had normal vaginal delivery and cesarean section accounted for 39% of cases. The major indication for cesarean section was meconium stained liquor (52%) followed by oligohydraminos (15%) and cephalopelvic disproportion (11%). The maternal complication accounted for 59% of total cases. Among them, anaemia was highly prevalent comprising 11% of cases followed by PPROM (9.8%) and hypertensive disorders in pregnancy (8.5%). In perinatal outcome, the incidence of preterm birth was 15.9% and low birth weight was 13.4%. The rate of NICU admission was 2.4% and there was one case of still birth.

Conclusions: The study showed that teenage pregnancy is at increased risk of adverse maternal and perinatal outcome. So if we lay an effort for reducing the incidence of teenage pregnancy, we can bring in positive changes in the indicators of maternal and perinatal morbidities.

Keywords: adolescent; anemia; low birth weight; pregnancy; perinatal; teenage

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INTRODUCTION

Adolescence is the period between the ages of 10-19 years that encompasses time from puberty onset to full legal age (WHO, 2002b). It is generally a complex period where a number of factors may lead to sexual behaviors and reproductive health (RH) risks. Pregnancy in this period of life is often associated with pregnancy related complications such as anemia, hypertensive disorders, preterm delivery, low birth weight babies, maternal mortality, perinatal and neonatal morbidity and mortality.[1,2]

Adolescent pregnancy is a rising public health issue globally especially in developing countries due to tradition of early marriage, low socioeconomic status and illiteracy. Every year, an estimated 21 million girls aged 15 to 19 years and 2 million girls aged under 15 years become pregnant in developing countries.[3,4] Approximately 16 million girls aged 15-19 years and 2.5 million girls under age 16 give birth in developing countries.[3,5]

CORRESPONDENCE

Dr Anjali Subedi
Lecturer, Manipal College of Medical Sciences, Pokhara
Email- anzee739@gmail.com
Phone : +977-9856080108

Adolescents make up about 23% of population in Nepal (UNICEF, 2013). NDHS (2011) reported that 17% of teenage girls had already given birth or were pregnant with their first child. This percentage is increasing rapidly from 1% among those aged 15 to 39 % in those aged 19. A WHO study stated that adolescents aged <16 years face four times the risk of maternal death than those women aged in their 20s, and the death rate of their neonates is about 50%. It has been projected that the incidence of teenage pregnancy will rise by 2030 due to early engagement of adolescents in sexual life and reluctance and ignorance of contraception.[6] Hence this issue has been prioritized by UN in sustainable developmental goal.

This study aims to evaluate the maternal and perinatal outcome in adolescent pregnancy.

METHODS

This was a prospective cross-sectional study conducted in Department of Obstetrics and Gynecology, Manipal Teaching Hospital (MTH), Pokhara from October 2017 to March 2018 for duration of 6 months. All pregnant women aged 13-19 years who were admitted to Obstetric ward of MTH were enrolled in the study after their consent. Information was

noted in a predesigned performa. Maternal outcome measures recorded were anemia, hypertensive disorders in pregnancy, operative deliveries with their indications and maternal mortality. Perinatal outcomes recorded were stillbirth, low birth weight, any NICU admissions with their indications and early neonatal death. The cases were followed till the time of discharge from the hospital. The data were entered and analyzed using SPSS software version 17. Descriptive statistics in terms of mean and standard deviation were calculated for continuous variables while frequencies and percentage were calculated for categorical variables.

RESULTS

There were 82 (6%) teenage pregnancies with mean age of 18.4 years (range= 14-19) and 46.35% were at 19 years of age. Around 93% of cases were primigravida and the mean gestational age was 38 weeks. There were 3 cases below 28 weeks, out of which two were cases of incomplete abortion and one was case of molar pregnancy. There was increased tendency of postdate (40 weeks or above) pregnancy among adolescents by 41.5%. Cesarean Section appears to be high [Table-1]. There were two cases of manual vacuum aspiration for incomplete abortion and one suction and evacuation for molar pregnancy.

Table-1: Mode of delivery

Mode of delivery	Frequency	Percentage
Vaginal	45	54.9%
Cesarean Section	32	39%
Instrumental (vacuum)	2	2.4%

The most common indication for Cesarean Section was meconium stained liquor (52%) followed by oligohydraminos (15%), prolonged labor (11%) and cephalopelvic disproportion (11%).

There were two cases of vacuum delivery and both applied for prolonged second stage of labor [Figure-1].

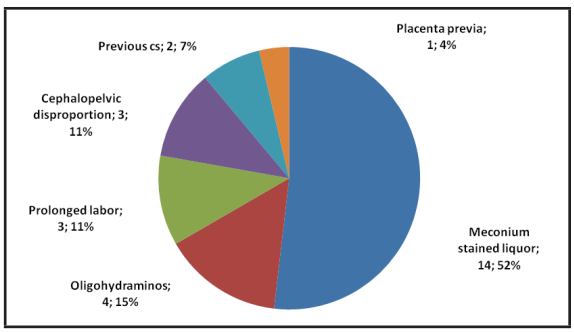

Figure-1: Indication for cesarean section

There were total 49 cases of maternal complications among teenage pregnancy accounting for 59%. Anemia was the most common complication followed by PPROM, hypertensive disorders, PROM and preterm. There were 3 cases of early pregnancy complications out of which two were incomplete abortion and 1 was molar pregnancy [Table-2].

Table-2: Maternal complications

Maternal complications		Frequency (n=49)	Percentage
Anemia		9	10.97%
Preterm premature rupture of membranes (PPROM)		8	9.75%
Hypertensive disorders in pregnancy	Gestational hypertension	3	8.53%
	Severe preeclampsia	3	
	Eclampsia	1	
Premature rupture of membranes (PROM)		7	8.53%
Preterm labor		3	3.65%
Early pregnancy complications (Incomplete abortion/molar)		3	3.65%
Twin pregnancy		2	2.43%
Rh -ve		2	2.43%
Infectious desease (chicken pox, syphilis)		2	2.43%
Previous cesarean section		2	2.43%
Antepartum hemorrhage		1	1.2%
Malpresentation (breech)		1	1.2%
Rheumatic heart disease		1	1.2%
Gestational diabetes mellitus		1	1.2%

The mean birth weight of newborn was 2.8 kg with minimum of 1.5 kg to maximum of 3.7 kg. Greater proportion of newborns had appropriate birth weight i.e. 2.5 kg or more. Only 13.4% had low birth weight. Preterm birth accounted for 15.9% of cases. There were only two neonates admitted in NICU and both for preterm. And there was one case of still birth with no any early neonatal death. Regarding the sex of newborns, female baby predominated with 50.63% of total newborns [Table-3].

Table-3: Perinatal complications

Perinatal complications	Frequency	Percentage
Low birth weight	11	13.4%
Preterm	13	15.9%
NICU admission	2	2.4%
Still birth	1	1.2%

DISCUSSION

Teenage pregnancy is on the rise due to increased vulnerability of adolescents in unsafe sex, lack of knowledge regarding contraception and also their reluctance to its use. The incidence of adolescent pregnancy in this study was 6%, which was similar to the study done by Suwal A. in one of the tertiary care centre in Bharatpur, Nepal.[7] cross sectional study was carried out in College of Medical Sciences Teaching Hospital (CMSTH). However, in contrast to this study, the incidence of teenage pregnancy was high (10-15%) in other studies done outside Nepal.[8–10] The reasons for low incidence in our study may be due to the fact that majority of teenagers have no antenatal care, and they prefer home delivery because of their illiteracy and low socioeconomic status as shown by various studies.[11-12]

Majority of adolescent mothers were of age 19 in this study, which is similar to other studies as well.[11,13–15] As expected majority of cases were primigravida. Regarding the mode of delivery, around 55% cases had normal vaginal delivery and 39% cases had Cesarean Section. Findings similar to this study have also been shown by studies of Kamini S and Suwal A.[7,11] We usually anticipate the increased rate of cesarean and instrumental deliveries in teenagers due to gynecological immaturity leading to cephalopelvic disproportion and obstructed labor.[8,16] However, our study showed increased proportion of vaginal delivery and this may be due to the reason that majority of cases were late teenagers and also may be due to good prenatal and intranatal care received in our centre. The mean birth weight of newborn in this study was 2.8 kg which might have also contributed to increased rate of vaginal delivery. Various studies have shown that pregnancy outcomes in late teens were better than that of early teens.[17]

For cesarean section deliveries, the most common indication was meconium stained liquor followed by oligohydraminos, prolonged labor and cephalopelvic disproportion in our study. The increased incidence of meconium stained liquor can be attributed to the fact that the majority of cases (41.5%) were postdate in this study. In contrast to our study, the literature shows that the common indications for cesarean in adolescents were cephalopelvic disproportion, hypertensive disorders and acute fetal distress.[8,18] All LSCS were emergency may be due to arising complications (low maternal age, maternal illness and fetal complications) during pregnancy and during delivery.[19]

Maternal complications accounted for 59% of cases in our study which signifies that teenagers are at higher risk for pregnancy related adverse outcomes. Varying degrees of anemia was the most common complication among the study population which was a consistent finding in other studies as well.[15,18,20] Low iron stores are common in these growing teenagers before pregnancy and are hence predisposed to the risk of developing iron deficiency anemia during pregnancy, which is further aggravated by their insufficient dietary intake.

The incidence of hypertensive disorders among teenagers in our study was 8.53%, with three cases of severe preeclampsia and one case of eclampsia. In the study by Kumar et al found the frequency of hypertensive disorders significantly higher in teenagers than in adult women. Although various studies have documented increased maternal mortality among adolescents, there were no cases of maternal mortality in the present study, most likely due to small sample size. [19]

Among the perinatal outcome, our study showed 15.9% cases of preterm birth. The incidence of PPROM was around 10% in our study and this fact can be attributed to increased cases of preterm birth. The incidence of low birth weight was 13.4 % with neonatal admission rate of 2.4% and indication of both neonatal admissions was preterm. There was only one case of still birth accounting for 1.2%. In the study conducted by Rita D, the incidence of low birth weight was 12% and perinatal mortality was 2% which was similar to our study. Aparna J[8] did a study where the incidence of low birth weight was 16.7%, preterm birth was 11.7% and rate of NICU admission was 3.3%.[17] Hence the findings of our study correlated to other studies as well. Various studies have compared the perinatal outcome of adolescent pregnancy with that of adult mothers and the results have shown poor perinatal outcome in teenagers.[19,21] The increased incidence of poor maternal health, increased prevalence of anemia, hypertensive disorders in teenagers, and inadequate antenatal care may have major contribution to preterm birth, low birth weight and increased rate of still birth and early neonatal death in teenage pregnancy.

CONCLUSIONS

Anemia, hypertensive disease and prelabor rupture of membrane were thr common complications among teenage pregnancy. One-third of teenage pregnancy had adverse perinatal outcome as low birth weight,

preterm labor and NICU admission.

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Risk Factors for Adverse Outcome in Pregnant Women with Obstructed Labor.

Dixit Thapa B[1], Regmi MC[1], Rai R[1]
[1]Department of Obstetrics and Gynecology, BP Koirala Institute of Health Sciences, Dharan, Nepal

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Aims: The aim of the study was to assess the risk factors for adverse outcomes in pregnancy with obstructed labor.

Methods: It was a prospective descriptive study conducted at BP Koirala Institute of Health sciences (BPKIHS).The patients with obstructed labour were managed and followed up until delivery and six weeks postpartum from Jan to Dec 2012.

Results: There were 57 (0.6%) cases of obstructed labour out of 9500 deliveries. The main cause was cephalopelvic disproportion in 36 (63.2%). The majority of the cases were from rural areas, low socioeconomic status, non salaried and illiterate. Risk for maternal mortality, peripartum hysterectomy and perinatal mortality as adverse outcomes was significantly associated with low socioeconomic status (AOR 12.5, P=0.02) and literacy status (AOR 21.9, P=0.001). If only the risk of perinatal mortality is taken as an adverse outcome, it is significantly associated with booking status (AOR 7, P=0.001), low socioeconomic status (AOR 9.62, P=0.037) and literacy of the patient (AOR 15, P=0.001). Perinatal mortality rate was 100 per 1000 live births in women with obstructed labour. The case fatality rate was 1.2%.

Conclusions: Individual socio-demographic and health system factors are strongly associated with obstructed labor.

Keywords: maternal mortality; obstructed labor; perinatal mortality; peripartum hysterectomy

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INTRODUCTION

Labor is said to be obstructed when in spite of good uterine contractions, the progress of labor comes to a standstill due to mechanical factors causing obstruction to delivery and without external assistance spontaneous delivery is not possible.[1,2]

It comprises one of the five major causes of maternal morbidity and mortality in developing countries.[3,4] It accounts for approximately eight percent of maternal deaths globally,[5,6] 75% of spontaneous rupture of uterus during labor[7,8] and 80% of genital fistula seen in developing countries.[9] Incidence in developing countries is about 1-5% depending on health care and transport facilities available.[10,11,12] and an important cause of perinatal mortality.

The main obstetric causes of obstructed labour in low income countries include cephalopelvic disproportion, malposition and malpresentation and fetal anomalies like hydrocephalous.[13] The chain of factors affecting the outcome of obstructed labour in low-income settings includes both cultural and socio-economic factors. Adherence to traditional childbirth practices and individual beliefs as well as poverty restricting the family's ability to pay for transport is directly related to delay in seeking skilled care at birth. In our country the childhood marriage, teenage pregnancy and grand multiparity are common; who are high risk for cephalopelvic disproportion and more delivery takes place outside the hospitals. So obstructed labor is expected to be a common problem of our obstetric practice.[14]

No study had been conducted in BPKIHS regarding this subject. So this study had been designed to have an insight in this condition as the centre is referral centre for all the complicated obstetric conditions of the region. Obstructed labor is associated with different adverse maternal and fetal outcomes. This study was designed to know the risk factors for adverse outcomes in obstructed labor.

METHODS

It was prospective descriptive study done in patients who were admitted in BPKIHS with diagnosis of obstructed labor in 2013. All cases with clinical diagnosis of obstructed labor after 28 weeks period of gestation without co-morbid medical conditions were taken.

Uterine rupture was assessed and managed according to hospital protocol. Obstruction was released either

CORRESPONDENCE

Dr. Baburam Dixit(Thapa)
Assistant Professor, Department of Obstetrics and Gynecology
BP Koirala Institute of Health Sciences, Dharan, Sunsari, Nepal
Phone Number: 9842352481,
E mail address: baburamdixit@yahoo.com

by vacuum assisted vaginal delivery (VAVD) or Cesarean section. Foley catheter was left in situ for 14 days postpartum and followed up till six weeks.

Data was collected in pre designed Proforma and expressed as frequencies, percentages, mean and standard deviation and recorded in tabular form, histogram and pie charts. Crude odds ratios (COR), adjusted odds ratios (AOR) and their 95% confidence intervals (CI) were calculated. Kaplan and Mayer coefficient was used to see the association between the risk factors and adverse outcomes of obstructed labor.

Data analysis was done by using SPSS software version 11. Chi square test was used for comparison of data for statistical significance. A p-value of < 0.05 was taken as significant.

RESULTS

During the study period, total number of deliveries was 9500, out of which 57 ended up with obstructed labor, the incidence being 0.6 %. Among the 57 women who presented with obstructed labor 61% were aged between 20 to 29 years while 51% were nulliparous. Majority of them were from rural areas (82.5%) with low socioeconomic status 45(78.9%), non salaried 51(89.5%) and illiterate 34(59.6%) [Table-1].

Table 1: Sociodemographic characteristics (n=57)

Characteristics	n(%)
Age (years)	
15-19	10(17.5)
20-29	35(61.4)
≥30	12(21.1)
Parity	
Primi	29(50.9)
2-4	18(31.6)
>4	10(17.5)
Literacy	
Illiterate	34(59.6)
Literate	23(40.4)
Occupation	6(10.5)
Salaried	51(89.5)
Unsalaried	
Socioeconomic status	
Low	45(78.9)
Not low	12(21.9)
Residence	
Rural	47(82.5)
Urban	10(17.5)

The most common cause of obstructed labor was cephalo-pelvic disproportion (63.2%); 75.4% underwent Caesarean section (4 four had uterine rupture), 14.1% laparotomy and 10.5% vacuum extraction.

Maternal complications observed among the women with obstructed labor were postpartum hemorrhage (10.5%), ruptured uterus (17.5%), puerperal pyrexia (24.5%), bladder injury (5.2%), and vesico-vaginal fistula in one patient. Hysterectomy was required in eight patients and three women died as a result of obstructed labor (5.2%). There were 22 (38.6%) perinatal mortality. [Table 2]

Table-2: Maternal complications (n=57)

Complications	n(%)
Postpartum hemorrhage	6(10.5)
Ruptured uterus	10(17.5)
Hysterectomy	8(14)
Bladder injury	3(5.2)
Puerperal pyrexia	14(24.5)
Wound infection	6(10.5)
Broad ligament hematoma	1(1.7)
Vesico-vaginal fistula	1(1.7)
Maternal mortality	3(5.2)

The study showed that the patient who are non salaried, unsupervised and are from rural area have higher odds of having adverse outcomes (maternal mortality, perinatal mortality, hysterectomy) but are not statistically significant whereas low socioeconomic status (OR 12.5, P=0.02) and illiteracy (OR 21.9, P=0.001) are statistically significant. [Table 3]

Table -3: Association between socio-demographic characteristics and adverse outcomes (maternal mortality, hysterectomy and perinatal mortality in composite)

Charac teristics	Category	Group Adverse	normal	OR (95% CI)	P value
Occupation	Non salaried Salaried	24 1	27 5	4.44 (0.484-40.7)	0.187
Supervision	Unsupervised supervised	17 8	4 28	14.8 (3.8-56.9)	0.128
Residency	Rural urban	23 2	24 8	3.83 (0.735-19.9)	0.111
Socio economic status	Low Middle	24 1	21 11	12.5 (1.49-105.7)	0.02
Literacy	Illeterate Literate	23 2	11 21	21.9 (4.35-110.7)	0.001

The study showed that unsupervised pregnancy (OR 7, P=0.001), low socioeconomic status (OR 9.62, P= 0.037) and illiterate women (OR 15, P=0.001) were at a statistically significant higher risk of having perinatal deaths as an adverse outcome. However, women with obstructed labor who are non-salaried and who are from rural areas have higher chance of perinatal mortality but not statistically significant. [Table 4]

Table -4: Association between socio-demographic characteristics and perinatal mortality

Characteristics	Category	Group Adverse	normal	OR (95% CI)	P value
Occupation	Non salaried Salaried	22 0	29 6	1.76 (0.53-38.4)	0.99
Supervision	Un supervised supervised	14 8	7 28	7.00 (2.10-23.24)	0.001
Residency	Rural urban	20 2	27 8	2.96 (0.567-15.48)	0.198
Socio economic status	Low Middle	21 1	24 11	9.62 (1.145-80.99)	0.037
Literacy	Illeterate Literate	20 2	14 21	15.0 (3.019-74.53)	0.001

DISCUSSION

The incidence of obstructed labor in our study was 0.63 %. However, studies conducted elsewhere in Africa have reported incidence rates of between 0.9% - 7%,[2,15] this was lower than 2.3% reported by Dutta[16] in 1979, 1.27% by Daff Allah et.al[17] from Sudan in 2003. There is as high as seven percent in a retrospective study done at Jimma University Specialized Hospital, Ethiopia[18] and also less than other studies of Adhikari et al, [19]Anjum Ara[20] and Shahida et al.[21]

The main obstetric causes of obstructed labor in our study were cephalo-pelvic disproportion (63.2%), malpresentation (17.6%) and malposition (19.3%) which have also been reported by other authors elsewhere.[2]

Our study provides baseline information on the individual socio-economic and sociodemographic and health system factors associated with obstructed labor and and its adverse outcomes which is similar to study conducted by Kabakyega et al[22] in south western Uganda. In our study, the main maternal complications observed were ruptured uterus, puerperal sepsis, bladder injury, postpartum hemorrhage and fistulae and are similar to what has been reported by other authors.[11,23]

Moreover, we found out that adverse outcomes of obstructed labor such as perinatal death and maternal mortality was strongly associated with socioeconomic status, supervised pregnancy, literacy occupation and residency. Resource poor women may not be able to pay the money required for obstetric emergency and therefore face delay I and II. The association between low socio-economic status and obstructed labor has also been reported by other authors.[24-26]

CONCLUSIONS

Obstructed labor remains a major obstetrical problem. Adequate antenatal care and proper care at delivery could prevent it. Individual socio-demographic and health system factors are strongly associated with obstructed labor and its adverse outcome in country like Nepal.

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A Comparative study of intrathecal hyperbaric Bupivacaine with or without Morphine for Post-Operative Analgesia in Hysterectomy

Basnet U[1]
[1]Department of Anesthesiology, Paropakar Maternity and Womens' Hospital, Thapathali, Kathmandu

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Aims: The aim of the study is to compare the effect of addition of morphine with bupivacaine and bupivacaine alone in intrathecal anesthesia for the quality and the duration of analgesia in hysterectomy.

Methods: Prospective randomized analytical study was conducted in patients undergoing hysterectomy under spinal anesthesia over period of one year. Patients were randomized into two groups: hyperbaric bupivacaine (15mg) only or hyperbaric bupivacaine (15mg) plus morphine (0.2mg). The mean duration for the request of first analgesia in post-operative period, mean visual analogue scale (VAS) score at the time of request of analgesia and common adverse effects were compared.

Results: The post-operative analgesia was prolonged (260.32 Vs. 154.34 minutes) along with low VAS pain scale (5 vs. 7.5) in combination group but the respiratory depression was significantly high.

Conclusions: The addition of morphine to hyperbaric bupivacaine prolongs the total duration of sensory analgesia, causes significantly greater frequencies of respiratory depression and causes no significant increase in other complications like hypotension, bradycardia, nausea and vomiting and pruritus, in comparison to patients receiving intrathecal hyperbaric bupivacaine only.

Keywords: adverse effects; hyperbaric bupivacaine; morphine; post-operative analgesia; spinal anesthesia

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INTRODUCTION

Pain is generally considered an important postsurgical complication, which may result in serious morbidities if left unaddressed.[1] Hysterectomy is associated with severe or moderate postoperative pain. Postoperative pain management remains a significant challenge after abdominal surgery.[2] It is also a main challenge for anaesthesiologists and even with the help of multimodal analgesia techniques patients still remain undertreated.[3]

The usual method of the pain control in half of the patients often does not provide an adequate analgesia and postoperative pain can delay patient's recovery.[4] Anesthetic technique appears to be effective in postoperative pain.[5]

Spinal blocks are major regional techniques with a long history of effective use for a variety of surgical procedures and pain relief. Spinal anesthesia (SA) is one of the most versatile regional anesthesia techniques available today. [6]

CORRESPONDENCE

Dr Ujjwal Basnet,
Registrar of Anesthesiology,
Cell:+977-9841364705,
email: ujjwalbasnet05@gmail.com

Intrathecal opioid administration is an attractive analgesic technique since the opioid is injected directly into the cerebrospinal fluid, close to the structures of the central nervous system where opioid acts. Morphine is the prototype opioid agonist to which all other opioids are compared. Analgesia is the most prominent when morphine is administered before painful stimulus occurs.[7]

Since 1979 intrathecal morphine has been used for postoperative pain management.[8] Doses of intrathecal morphine ranging from 0.1 to 0.25 mg have been used to reduce side-effects and complications. In current study, we tested hypothesis that SA with hyperbaric bupivacaine 0.5% in addition to 0.2mg intrathecal morphine is superior to hyperbaric bupivacaine 0.5% only to reduce postoperative pain and analgesic consumption after elective hysterectomy surgery.

METHODS

This randomized prospective comparative study was conducted in department of anesthesia, Nepalgunj Medical College, Teaching Hospital, Kohalpur, over a period of one year (from 1st November 2012 to 31st October 2013) after ethical approval obtained from

the ethical committee, written informed consent obtained from the patients. This study was conducted in 100 patients of ASA physical status of I and II of age group between 20 to 60 years undergoing routine abdominal or vaginal hysterectomy. The patients were divided randomly into two equal groups using envelop technique - Group A: 50 cases with hyperbaric bupivacaine (15mg) and Group B: 50 cases with hyperbaric bupivacaine (15mg) and Morphine (0.2mg). Patient who refused to participate, sensitivity to study drugs, patients on anticoagulant or antiplatelet therapy or with bleeding diathesis or coagulopathy, haemodynamic instability, raised intracranial pressure, local infection at back; severe spinal deformity and emergency surgery were excluded from the study.

Following a detailed pre-anesthetic examination, all patients were admitted to the hospital at least a day before surgery had undergone pre-anaesthetic physical check-up and biochemical examination which was noted in the proforma. The patients were kept fasting from 24.00hrs the night prior to surgery. All the patients received Pantaprazole 40mg and diazepam 5mg orally at 22:00hrs the night before surgery and the same dose in the morning of surgery day at 6:00 hrs.

Patient was brought to pre-anaesthetic room and IV line was opened with 18 gauze cannula and fluid preloading was done with 1litre Ringer lactate over 20 minutes. Patient was attached to ECG, non-invasive blood pressure (NIBP) monitor, and pulse oxymeter on OT table. Patients were randomly allocated, using closed envelope technique, to receive either heavy bupivacaine alone (15mg) or heavy bupivacaine (15mg) and morphine 0.2mg Under strict aseptic preparation, lumbar dural puncture was performed at L3/4 inter space with 25G sterile disposable Quincke's type spinal needle, using standard midline approach in the sitting position. Free flow of CSF was confirmed in each quadrant during the 360 degree rotation of the needle on removal of the stylet. Intrathecal administration of the drugs was done at the rate of 0.2 ml/second. At the end of the injection, a small sterile dressing was applied and the patient immediately turned into horizontal supine position, with a pillow under the head and neck. For intra operative monitoring and management following parameters were recorded: quality of spinal anesthesia by using bromage scale of motor block, intraoperative VAS pain score from the time of surgical incision at 10 minutes interval till the end of surgery, duration of surgery, NIBP, pulse rate, respiratory rate, ECG and SPO_2 - baseline values and then every 10 minutes interval till the end of surgery and adverse effects occurring in perioperative period.

Intraoperative fluid management was done in relation to body weight of the patient, vital signs and intraoperative losses. At the end of the surgery, the patient was shifted to the postoperative ward for clinical monitoring of vital signs, appropriate fluid therapy and other treatment. Postoperatively vital signs (pulse, NIBP, SpO2 respiratory rate) were measured at 10 minutes interval up to 100 minutes from initiation of surgery.

At 24 hour postoperatively, the patients were evaluated for the duration of effective analgesia (time from SA to the first request of analgesics) and the VAS pain score at that time. Pruritus, PDPH (headache within first 24 hours postoperative), nausea and vomiting if present were noted.

Data were entered in Excel Master Sheet with coding of the variables and analyzed using Statistical Package for Social Sciences (SPSS software version 20.0). Frequencies, percentages, means with standard deviations were calculated. Paired sample t-test: used to compare the means between the two groups; p-value was taken as significant at 0.05.

RESULTS

The age wise distributions of the cases in both groups were comparable, without any statistically significant difference [Table-1].

Table-1: Age group comparison

Age group (years)	Group A	Group B	Total
20-30	3	3	6
31-40	16	14	30
41-50	21	14	35
51-60	10	19	29
Total	50	50	100

There was no statistically significant difference in age, weight, ASA physical status on either group [Table-2].

Table-2: Mean age among the two study groups

	Group A		Group B		Total		p-value
	Mean	SD	Mean	SD	Mean	SD	
Age	44.56	8.33	46.42	9.74	45.49	9.03	0.800
Weight	53.16	7.45	49.90	7.06	51.53	7.25	0.769

Cases at ASA grade I were 76 and 70, and ASA II were 24 and 30 in group A and B respectively.

In group A, the mean duration for the request of first analgesia in post operative period was significantly less ($p<0.05$) than in group B [Figure-1].

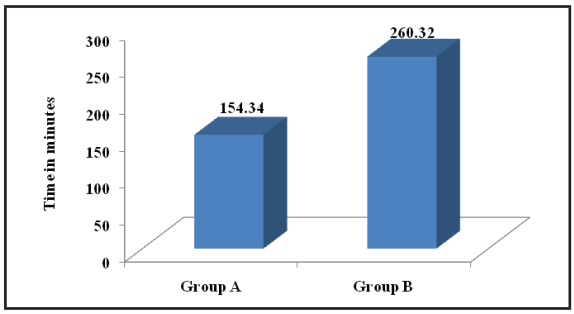

Figure-1: Indication for cesarean section

In group A, the mean VAS score at the time of request of analgesia was 7.50 with standard deviation of 1.14 whereas in group B, the mean VAS score at the time was 5.00 with standard deviation of 1.60. The difference was statistically significant ($p<0.05$) [Figure-2].

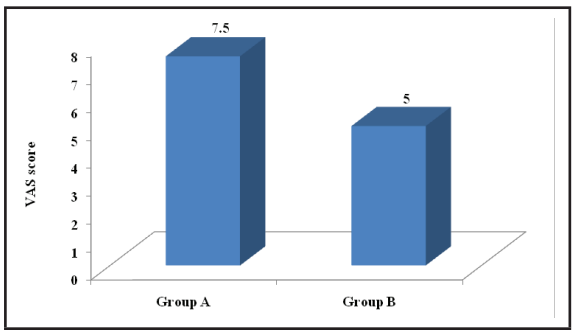

Figure-2: Mean value of visual analogue score at first analgesia

Intra-operative vitals sign, heart rate, respiratory rate and mean arterial blood pressure (MAP) were comparable in both groups. Hypotension, bradycardia, nausea and vomiting were the common adverse effects encountered in both the groups; but there was no statistically significant difference. Pruritus and respiratory depression were not observed in either of the group [Figure-3].

In post-operative period: hypotension, nausea and vomiting, pruritus were present but there was no statistically significant difference. None of the patients had bradycardia but respiratory depression was observed in 6 patients out of 100 cases and all of them were from group B that was statistically significant ($p= 0.013$) [Figure-4].

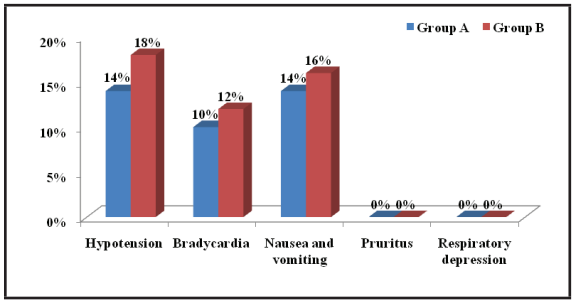

Figure-3: Intra operative complications

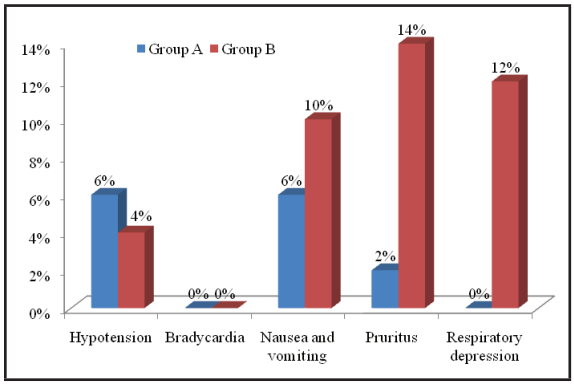

Figure-4: Post-operative complications

DISCUSSION

Opioids and local anaesthetics administered together intrathecally have been shown to have a synergistic analgesic effect.[9]

The duration for the request of first analgesia in post-operative period was 362 vs 209 minute in patient receiving 0.2mg intrathecal bupivacaine with morphine and patient receiving intrathecal bupivacaine only, this finding was similar to other studies done by Singh et al[10], Tridevi et al[11], Nakamura et al[12] and Sharma et al[13].

In this study, the mean VAS pain score at the time of first request of analgesia was 7.5 receiving intrathecal bupivacaine whereas it was 5 in patients receiving intrathecal bupivacaine and morphine. This difference was statistically significant ($p<0.05$). This is comparable with the study done by Marion et al.[14]

The incidence of respiratory depression was significantly high among the patient who received intrathecal morphine (6 out of 50 patients), which was statistically significant ($p<0.05$) in this study. The administration of intrathecal opioids may provide benefits in augmenting intraoperative anaesthesia, but carries a risk of respiratory depression.[15,16]

In this present study, total 8 patients had nausea and vomiting out of 100 cases. Among them 5 patients

were from the group who received 0.2mg intrathecal morphine. All of them had more than one episode of nausea and vomiting. This finding was similar to the study done by others.[17-19]

Pruritus was experienced only in the morphine group which was similar study done by Hein et al[20] and Wodlin et al.[21] There was no statistical difference in the change of vital signs post-operatively in my study. In contrarary to this, a study done by Karman et al[22], post-operative mean arterial blood pressure was significantly lower in morphine group with p value less than 0.05. But they used intrathecal morphine at dose of 5 microgram/kg.

CONCLUSIONS

The addition of 0.2mg morphine to 15mg of bupivacaine in comparison to 15mg bupivacaine only prolongs the total duration of sensory analgesia; causes significantly greater frequencies of respiratory depression; and causes no significant increase in other complications like hypotension, bradycardia, nausea and vomiting, and pruritus.

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Evaluation for Screening of Cervical Cancer by Visual Inspection with Acetic Acid (VIA) Method

Thapa K[1], Parajuli U[1]
[1]Department of Obs. & Gynae, Bheri Zonal Hospital, Nepalgunj, Nepal

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Aims: To evaluate pre-cancer lesion and presence of risk factors by visual inspection with acetic acid.

Methods: A retrospective study was done to evaluate VIA positive women by demographic and reproductive history and presence of risk factors from the period 16th March, 2016 to 15th March, 2017.

Results: A total of 605 women were included and counseled for screening mean age of patient in year's was 39.46±9.4 years and VIA positive rate was 4.63% (28/605).

Conclusions: Cervical pre-cancer and cervical cancers were detected by VIA testing.

Keywords: Cervical Cancer, screening, VIA

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INTRODUCTION

Worldwide, cervical cancer is the fourth most frequent cancer in women with an estimated 530,000 new cases in 2012 representing 7.5% of all female cancers approximately estimated 270,000 deaths every year more than 85% of these deaths occur in low and middle income countries.[1] The World Health Organization estimate that a crude incidence rate of cervical cancer in Nepal is 24.2 per 100,000 women per year with 3,504 new cases diagnosed every year and 1,872 deaths.[2] In Asia, 6.4 per 1000 women die each year because of this disease.[3] It often affects women who are within the reproductive age group.[4] The important reasons for these high incidences are lack of valuable screening curriculum and poor organized resources.[5] It is an avoidable and curable disease if it is diagnosed or treated early because of slow progression of pre-cancer lesion to invasive cancer stage, could long till 10 years.[6] Cytology based screening is not feasible in many developing countries in view of the considerable, financial, technical and manpower resources required for such programmes.[7]

CORRESPONDENCE

Dr. Kalpana Kumari Thapa
Department of Obstetrics and Gynaecology,
Bheri Zonal Hospital, Nepalgunj, Nepal
Email: drkalpanathapa@icloud.com
Phone No.: 9858026961

There has been strong need for a screening test that is simple and can be interpreted immediately and combined with treatment if necessary.[8] Visual Inspection with Acetic Acid (VIA) doesn't depend laboratory services could be possible and promising alternative screening tool for early detection of cervical cancer.[9] The National Cervical Cancer Screening and Prevention Programme (NCCSP) by the government of Nepal initiated in 2011 and VIA as the screening test and Cryotherapy as the treatment of choice for positive lesion.[10]

METHODS

A retrospective study on cervical cancer screening by VIA was done from 16th March 2016 to 15th March 2017 at Bheri Zonal Hospital, Nepalgunj. An inclusion criterion was married women between 30 to 60 years and younger women less than 30 years who were married for more than 10 years. Unmarried, pregnant, women with lower genital tract infection and vaginal bleeding were excluded. Before VIA testing women were counseled about the importance of test and its possible result, treatment option in case of positive result and post-test follow up for negative result. The objective was to evaluate the VIA positivity and risk factors.

Freshly prepared 5% Acetic acid was used to see aceto-white lesion over the cervix if any and recorded in a special VIA form. The risk factors like early

marriage (age of first intercourse), smoking, number of sexual partners, parity, current contraceptive use, family history of cervical cancer, postcoital bleeding and previous abnormal pap smear were also recorded. Positive cases were counseled for cryotherapy and suspicious lesion had biopsy.

Eligible criteria for cryothaerapy were the lesion aceto-white less than 75% of the area of cervix, no vaginal extension and lesion not more than 2mm of cryotip. Double freezing technique was used for cryotherapy. Follow up was scheduled at 1 month, 3 month and retested by VIA at 1 year. If found negative client were asked for follow up after 5 years. Data were entered in the excel sheet and analyzed.

RESULTS

A total of 605 women were included who met the eligible criteria and 28 (4.63%) were VIA positive; 16 received cryotherapy, seven could not get treatment due to lack of cryo-machine and five (0.82%) had suspected cervical cancer who got referred for treatment after confirmation with histopathology. The mean age was 39.5±9.4 years, the median age of marriage was 17.6±3.4 years and median age of parity was 3±1.76 [Table-1].

Table-1: Demographic parameters of the study population (n=605)

Characteristics	Frequency	Percent
Age Group (years)		
<30	21	3.77%
31-40	320	57.45%
41-50	170	30.52%
51-60	46	8.26%
Mean age of Patients ± SD = 39.46 ± 9.40		
Age of Marriage (years)		
<18	313	51.74%
≥18	292	48.26%
Mean age of marriage ± SD = 17.59 ± 3.40		
Parity		
0	26	4.29%
1	36	5.94%
2	179	29.54%
3	165	27.23%
4	102	16.83%
≥5	98	16.17%
Median parity of patients ± SD = 3 ± 1.76		
Regularity of menstruation		
Regular	403	66.61%
Irregular	165	27.27%
Menopause	37	6.12%

Only 9% of cases had some associated risk factors and smoking was the most common one [Table-2].

Table-2: Risk factors for high grade lesion (n=605)

Risk factors	Frequency	Percent
None	551	91.07%
Smoker	35	5.79%
History of postcoital bleeding	12	1.98%
Family history of cervical cancer	5	0.83%
Previous abnormal pap smear	2	0.33%

Two-third of the clients did not practice any contraceptive measures. The common type of contraceptive is tubectomy followed by injectable and barrier method [Table-3].

Table-3: Contraceptive used (n=605)

Contraceptives	Frequency	Percent
None	398	65.79%
Tubectomy	99	16.36%
Depoprovera	38	6.28%
Barrier	31	5.12%
Implant	16	2.64%
Vasectomy	16	2.64%
IUCD	7	1.16%

Among those treated with cryotherapy 3 patients came within four weeks with complaint of vaginal discharge and on examination it was found normal. Among 16, who had got treatment, only 12 patients came for one year follow up, and 2 patients had persistent small lesion with negative Pap smear who received repeat cryotherapy. .

DISCUSSION

Simple and inexpensive methods based on visual examination of the cervix being investigated an alternative method of cervical screening.[11] In the present study, VIA positive women were 4.62% which is less in comparison to other's study.[12,13,14] It may be due to large population or presence of large high risk group in those studies. It indicates people are not much aware of cervical screening programme facility in hospital. Study also shows low prevalence of contraceptive use that is 34.16% in comparison of NDHS (Nepal Demographic and Health Survey) report 2016 which is 42.8%. Barrier method was used by 5.12% of people in comparison to other's study (10.5%).[13] It may be due to unmet need or due to ignorance of the people. It indicates need of strengthening of family planning program in this area.

CONCLUSIONS

VIA testing only could detect around 5% of abnormal cervical lesion and 1% of cervical cancer which were treated on time.

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Fetomaternal outcome in elevated Glucose Challenge Test and gestational diabetes

Shrestha A[1], Kayastha B[1], Pradhan N[1]
[1]Department of Obstetrics and Gynecology, Dhulikhel Hospital - Kathmandu University Hospital, Kavre

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Aims: To observe the maternal and fetal outcome among those having elevated Glucose Challenge Test (GCT) level and gestational diabetes mellitus (GDM).

Methods: Medical record of 15,413 pregnant women booked and delivered between June 2012 and January 2018 were evaluated. GCT was performed by using 50gm glucose and diagnosis of gestational diabetes performed by using the Carpenter Coustan Criteria. Pregnancy outcomes were assessed by the antenatal events, gestation and mode of delivery. Similarly, neonatal outcomes assessed in terms of birth weights, Apgar score, congenital abnormalities, hyperbilirubinaemia, hypoglycaemia and respiratory distress syndrome.

Results: The detected incidence of gestational diabetes was 2.35%. With the threshold plasma glucose level at 140 mg/ dl, 1843 women needed to undergo 100g oral glucose tolerance test and 363 women had gestational diabetes.

Conclusions: It is very important to find out GDM in pregnancy as it has adverse outcomes which are preventable; it is worthwhile to detect GDM by screening in pregnancy. The 50g GCT is feasible and 100gm OGTT to find out GDM.

Keywords: fetomaternal outcome, gestational diabetes, glucose challenge test, oral glucose tolerance test, pregnancy

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INTRODUCTION

Gestational diabetes (GDM) is defined as glucose intolerance of variable severity with onset or first recognition during the present pregnancy and reverting to normal after the puerperium.[1] The frequency of gestational diabetes mellitus is 0.6% -15% of pregnant woman.[2] Figures vary considerably depending upon the criteria used and demographic characteristics of the population. The prevalence is expected to increase as the epidemic of obesity continues.[3] Whereas the study performed in Singapore showed the incidence ranges from 1.1% to 13.3% of the population. Pregnancies affected by GDM impose a risk for both mother and child as the risk of cesarean and operative vaginal delivery, macrosomia, shoulder dystocia, neonatal hypoglycemia and hyperbilirubinemia is increased.[4] Women with a history of GDM are also at an increased risk of developing type 2 diabetes mellitus (T2DM) in the years following their pregnancy and their children have a higher risk of developing obesity and T2DM early in life.[5-7] For those reasons it is important to pay rigorous attention to GDM and the purpose of this study is therefore to cover a wide range of clinical issues related to GDM its treatment and prevention and the long and short term consequences of GDM for both mother and child.

CORRESPONDENCE

Dr Abha Shrestha
Associate Professor, Department of Obstetrics and Gynecology, KU
Email:abhaobgy@gmail.com
Mobile: +977-9849230060

METHODS

It was a retrospective, study carried out in all the pregnant women attending Kathmandu University School of Medicine between January 2012 to January 2018 after the IRC approval. There were total 15,413 pregnant women who were booked as our antenatal cases having no previous history of diabetes mellitus.

These patients underwent the 50g GCT between 24 and 28 weeks of gestation or at booking visit if they come after 28 weeks of gestation. A 50g glucose drink was administered after the antenatal consultation and 60 minutes later venous blood was drawn for plasma glucose estimation. The glucose oxidase method was performed to estimate the plasma glucose level. A plasma glucose level of 140mg/dl or higher was considered a positive test and these women were considered for 100g OGTT. Using the Carpenter Coustan criteria (based on proceedings of the fourth International Workshop- Conference on Gestational Diabetes Mellitus), a diagnosis of GDM was made if the plasma glucose level: fasting,

95mg/dl, in 1hour=180mg/dl; 2h=155mg/dl; and 3hour= 140mg/ dl. (). All patients who had GDM were referred to a dietician and jointly managed by dietician, physiotherapist and an obstetrician. They were put on 1800 kilocalorie diet and started on insulin when indicated. For those women whose sugar levels were well controlled on diet, pregnancy was allowed to progress for spontaneous labour, while for those women who required insulin therapy; pregnancy was terminated at 38 completed weeks of gestation. The client was sent for fetal ECHO at 26-28of weeks of gestation. After delivery, all infants of diabetic mothers were assessed for congenital malformations, hypoglycaemia and other electrolyte and respiratory disorders. The outcome of the pregnancies was assessed by the gestation and mode of delivery and neonatal outcomes in terms of birth weights, Apgar scores, congenital abnormalities, hyperbilirubinaemia, hypoglycaemia and respiratory distress syndrome. The results were analyzed by Microsoft Excel 2010 using simple manual analysis of frequency and percentage.

RESULTS

A total of 15,413 pregnant women were screened antenatally with the 50g GCT. Of these, 1843 (11.95%) women were found to have a 50g GCT value of greater or equal to 140mg/dl. They underwent formal OGTT and 363(2.3%) women were found to have abnormal OGTT. In our study, we noticed that women in between 15-29 years were 14,527 and those with age more than 30 years were 886. Those with age >30 were found to have high GCT and abnormal OGTT compared to women lesser than 30 years, as we can see in table 3 that only 886 of women were in this age group and 97 of them had high GCT and 89 had abnormal OGTT, this gives us 10.94% among 886 patients and 10.01% with abnormal OGTT [Table-1].

Table-1: Demographic Profile

Age (years)	GCT>140mg/dl (n=1843)	Abnormal OGTT (n=363)
15-19	335 (18%)	-
20-25	894 (48.50%)	212(58.4%)
26-30	517 (28%)	62 (17.07%)
31-35	65 (3.52%)	57 (15.7%)
36-40	30 (1.62%)	30 (8.26%)
>45	2(0.1%)	2(0.5%)

In women with Body mass index (BMI) of >25, the prevalence of diabetes is higher. [Table-2] As compared to women with no risk factor the women who had risk factors are at more risk of developing diabetes [Table-3]. Ethnicity seems to play a role in development of GDM. In our study we observed that 1087 (59 %) women were Tamang, 718 (38.9%) women were from Newar ethnicity. We observed that abruption of placenta was seen in 11 patients with polyhydramnios and abnormal OGTT [Table-4]. Fetal Echocardiography was performed at 24.7±2.4, in patients with abnormal OGTT. Congenital heart disease like ventricular septal defect (VSD) was the commonest amongst women with abnormal OGTT. It was seen amongst 13 (3.58%) patients with abnormal OGTT [Table-5].

Table-2: Relation between BMI and high GCT and abnormal OGTT

BMI (n=15413)	GCT>140 (n=1843)	Abnormal OGTT (n=363)
18-20	184(9.98%)	12(3.30%)
21-25	1460(79.21%)	206(56.74%)
26-30	154 (8.35%)	120(33.05%)
31-35	28(1.51%)	20 (5.56%)
>35	17 (.92%)	5(1.37%)

Table-3: Abnormal GCT and OGTT in pregnant women with different risk factors

Risk factors	**Total patients (n=15413)**	**GCT> 140mg/dl (n-1843)**	**Abnormal OGTT (n=363)**
Age >30 years	886 (4.8%)	97(5.2%)	89 (24.51 %)
Obesity	385(2.49%)	199(10.79%)	25(6.88%)
Family history of Diabetes	308(1.9%)	35(2.9)	27(7.43%)
Grand Multipara (>4 births)	164 (1.06%)	110 (5.9%)	30 (8.26%)
Previous big baby	51 (0.33%)	38(0.9%)	33(9.09%)
Previous unexplained Intrauterine death	67 (0.43%)	19(1.03%)	12 (3.3%)
Previous baby with congenital anomaly	16 (0.10%)	12 (0.65%)	9(2.4%)
No risk factor	13,536 (87.82%)	1333 (72.32%)	138 (38.01%)

Table-4: Maternal outcome in women with high GCT and abnormal OGTT

Parameters	GCT>140mg/dl (n=1843)	Abnormal OGTT (n=363)
Preclampsia	214(11.61%)	95 (26.15%)
Ecclampsia	2(0.1%)	-
Abruptio placentae	107(5.8%)	35(9.6%)
Polyhydramnios	45 (2.4%)	32(8.8%)
Preterm labour	42(2.2%)	10(2.7)

Table-5: Perinatal outcome in women with abnormal OGTT

Parameters	Abnormal OGTT
Gestational age at birth	38.2±1.4
Birth weight	3720±328.5
Length (cm)	49±2.3
Macrosomia(>4000gms)	18(4.9%)
Premature birth	48 (13.22%)
Neonatal jaundice	43(11.8%)
Congenital heart disease	5(1.37%)
Other congenital anomalies	2(1.37%)

DISCUSSION

In a country like Nepal where women need to be encouraged to come for antenatal check up, The glucose challenge test (GCT) is a very appropriate test to screen for diabetes. It can be performed in all the pregnant women in out patient basis as it is easy, work friendly, cheap and convenient for screening purpose as stated by Wong L et al [8]. Apart from that, the women did not require to fast and they also appreciated the test after explaining the importance. No women complained about the adverse effects of test. So, it is feasible to perform 50g GCT in all pregnant women. It helps us to screen out the women with GDM. As GDM is notorious for causing adverse effects in pregnancy and also fetal outcome, so there is clear benefit by screening of GDM as it helps in early treatment.[9] Women with gestational diabetes had an increased risk of developing type 2 diabetes compared with those who had a normoglycaemic pregnancy.[9]

Amongst 15,413 women who underwent screening for GDM with 50g GCT, 1843 (11.95%) women were found to have an elevated level greater or equal to 140mg/dl and 363 (2.35%) women were found to have GDM. So, the incidence of GDM was 2.35% in pregnant women attending Dhulikhel Hospital, and the diagnostic yield was 6.06%. The incidence in our study is similar to Andrew Collier et al[6] and Yang HX et al which showed the incidence of GDM 2.7% [10], but is lower than that of the study performed by Wong L and Tang ASA which reported the incidence of 8.2% and diagnostic yield of 22.6%.[8] Similarly study performed by King H and Ray R et al showed the incidence comparable to our results.[11]

The study performed by Wong L and Tang ASA[8] showed that every one in five elevated GCT found to have GDM which was similar to our results as in our case every one in six elevated GCT found to have GDM. So study performed in 19,798 women, O'Sullivan reported a sensitivity of 79% and specificity of 87% using a threshold value of 130 mg/dl whole blood (or 7.9 mmol/l plasma). Based on his study, OGTT done for positive history or obstetrical risk factors yielded poor results with a sensitivity rate of 63% and specificity rate of 56%.In the 1980s those cut-off points were adapted to modern methods for measuring glucose and applied to the modern definition of gestational diabetes - glucose intolerance with onset or first recognition during pregnancy.[12]

Cousins, favored a cut-off of 130 mg/dl (7.2 mmol/l) while Carpenter, suggested the threshold value be set at 135 mg/ dl (7.5 mmol/l).[7,13] When the threshold was set at 140mg/ dl, we discovered that 12.39% of the population would need to be further tested with the OGTT and the diagnostic yield was 6. 06%. Since we do have poor patients came to our outpatient service so, for economic reasons, we recommend the threshold of 140mg/dl. At this threshold value, only one out of six of the screened population needs to undergo the OGTT.

We observed the epidemiological data to see any epidemiological risk factors associated with a raised GCT or OGTT result, we observed that high GCT and GDM were more amongst women of Mongol ethnicity. According to a study by Wild S et al, the total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030, largely because of an increase in the proportion of people over 65 years of age.[13] The regions with the greatest potential increases are Asia and Africa, where diabetes rates are predicted to rise to two or three times those experienced today. The "top three" countries with the maximum prevalence of diabetes are India, China, and the USA [13]. Study performed by Ray R et al showed that older age that is 30 years and above, Chinese ethnic group, maternal obesity (body mass index > or = 25) and history of > or =

4 pregnancies were associated with raised GCT levels.[11] Our results also showed that the patient with BMI>26 had raised GCT and abnormal OGTT which is similar to study performed by Ray R et al but differ in presentation of age group as in our case the raised GCT and abnormal OGTT was in age group >20years.[11] It may be because in our study population women become pregnant in their younger age. Similarly study performed by Wong L and Tand ASA showed no statistical significant between the raised GCT with respect to age.[8]

Our finding indicates that the risk of GDM becomes significantly and progressively increased from 30 years onwards. This supports the American Diabetes Association recommendation on the use of age ≥25 years as the cutoff for screening and the observation that maternal age ≥25 years is the factor most predictive of GDM.[14] American Diabetes association has also recommended that In clinical practice, maternal age of ≥25 years should be adopted instead of ≥35 years or 40 years as a risk factor for the development of GDM.[14] We observed that Preeclampsia and Eclampsia is more common amongst women with high GCT and GDM compared to non diabetics, which is similar to a study by Chris L. Bryson et al.[15] We observed that with poor glycemic control polyhydramnios sets in in third trimester and it may lead to complications like abruption placentae.Though we did not see any adverse perinatal outcome as this was seen in the labour room. We could immediately take up the women for ceasarean section.We noticed that neonatal complications like hypoglycemia, hyperbilirubinemia, transient tachypnea of newborn and macrosomia was more common amongst women with high GCT and abnormal OGTT as in the study by Rashid FB et al.[16] Congenital heart disease like ventricular septal defect (VSD) was the commonest amongst women with abnormal OGTT. Our results also similar to the study performed by different authors.[17-19]

CONCLUSIONS

It is very important to find out GDM in pregnancy as it has adverse outcomes which are preventable; it is worthwhile to detect GDM by screening in pregnancy. The 50g GCT is easy, work friendly, cheap and convenient for screening purpose. It was well tolerated by all the patients. We recommend that the threshold value be set at 140mg/dl because only one-fifth of the population would need to undergo the OGTT and the diagnostic yield was 6.06 %.

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Isolation of Organism and its Drug Sensitivity Pattern in Patients with Urinary Tract Infection at Kathmandu Model Hospital

Joshi RD[1], Khadka S[1], Joshi DM[1], Dahal A[1], Shrestha B[2], Dangal G[3]

[1]Department of Medicine, Kathmandu Model Hospital, Kathmandu, Nepal, [2]Department of Microbiology, Kathmandu Model Hospital, Kathmandu, Nepal, [3]Department of Obstetrics and Gynecology, Kathmandu Model Hospital, Kathmandu, Nepal.

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Aims: Lack of compliance and unjustified antibiotic prescriptions has resulted in increasing bacterial resistance and is proving as a major challenge in the management of infections. Knowing the commonly isolated uropathogens and their antimicrobial susceptibility is beneficial in planning treatment protocols.

Methods: A retrospective review of records of patients with urinary tract infection from January 2012 to December 2016 was conducted at Kathmandu Model Hospital. All patients who were diagnosed as having culture positive urinary tract infection in medical ward of Kathmandu Model Hospital during 5 years period were analyzed for demographic data, prevalence of organism and antibiotic susceptibility patterns.

Results: A total of 315 samples were culture positive. The majority of bugs were gram negative E.coli (48.57%) followed by multi-drug resistant E.coli (28.89%). The other major pathogens were *E. faecalis* (6.03%), *S. epidermidis* (4.44%), *K. pneumoniae* (4.13%), respectively. The highest level of sensitivity in first line antibiotics was seen in nitrofurantoin (84.9%), whereas least sensitivity was shown by amoxicillin/clavulanic acid (21%). Similarly, in second line antibiotics, highest sensitivity was seen in tetracycline (100%), imipenem (91.9%) and least to meropenem (49.2%). Ceftazidime is mostly (93.3%) resistant antibiotics among uropathogens. All the third line antibiotics such as polymyxin B, tigecycline and colistin were 100% sensitive to all our isolates.

Conclusions: Nitrofurantoin may be an appropriate choice for initial empirical therapy of urinary tract infection. Similarly, the multi-drug resistant *E.coli* is increasing but it can be tailored if antibiotics are used appropriately on the basis of susceptibility data.

Keywords: Colistin Sulphate; multi-drug resistant E.coli; Nitrofurantion

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INTRODUCTION

Urinary tract infection (UTI) presents with lower abdominal pain, increase in urinary frequency, dysuria, low backache and fever, including acute and chronic pyelonephritis, cystitis, urethritis, epididymitis and prostatitis. It is one of the commonest infections in clinical practice and the second most common infectious presentation in community. Worldwide, there is an estimated 150 million UTIs per year.[1, 2] Lack of compliance and unjustified antibiotic prescriptions has resulted in increasing bacterial resistance and is proving as a major challenge in the management of this infection.[3] Knowing the common isolated uropathogens and their antimicrobial susceptibility is beneficial in planning treatment protocols. Therefore, this study aimed to determine the bacteriological profile and antibiotic sensitivity patterns in UTI cases in our hospital over past five years.

METHODS

A retrospective review of records of patients with UTI from January 2012 to December 2016 was conducted at Kathmandu Model Hospital. All patients who were diagnosed as having culture positive UTI in medical ward of Kathmandu Model Hospital during 5 years period were analyzed for demographic data, prevalence of organism and antibiotic susceptibility patterns. Only the patients with urine cultures yielding significant growth of pathogens from a freshly voided midstream urine specimen were included in the study. Any patient records with incomplete information were excluded from this study. An antibiotic susceptibility pattern was further confirmed from the

CORRESPONDENCE

Dr.Sachin Khadka,
Department of Medicine, Kathmandu Model Hospital,
Exhibition Road, Kathmandu, Nepal.
Email:sachin_khadka18@hotmail.com,
Phone: +9779840051772

laboratory records. Antimicrobial susceptibility of the isolates was tested by the disc diffusion method. Due necessary permission from the concerned departments and Institutional Review Committee (IRC) of *phect*-NEPAL/ Kathmandu Model Hospital were obtained. Data were entered and analyzed using Excel and SPSS version 21. Data has been summarized using percentage, graph, bar diagram, and tables.

RESULTS

Table 1.Demographic and clinical variables of Urinary tract infection (n=315).

Characteristics	Total (n)=315	
	Number	Percentage (%)
Age		
≤ 20	20	6.3
21 to 40	62	19.7
41 to 60	79	25.1
61 to 80	114	36.2
≥ 81	40	12.7
History of UTI		
Yes	55	17.5
No	260	82.5
Risk Factors (Diabetes, renal calculus, history of cauterization ,VUR)		
Yes	113	35.9
No	202	64.1
Symptoms of UTI		
Yes	174	55.2
No	141	44.8
Pus cells in urine		
Yes	222	70.5
No	93	29.5

The mean age of study population is 56.1 years with a standard deviation of 21.19 (age distribution was 15 to 94). The data illustrates that the age group 61-80 years is highly vulnerable (over one third) to UTI followed by 41-60 years group (a fourth) with the least vulnerable (marginally over a twentieth) being the population under 20 years of age. Majority (82.5%) of patients did not have any history of UTI, lesser patients (35.9%) presented the risk factors and almost similar number (55.2%) of patients presented clinical symptoms. Lastly, while analyzing the presence of pus cells in the urine of culture positive patients, majority (70.5%) showed positive result. [Table-1]

Table 2: Organisms causing urinary tract infection (n=315).

Bacteria isolated	Number (n)	Percent (%)
E. coli	153	48.57%
MDR E. coli	91	28.89%
E. faecalis	19	6.03%
S. epidermidis	14	4.44%
K. pneumoniae	13	4.13%
Enterobacter Spp	6	1.9%
S. saprophyticus	3	1.0%
C. freundii	3	1.0%
P. vulgaris	3	1.0%
P. mirabilis	2	.6%
Acinetobacter spp	2	.6%
K. oxytoca	2	.6%
P. aeruginosa	2	.6%
C. koseri	1	.3%
Coagulase Negative Staphylococci	1	.3%
Total	315	100%

The majority of bugs were gram negative aerobic rods. Among the gram negative rods, *E.coli* was most frequently UTI causing uropathogens, which accounted for 48.57% followed by multi-drug resistant *E.Coli* (28.89%). The other major pathogens were *E. faecalis* (6.03%), *S. epidermidis* (4.44%), *K. pneumoniae* (4.13%), respectively. The prevalence of other uropathogens were almost similar in proportion. [Table-2]

Table 3 illustrates the sensitivity patterns of uropathogens to the first line, second line and third line antibiotics**.** The highest level of sensitivity in the first line antibiotics was seen in nitrofurantoin (84.9%), gentamycin (72.9%), levofloxacin (54.5%), cotrimoxazole (44.1%), norfloxacin (42.8%), ofloxacin (42.2%), and ciprofloxacin (41.8%), whereas least sensitivity was shown by amoxicillin/clavulanic acid (21%), amoxicillin (23.7%), ceftriaxone (29.7%), cefixime (37.4%) and cefotaxime (39.7%), respectively.

Similarly, the second line antibiotics also showed the mixed sensitivity patterns with highest sensitivity in tetracycline (100%), imipenem (91.9%), vancomycin (75%) and piperacillin/tazobactam (74.4%). Unfortunately, other carbapenen, mainly meropenem was sensitive in only 49.2% patients. Contrary to this, ceftazidime is mostly resistant antibiotics among uropathogens with 93.3% resistance. Fortunately, all the third line antibiotics polymyxin B, tigecycline and colistin were 100% sensitive to all our isolates.

Table 3: Overall sensitivity of uropathogens (n=315)

Antibiotics	Number (n)	Sensitivity (%)	Resistance (%)	Intermediate (%)
1st Line				
Amoxicillin	152	36 (23.7%)	115 (75.7%)	1 (0.6%)
Amoxicillin/Clavulanic Acid	38	8 (21%)	29 (76.3%)	1 (2.6%)
Cefixime	278	104 (37.4%)	168 (60.4%)	6 (2.2%)
Cefotaxime	295	117 (39.7%)	175 (59.3%)	3 (1%)
Ceftriaxone	229	68 (29.7%)	159 (69.4%)	2 (0.9%)
Ciprofloxacin	306	128 (41.8%)	167 (54.6%)	11 (3.9%)
Norfloxacin	306	131 (42.8%)	164 (53.6%)	11 (3.6%)
Ofloxacin	282	119 (42.2%)	155 (55%)	8 (2.8%)
Nitrofurantoin	312	265 (84.9%)	39 (12.5%)	8 (2.6%)
Cotrimoxazole	299	132 (44.1%)	165 (55.2%)	2 (0.7%)
Gentamycin	214	156 (72.9%)	52 (24.3%)	6 (2.8%)
Levofloxacin	145	79 (54.5%)	50 (34.5%)	16 (11%)
2nd line				
Amikacin	180	117 (37.1%)	6 (5.1%)	2 (.6%)
Cefoperazone/Salbactam	110	54 (49%)	50 (45.5%)	6 (5.5%)
Ceftazidime	132	5 (3.8%)	124 (93.9%)	3 (2.3%)
Doxycycline	46	24 (52.2%)	20 (43.5%)	(4).30%
Imipenem	99	91 (91.9%)	8 (8.1%)	—
Meropenem	130	64 (49.2%)	60 (52.2%)	6 (4.8%)
Piperacillin/Tazobactam	115	81 (74.4%)	30 (26%)	4 (3.5%)
Tetracycline	3	3 (100%)	—	—
Vancomycin	8	6 (75%)	2 (25%)	—
3rd Line				
Polymyxin B	5	5 (100%)	—	—
Tigecycline	9	9 (100%)	—	—
Colistin	10	10 (100%)	—	—

DISCUSSION

Urinary tract infections are the most frequent bacterial infection in women. In a study done in a rural area of India where the prevalence of UTI in female was 78.8%.[4] The close proximity of the female urethral meatus to anus, short urethra, altered vaginal biota and sexual intercourse influence the higher prevalence of UTI in female.[5] In addition, elderly populations have increased vulnerability towards UTI for various associated risk factors such as age-associated altered immunity, increased comorbid conditions and exposure to nosocomial pathogens.[6] Our study showed almost three-fourth of the UTI patients were over 40 years, indicating the higher prevalence of UTI in elderly people. A similar finding was demonstrated by the study done by Prakash and Saxena where the highest susceptible age group of patient to UTI was over 48 year with 63.51% prevalence.[7]

In our study, majority (82.5%) of the patients did not have any history of UTI which is similar to the study done by Derese et al where 73.1% patients had no history of UTI.[8] Similarly, we observed predisposing factors for UTI were present in 35.9% patient contrast to 64.1% with no risk factor. In this study, condition like diabetes, renal calculus, history of cauterization, VUR are considered as predisposing factor. Overall, these entire predisposing factors play role in causing UTI but the association with UTI is not very strong as shown in study done in Nepal by Subedi et al[9] and in study done by Holmgrem.[10] Over viewing the clinical symptoms, almost similar number of patient had clinical symptom (55.2 vs. 44.8%). Previous study also showed clinical symptoms were present in 47.3% which is nearly similar to our study.[8] When analyzing the presence of pus cells in culture growth patients, 70.5% patients showed positive result. In this study, pus cells more than 6/HPF is considered positive.[11] A cross sectional study from Bangladesh showed out of 100 urinary samples having pus cells >5/HPF, 93.3% culture positive patients showed significant pyuria.[12]

Increasing resistance in bacterial pathogens is of world-wide concern. In this study, the majority of

bugs were gram negative aerobic rods. Among the gram negative rods, *E.coli* was most frequently UTI causing uropathogens, which accounted for 48.57%. Frequency of pathogens causing urinary tract infection in a tertiary care hospital in Western Nepal was studied, where the most common pathogens isolated were *E. coli* (59.4 %).[13] Similarly, the study done in india showed *E. coli* was found positive in 61.02% samples. The second frequently occurred organism in our study is multi-drug resistant *E.coli* (28.89%). In most of the study done in Nepal, other organisms like *E. faecalis, S. epidermidis, K. pneumoniae* are the second most causatives of UTI,[14] but in our study MDR *E. coli* is the second most frequently occuring organism which is similar to the study done in Thailand where MDR *E. coli* is higher.[15] The other major pathogens were *E. faecalis* (6.03%), *S. epidermidis* (4.44%), and *K. Pneumoniae* (4.13%), respectively. Antibiotic susceptibility pattern of urinary isolates from Manipur showed *Klebsiella* species (14.4%) is the second most common after *E. coli*.[16] In a prospective study undertaken over a 14-month period in Iran, *E. coli* was the most common etiological agent of UTI (74.6%), followed by *Klebsiella* spp (11.7%), *S. saprophyticus* (6.4%), and *P. aeruginosa* (2.2%).[17] In another study, *Klebsiella* species caused urinary tract infection in maximum number of cases (124, 37.35%) followed by *E. coli* (114, 34.4%).[18] The prevalence of antimicrobial resistance in both out and hospital patients with UTI is increasing and can vary according to geographical and regional location, but in overall, *E. coli* is causing UTI in most of the people worldwide.

Regarding the sensitivity patterns of uropathogens to first line antibiotics**,** the highest level of sensitivity was seen with nitrofurantion (84.9%), gentamycin (72.9%), levofloxacin (54.5%) , cotrimoxazole (44.1%), norfloxacin (42.8%), ofloxacin (42.2%), and ciprofloxacin (41.8%), whereas the least sensitivity was shown by amoxicillin/clavulanic acid (21%), amoxicillin 36 (23.7%), ceftriaxone (29.7%), cefixime (37.4%) and cefotaxime (39.7%). Considering antibiotic sensitivity, our results were different from a year-long study conducted in Shankarapur Hospital in Kathmandu valley in 2015 where the sensitivity rates of nitrofurantion (59.4%), gentamycin (56.4%) were lesser than our findings. Whereas similar comparable sensitivity was seen with cotrimoxazole (47.3%), ofloxacin (50%), ciprofloxacin (49.7%), and cefixime (48.5%). In addition, a higher antibiotic sensitivity to ceftriaxone (73.3%%) and amoxicillin/clavulanic acid (60.6%%) was seen which is contrary with our finding.[9] Other study done at Bangladesh showed cotrimoxazole and amoxicillin are virtually useless against uropathogens as they were effective against 31.81%and 11.81% of all isolated organisms respectively. This study also showed gentamycin is sensitive in 74.54% which is almost similar to our study but amikacin sensitivity is much higher than our study (86.3%).[19] Reduced susceptibility to amoxicillin in our study may indicate patients presenting to primary care which may have less severe symptoms and likely to present earlier or may reflect changes in antibiotic susceptibilities due to physicians' prescribing behavior.[20]

Similarly, second line antibiotics also showed the mixed sensitivity patterns with highest sensitivity with tetracycline (100%), imipenem (91.9%), vancomycin (75%) and piperacillin/tazobactam (74.4%). The study done by Subedi et al showed similar sensitivity to tazobactam (73.3%).[9] Similarly, study from Bangladesh showed imipenem and meropenem is 98.18% sensitive to uropathogens whereas our study shows similar result with imipenem (91.9%) but, unfortunately meropenem was sensitive in only 49.2% patients. According to our results, ceftazidime was 3.6% sensitive which differ from a Pakistani study done by Tabish and Iqbal where ceftazidime sensitivity was 46.66%.[20]

In our study, overall the third line antibiotics polymyxin B, tigecycline and colistin were 100% sensitive to all our isolates. Identical results are reported in a study from USA where tigecycline were found to be most efficacious.[21]

CONCLUSIONS

In conclusion, nitrofurantion may be an appropriate choice for initial empirical therapy of UTI though the uropathogens showed high levels of resistance to multiple urinary antimicrobial agents. Similarly, the multi-drug resistant *E.coli* is increasing but it can be tailored if antibiotics are used appropriately on the basis of susceptibility data. The third line antibiotics polymyxin B, tigecycline and colistin could be used only if needed to preserve it for future for MDR uropathogens.

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Ruptured Right Cornual Pregnancy

Pokharel S[1], Dangal G[1], Karki A[1], Pradhan HK[1], Shrestha R[1], Bhattachan K[1], Thapa S[1], Paudel R[1], Bajracharya N[1]
[1]Department of Obstetrics and Gynaecology, Kathmandu Model Hospital Kathmandu. Nepal

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The ectopic implantation is implantation of fertilized ovum outside the uterine cavity, ampulla of fallopian tube being the most common site. A cornual or interstitial pregnancy is an ectopic pregnancy that develops in the interstitial portion of the fallopian tube which is one of the most hazardous type of ectopic gestation. Treatment depends on the week of gestation at the time of diagnosis, level of serum β HCG, findings of ultrasonography, hemodynamic stability of the patient and the choice of future fertility. In this case report, we present a case which was previously misdiagnosed as a case of missed abortion at 8 weeks of gestation by transabdominal ultrasound and patient underwent medical abortion with mefipristione and misoprostolandafter 1 month presented with pain abdomen and was confirmed as extrauterine pregnancy by transabdominal ultrasound followed by surgical management.

Keywords: cornual pregnancy; ectopic pregnancy; laparascopy

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INTRODUCTION

Ectopic pregnancy is a the one which develops following implantation anywhere other than endometrial cavity of the uterus. Ectopic pregnancy is one of the serious complication of pregnancy and is one of the leading causes of maternal morbidity and mortality. About 95% of ectopic pregnancy occurs in fallopian tube and of these 55% occurs in ampulla. Cornual(interstitial) pregnancy is a rare form of ectopic pregnancy accounting for 2-4% of ectopic pregnancy or once every 2,500 to 5000 live birth.[1]Risk factors for interstitial pregnancy are similar to other type of ectopic pregnancy.[2]

CASE

A 41 years multigravida, G3P2L2, presented to emergency of Kathmandu Model Hospital on Mangsir 21, 2074 with the complaint of pain lower abdomen 5 hours prior to presentation to hospital. Her vitals were stable. Lower abdomen was tender over right iliac region. On her pelvic examinationuterus was retroverted, 12 weeks size, tenderness present in right fornix, cervical motion tenderness present. Urine pregnancy test was positive and she gave history of medical abortion at some other health center for missed abortion at 8w6d of gestation 1 month ago and had minimal bleeding after taking medicine for abortion. No other significant past medical and surgical history. Her previous two pregnancy were uneventful vaginal deliveries. The initial laboratory test included Hb 12.4gm%, total count, differential count, platelets, renal function test, serum amylase were within normal limit. On the abdominal ultrasonography, single live embryo of 12+ weeks of gestation (CRL 59mm= 12w3d) noted at right side of uterus possibly right cornu, moderate amount of free fluid noted in the abdomen and pelvis.

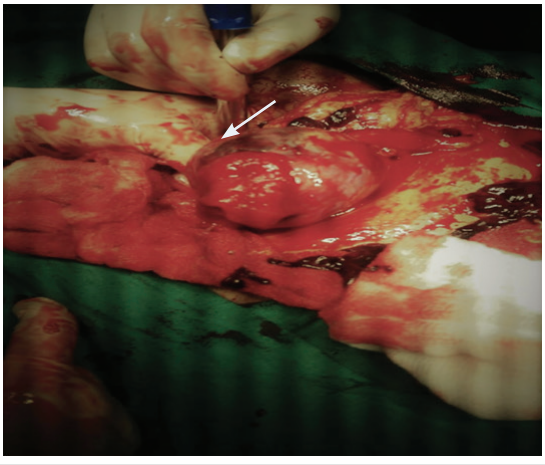

Figure-1: Intra-operative picture of ruptured right ectopic interstitial pregnancy. Arrow shows the rupture site

An emergency laparotomy with bilateral tubal ligation was performed under general anaesthesia. There was approximately 2000 ml blood in abdominal cavity with a male foetus protruding from the right

CORRESPONDENCE

Dr Shreesiya Pokharel
Department of Obstetrics and Gynaecology
Paropakar Maternity and Women's Hospital, Thapathali, Kathmandu
Email: shreesiya03@gmail.com
Phone: +977-9843-051234

ruptured cornual region. The rupture measured 10-12 cm in length and placental tissue protruding through it. Normal left fallopian tube and both ovaries were normal. Three pints of whole blood was transfused. Postoperative period was uneventful and she was discharged on third postoperative day in good condition.

Figure-2: Single non-viable male fetus with placenta.

COMMENTS

Cornualgestation is one of the most hazardous type of ectopic gestation. The diagnosis and treatment are challenging and mostly is a medical emergency. The interstitial part of the fallopian tube is the proximal portion that lies within the muscular wall of the uterus and the pregnancies implanted in this site are called interstitial(cornual) pregnancy.[3] It should be differentiated from the angular pregnancy in which the embryo implants in the lateral angle of the uterine cavity medial to the internal ostium of the fallopian tube. The gestational sac is better protected in the interstitial portion than in other portion of the tube , the symptoms of interstitial pregnancies usually manifest later (>12 weeks of gestation).Due to its location there is difficulty in the diagnosis and treatment, leading to high mortality compared to other ectopics. Pelvic pain and vaginal spotting are common early symptoms and because the pregnancy occurs at the most vascularized area of the female pelvis, that is, the junction of uterine and ovarian vessels rupture usually causes profound and sudden shock.[1]

Clinically, risk factors are as for other type of ectopic pregnancy: PID, previous pelvic surgery, previous ectopic pregnancy, in vitro fertilization, ipsilateral salpingectomy.[3] The combination of a high index of suspicion, sensitiveserum β-hCG assays, and transvaginalsonography has revolutionizedthe diagnosis of tubal pregnancy. Interstitialpregnancy, however, remains the most difficult ectopic pregnancyto diagnose preoperatively. An eccentrically located gestational sac surrounded by anasymmetric myometrial mantle and a separate empty uterine cavity with endometrial echoes were the most common ultrasonographic findings of interstitial gestations.[4]Timor-Tritsch et al[6] adopted the same parameters and diagnosed interstitial pregnancy according to three sonographic criteria: an empty uterine cavity, a chorionic sac seen separately and 1 cm from the most lateral edge of the uterine cavity, and a thin myometrial layer surrounding the chorionic sac.

The traditional treatment of interstitial pregnancy has been cornual resection or hysterectomy in cases with severely damaged uteri.[3]Ruptured interstitial pregnancy may present with hypovolemic shock, necessitating emergency laparotomy and cornual resection or hysterectomy. However, in patients who are hemodynamically stable, conservative measures may be attempted, including laparoscopy or medical management. Laparoscopic resection may be assisted by direct injection of vasoconstrictive agents such as diluted vasopressin.There is no general consensus on the best surgical procedure for interstitial ectopic pregnancy. Increasingly moreconservative approaches are being used, such as cornuostomy instead of cornual resection, as well as laparoscopy in place of laparotomy.[5] The Royal College of Obstetricians and Gynaecologists recommends that the women with tubal pregnancy who are most suitable for methotrexate therapy are those with a serum hCG level of <3000 iu/l and with minimal symptoms.Future fertility is possible in patients with a history ofinterstitial pregnancy. There is a concern regarding uterine rupture because of the weakened myometrial scar.[5]

CONCLUSIONS

Cornual pregnancy poses a significant diagnostic and therapeutic challenge and carries a greater maternal mortality risk than tubal pregnancy. Transvaginal sonography can be helpful but often is not conclusive. Early clinical diagnosis aided by ultrasound or laparoscopy may help to contribute towards effective conservative management.The serious consequences of cornual pregnancy are caused mainly by rupture after 12 weeks of pregnancy, leading to catastrophic haemorrhage and even death. Cornual excision or hysterectomy used to be the treatment for such

cases.Conservative management has, however, been increasingly practiced successfully. This includes laparoscopic conservative treatment and medical treatment with systemic methotrexate.Appropriate individual counseling is needed regarding risks of future pregnancy and mode of delivery.

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Creation of Functional Neo-vagina in Vaginal Atresia

Poudel R[1], Dangal G[1], Karki A[1], Pradhan H[1], Shrestha R[1], Bhattachan K[1], Bajracharya N[1]
[1]Department of Obstetrics and Gynecology, Kathmandu Model Hospital, Nepal

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Vaginal atresia is one of the common congenital anomalies of the female lower genital tract due to incomplete canalization of Mullerian ducts. It mostly presents as primary amenorrhoea with attacks of severe lower abdominal pain at monthly interval in presence of appropriate Tanner staging secondary sex characteristics. It is diagnosed by clinical presentation, examination and imaging, usually ultrasound scan and magnetic resonance imaging. There are conservative non-surgical as well as surgical methods to correct it. A 13 years pubertal girl presented at Kathmandu Model Hospital with complaints of cyclic severe lower abdominal pain since one year with presence of appropriate secondary sexual characteristics. Ultrasound showed features suggestive of hematometra. She underwent drainage of hematocolpos with neo-vaginoplasty followed by intravaginal mould placement. She also underwent dilatation of neovagina thrice under IVA to maintain the vaginal length and function. We present here a case of isolated vaginal atresia, who underwent Mc Indoe Vaginoplasty followed by serial dilatation.

Keywords: hematocolpos; neo-vaginoplasty; vaginal atresia

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INTRODUCTION

Vaginal atresia is a congenital defect in which the urogenital sinus fails to contribute to the caudal portion of the vagina resulting in uterovaginal outflow tract obstruction. Its incidence is 1 in 5000-10,000 live female births.[1] It may occur as an isolated developmental defect (extremely rare) or as part of a complex of anomalies (more common).[2]Diagnosis is made only when evaluation is done for primary amenorrhea or cyclic abdominal pain with otherwise typical growth and pubertal development.[3]

CASE

A 13 years girl from Lalitpur district presented to Kathmandu Model Hospital with complaint of cyclical pain over lower abdominal region since one year. This pain used to occur for 2-3 days and got repeated each month. It was moderate in intensity and sometimes severe enough which required hospital emergency visits. She had not had her menarche and had not been sexually active yet. She had undergone examination under Anesthesia (EUA) and drainage of hematocolpos thrice in one of the centers in Kathmandu itself with misdiagnosis of imperforate hymen. But she repeatedly had same problem and this time she came to our centre.

CORRESPONDENCE

Dr Rekha Poudel
Department of Obstetrics and Gynecology,
Kathmandu Model Hospital, Nepal
Email: drrekhapoudel@gmail.com
Phone: +977- 9803721075

At our center, findings of general physical examination were normal with appropriate Tanner staging secondary sex characteristics. Abdomen was soft with mild suprapubic tenderness. Gross examination of external genitalia revealed normal findings. There was an isolated blind-ending vaginal dimple about one cm in depth, without obvious bulging of the hymen. Per rectal examination revealed mass palpable anterior to the rectal wall. Ultrasound of abdomen and pelvis revealed bulky uterus (9x5x6 cm) with collection (150 ml) having low level internal echoes in the uterine cavity and extended down to the upper two-third of vagina, suggestive of hematometra. Bilateral ovaries appeared normal. Other basic investigations were within normal limit.

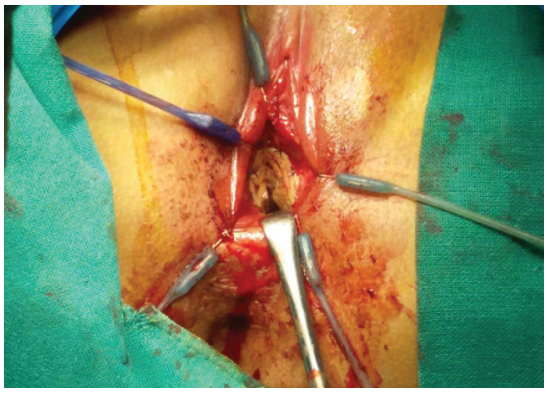

Figure-1: Neo-vaginoplasty with Split thickness graft in-situ (Mc Indoe Vaginoplasty)

She was admitted and started with parenteral antibiotics. Informed consent was taken and under spinal anaesthesia, previous examination findings

were confirmed. Split thickness skin graft was taken from right buttock and harvest site was dressed with an occlusive dressing. Vaginal mould was prepared. Then, 2-3 cm transverse incision was given over the vaginal dimple and dissection was done creating space between urethra and urinary bladder anteriorly and rectum posteriorly. Two canals were created on each side of median raphe; the latter was then cut creating a single canal. Hematocolpos of around 150 ml was drained and vagina was dilated with Hegar's dilators. Pathway to the uterus was identified. The graft was draped over the mould and lateral edges of the skin graft were approximated. Mould was then inserted into the vagina. Edges of the skin graft at the distal end of mold were reapproximated to the distal opening of the neovagina using interrupted stitches of delayed-absorbable suture.

The vaginal mould and Foley catheter was left in place for seven days following surgery. Parenteral antibiotics were continued for 48 hours followed by oral antibiotics. On seventh post-operative day, external stitches and mold were removed. Her post-operative stay was uneventful. On one week follow-up, patient was doing well and had no complaints. Then, after five weeks of surgery, she had her menses which was associated with dysmenorrhoea and it was relieved with oral analgesics. Then, she underwent EUA and vaginal dilatation under IVA thrice at interval of one month. Now, she is having regular menstrual cycles associated with mild dysmenorrhoea. She is on regular follow-up and her vaginal length is maintained at 6 cn

DISCUSSION

Only upper vagina is formed from Mullerian ducts while the lower vagina develops from the vaginal plate of the urogenital sinus. Vaginal atresia falls under Class I according to the American Fertility Society Classification of Mullerian Anomalies.[4] Vaginal atresia occurs in various degrees and forms. It is usually associated with various syndromes like Mayer-Rokitansky-Kuster-Hauser syndrome, Bardet-Biedl syndrome, Kaufman-McKusick syndrome, Fraser syndrome, and Winters syndrome.[5]

Isolated vaginal atresia mostly presents with primary amenorrhoea in background of appropriate Tanner's staging of secondary sex characteristics while it occasionally presents with severe lower abdominal pain at monthly intervals in background of cryptic menstruation. This condition can lead to haematometra, haemtocolpos, endometriosis or pyometrawhich, if left untreated can cause imminent threat to fertility.[6]Clinical examination, Ultrasound evaluation and MR imaging aids in the diagnosis.

In women with Mullerian agenesis with associated vaginal atresia, passive dilatation technique establishes the coital function of vagina in as many as 90% of cases.[7]In women with isolated vaginal atresia, creation of functional neo-vagina is the treatment goal.MC Indoe vaginoplasty is universally acceptable and widely practiced procedure for neocolposis reconstruction.[6]It creates a neovaginal cavity by dissecting between the bladder and rectum, and grafts skin to resurface a surgically created neovagina. It uses split or full thickness skin graft obtained from patient's buttocks or thighs. A space-occupying vaginal mold is required to maintain the skin graft.[8]Postoperative infection, haemorrhage, failure of graft take, vaginal stricture and fistula are few complications.[9]

Time of surgery is to be decided according to grade of atresia and clinical presentation. Modified Mc Indoe vaginoplasty, Colpoplasties using bowel segments, Vecchietti procedure, etc are other trending approaches. Scheduled postoperative passive dilatation is required to prevent vaginal stricture. Psychological support is a must to improve the overall quality of life.[9]

CONCLUSIONS

An adolescent female with cyclic lower abdominal pain and otherwise typical growth and pubertal development should be evaluated well to rule out any congenital genital anomalies. Timely surgical intervention is necessary to prevent further complications.

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Ovarian Adult Granulosa Cell Tumor – a rare case report

Joshi R[1], Baral G[1], Malla K[1]
[1]Paropakar Maternity and Women's Hospital, Kathmandu, Nepal

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Introduction: Adult granulosa cell tumor is a rare tumor which accounts for 1% of all ovarian tumors. They usually present with postmenopausal bleeding and abdominal mass. Inhibin is used as the tumor marker.

Case: A 76 years multiparous post-menopausal women presented with vaginal bleeding for past three years and painless huge mass in lower abdomen. She underwent total abdominal hysterectomy with bilateral salphingo-oophorectomy with bilateral pelvic lymphnode dissection with appendectomy. Histopathology showed the adult granulosa cell tumor with few mitosis, Stage IA. Her postoperative period was uneventful.

Conclusion: Surgery is the mainstay of treatment of granulosa cell tumor and chemotherapy is indicated in advanced cases. Although they have better prognosis, life-long follow up is advised to detect late recurrence.

Keywords: granulosa cell tumor, inhibin, ovarian tumor.

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INTRODUCTION

Ovarian sex-cord stromal tumors are rare hormone producing tumors.[1] It comprises of tumors arising from the variety of cells from the gonadal sex cords (granulosa cells, theca cells, stertoli cells) or stromal cells.[1,2] Ganulosa cell tumors (GCT) consist of granulosa cells often mixed with a variable number of fibroblasts and theca cells. Among the two distinct clinical and histological sub-types, adult GCT are more common (95%) than the juvenile counterpart (5%).[1,3] The adult type are common in middle aged and in postmenopausal women while the juvenile type is common in young age and children.[4,5] Adult GCT account for approximately 1% of all ovarian tumours.[4] They typically present with postmenopausal bleeding in older women while 10% may present with acute abdominal symptoms. They are often diagnosed on the histopathological examination following surgery.[1,2]

CASE

A 76 years multiparous post-menopausal lady presented to outpatient department of Paropakar Maternity and Women's Hospital with complaints of irregular and excessive per vaginal bleeding for past three years and painless mass in lower abdomen noticed since 2 months. She had attained menopause at the age of 50 years. On clinical examination, she was thin built with weight of 41 kg. A non-tender mobile cystic mass of 26 cm x 20 cm with smooth surface and regular margin was palpable in the lower abdomen. Fresh bleeding was noted from the endocervical region and cervix was flushed with the vagina.

In ultrasound examination there was a large hetrogenous intrapelvic lesion with multiple thin septa with solid component with increased vascular flow in left adnexa. Contrast enhanced CT scan of abdomen and pelvis showed extensively enlarged multilocular cystic mass of 21 x 15 x 9 cm at left adnexa with variable thickness of cyst wall and septations with solid component. Uterus was normal in size with endometrial thickness of 7 mm. Tumor marker (CEA, α-FP, LDH, β-hCG) were within normal range except for CA-125 which was double than normal (78 IU/ml).

Staging laparotomy with total abdominal hysterectomy with bilateral salphingo-oophorectomy with bilateral pelvic lymphnode dissection with appendectomy was done on 13/06/2018. Hemorrhagic peritoneal fluid of 50 ml was noted on opening of abdomen. Left ovarian cystic mass of around 25x 25 cm was seen with intact capsule and smooth surface. Uterus, fallopian tubes and right ovary were normal. There were no gross tumor deposits inside the abdomen. On cut section, cyst wall was thick; multiple loculi with thick and thin septa were present; most of the loculi had hemorrhagic fluid while some loculi had

CORRESPONDENCE

Dr Rijuta Joshi
Paropakar Maternity and Women's Hospital, Kathmandu
Email: dr.rijutajoshijha@yahoo.com;
Phone: +977-9851151830

clear fluid (total fluid-1500 ml); solid component of around 5x5 cm was also seen [Figure-1, 2 and 3]. Her post-operative period was uneventful and she was discharged from the hospital on 12th post operative day.

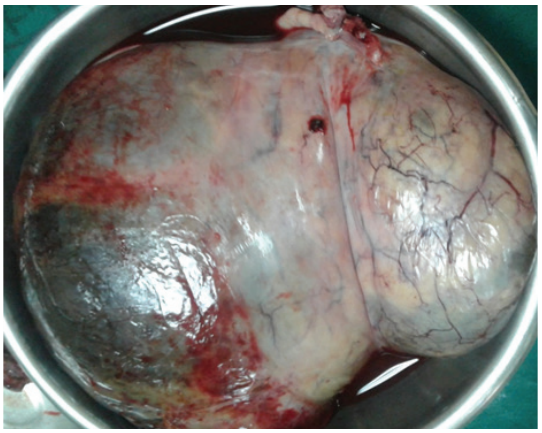

Figure-1: Gross specimen of left ovarian tumor

Figure-2 & 3: Cut section of tumor showing the solid component

Histopathological examination showed tumor cells arranged predominantly in inter-anastomosing trabaculae of ribbon, cords and sheets while few cells were arranged in micro-follicular pattern. The tumor cells were forming microcystic spaces containing eosinophilic secretions. The individual tumor cells were uniform with round to oval nuclei with single small nucleoli, longitudnal grooves and pale cytoplasm with few mitoses (0-2/10 HPF). Peritoneal fluid and pelvic lymphnodes were negative for malignant cells (0/10). There was no lymphovascular and perineural invasion. The histopathological diagnosis was pure sex-cord tumor – adult granulosa cell tumor, Stage IA [Figure-4 and 5]. Serum inhibin was was done on 14th post operative day which was 0.80 pg/ml (inhibin level for postmenopausal age <2.1 pg/ml).

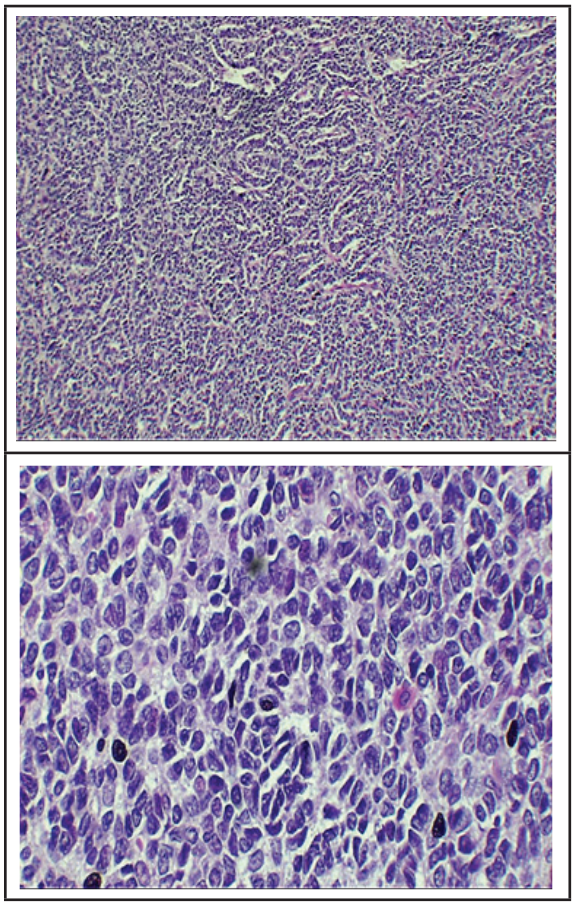

Figure-4 & 5: Low (100x) and high power (400x) of left granulosa cell tumor

Tumor cells arranged in inter-anastomosing trabeculae of ribbons and cords. (HE, 100x); Sheets of monotonous small cells with scant cytoplasm and nuclei with occasional longitudinal grooves (HE, 400x)

DISCUSSION

GCT is low malignant ovarian tumor which arises from the granulosa cells, the somatic cells of the sex cords of the ovary. The age ranges from 35 to 81 years and the peak incidence is at 50-55 years.[6-8] In three cases of GCT reported by Moustaide H and

colleagues age group ranged from 52 to 81 years.[9]

They have a long natural history with indolent growth. Granulosa cells are responsible for the production of sex steroids and peptides necessary for ovulation. These tumors may present with features of hyper-estrogenicity as precocious puberty, altered menstrual patterns and vaginal bleeding in postmenopausal age.[1,3,6] Small group may present with infertility due to unregulated inhibin and virilizing features due to androgen.[3] Among the post menopausal women, vaginal bleeding is the most common finding.[1,6] These tumors may also present with a large palpable abdominal mass.[1,3,6] In a study done by Dridi M et al abdominal mass and post menopausal bleeding was seen in 61% (19/31) and 32% (10/31) of cases respectively.[7] Similar presentation of abdominal mass and postmenopausal bleeding were seen in other case reports as in this case.[9] Minor problems like mastalgia and risk of breast cancer development is also increased in these women secondary to higher exposure to estrogen.[3,6,10] Some cases may present with features of acute abdomen due to the rupture of the tumor.[6,10] It may be associated with endometrial hyperplasia (32-85%) as well as the endometrial cancer (3-22%).[3,10] Continuous exposure to ovulation induction drugs like selective estrogen receptor modulators (SERM), clomiphene citrate, gonadotropins may also increase the risk of GCT. Chromosomal abnormalities like trisomy 12, monosomy 22, and deletion of chromosome 6 have also been seen in cases of GCT.[6]

In ultrasound, usually they present as the predominantly multi-cystic mass with variable solid components or solid masses, none of which are diagnostic.[1,3] Similar to this case, in majority of case reports unilateral cystic masses were seen on ultrasonography with median tumor size of 20 cm (4-33 cm).[7,9] Similar to the case, in a case report by Moustaide H, there was a heterogenous vascularised ultrasonographic picture of GCT.[9]

As in this case, elevated levels of CA-125 were seen in 42% of cases (13/31) of GCT in a retrospective study.[7] Suspicion arises when there is hyper-estrogenism, thickened endometrium and raised inhibin levels.[6,1] However, estradiol levels cannot be used as a reliable marker as its level does not correlate with the disease and has variable response to treatment.[10] Inhibin acts as the granulosa cell growth factor and its level reflects the tumor burden; so it can be used as the tumor marker.[6,10] Inhibin B is more specific than inhibin A.[1] However, not all granulosa cell tumors express inhibin.[6] As GCT are diagnosed usually in the pathological specimens, serum inhibin is usually not done in preoperative period.[1,6] Similar to this case, serum inhibin was not studied in any cases in a large retrospective study.[7]

Surgery is the diagnostic as well as therapeutic option for histological diagnosis, staging and cytoreduction.[1,6,,10] They are usually unilateral confined to the ovary at the time presentation.[3,4,6] Ascites, bilaterality and peritoneal seedlings are rarely seen in these type of tumors.[6] These features make it different from the epithelial ovarian tumors. Advanced disease is seen in 10% of cases.[10] As in this case, all had undergone surgery and disease was limited to Stage I in majority of the cases.[7,8,10-12] On gross examination, they are predominantly cystic and resemble mucinous cystadenoma while on cut section they have serous fluid or clotted blood.[10] The nuclei of the tumor cells have characteristic coffee-bean appearance (grooved nuclei).[1,9,10] Similar finding was noted on histopathological examination of the specimen of this case. Call-Exner bodies which consist of rosette arrangement of cells around an eosinophilic fluid space, are diagnostic of GCT.[1,10] However, this feature may not be sharply defined in many cases.[10] Extracellular expression of Vimentin, CD99, smooth muscle actin and inhibin aids on confirmation of the diagnosis of adult GCT which was seen in some case reports.[9,12]

Majority of them are symptomatic and detected at stage I. They have a long natural history and compared to the epithelial tumors, they have better prognosis.[6,10] Stage of the disease best correlates with the prognosis while other factors which are not well established for the prognosis are tumor size, tumor rupture, nuclear atypia and aneupoidy.[10] Associated endometrial cancers are usually the well differentiated early stage endometroid adenocarcinoma and have a good prognosis.[3,6] GCT is responsive to platinum based chemotherapy (bleomycin, etoposide and cisplatin).[5,6,10] Usually surgery is sufficient in stage I disease but when there is a large tumor with high mitotic index or ruptured capsule, chances of recurrences increases and then chemotherapy may be indicated.[10] Conservative surgeries can be done for Stage I adult GCT in young women.[5] For inoperable advanced and recurrent diseases, chemotherapy as

well as hormonal therapy (progestins) have been considered. Although radiotherapy has a limited role, it has been found to prolong survival in advanced cases.[10] In the study done by Sehouli J et al, majority of cases did not require chemotherapy.[8] Although five year survival is more than 90%, late recurrence has been noted, even with the stage I disease.[3,5,10] In one fourth of them, recurrence may be seen after many years, even decades of apparent clinical cure.[1,3] Recurrences have been found to be associated with increased fatality in majority of the cases.[1,6]

CONCLUSIONS

Majority of adult GCT presents with abdominal mass and postmenopausal bleeding. Surgery is the mainstay of treatment and chemotherapy is indicated in advanced cases. Serum inhibin test as a tumor marker of granulosa cell tumor is usually run in retrospect after histopathological report. However, life-long follow up is advised as it is a late recurring malignancy.

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Huge Ovarian Cyst Imitating Pregnancy

Bajracharya N[1], Karki A[1], Dangal G[1], Pradhan H[1], Shrestha R[1], Bhattachan K[1], Poudel R[1]
[1]Department of Obstetrics and Gynecology, Kathmandu Model Hospital, Kathmandu

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Ovarian cysts are common findings in females of reproductive age. Mostly, they are non neoplastic and hormonally dependent as follicular, simple, and corpus luteum cysts. Ovarian cysts are rarely grown to reach huge size without raising any symptoms. Most of the cases that have huge cysts present with pressure symptoms over the genitourinary system leading to urinary complaints or the respiratory system lead to respiratory embarrassment.

Dermoid cysts account for 10–20% of all ovarian neoplasms. They are common in young women, especially at the age of 30 years.In most of cases, they are asymptomatic and can be discovered accidentally on clinical examination or ultrasonographic scan. They are usually indolent tumors with very slow rate of growth about 1.8 mm per year. Giant dermoid cysts have been infrequently reported in the literature.

This is a case report of huge dermoid cyst weighing 25 kgs in a 42-year old perimenopausal lady that remained relatively asymptomatic. She underwent Laparotomy with ovarian cystectomy.

Keywords:laparotomy, pregnancy, ovarian cyst

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INTRODUCTION

Around 25-30% of all ovarian tumors are of Germ cell origin, 95% of which are benign and 3-4% are malignant. Benign cystic teratomas (Dermoid cyst) account for 10-20% of all ovarian tumors. Histologically, they are composed of variable proportions of tissue originating from the ectoderm, mesoderm, and endoderm. Cystic teratomas are commonly seen in active reproductive years but can occur in any age group and may be seen in postmenopausal women.[1]

They are usually indolent tumors with very slow rate of growth about 1.8 mm per year. With increasing availability of ultrasound services even in developing countries, the diagnosis of benign ovarian tumour is made earlier and the size of the ovarian tumour at diagnosis is relatively small. It is not common to find an ovarian cystic teratoma larger than 10 cm.Giant dermoid cysts have been infrequently reported in the literature.

CASE

Mrs. R.R. is a 42-year-old Para 1 (1 alive) woman who presented with a 16-years history of abdominal swelling. Swelling was localized to the lower abdomen, was initially small, and had been progressively increasing in size. There was no associated abdominal pain nor vomiting or change in bowel habits, no urinary symptoms or change in menstrual pattern. Neither history of shortness of breath, palpitation or edema was noted. Patient had amenorrhea since 9 months.

Figure 1- Appearance of the abdominal mass

Physical examination revealed an average built woman with wrinkled skin. She was not pale, febrile, or icteric. Her vital signs were within normal limit. Respiratory and Circulatory systemic findings were unremarkable. The abdomen was uniformly, globular with centrally placed and everted umbilicus. Whitish striae were noted in lateral abdominal wall. No venous dilatations were noted.On palpation, a firm mass of ~30x25 cm (Figure 1) was noted with limited mobility from side to side and top to bottom.

CORRESPONDENCE

Dr Nishma Bajracharya
2nd Year FCPS Resident, Department of Obstetrics and Gynaecology, Kathmandu Model Hospital, Kathmandu, Nepal.
Email: nishu_bajra@hotmail.com
Phone: 9860-157654

The mass was non-tender, had smooth and regular margins with dull note on percussion. Fluid thrills and shifting dullness was noted on flanks Pelvic examination revealed a normal vulva and vagina. The cervix was healthy looking, and the os was closed. An anteverted uterus was palpable separate from the abdominal mass. The lower border of the mass was felt at bilateral fornices, which was non tender. No nodules were palpated at posterior fornix.

CECT Abdomen done revealed a large well defined intraperitoneal cystic mass measuring 25x22x35 cm in right adnexae with dense wall calcifications and small internal area of fat. No internal enhancing solid components noted. The mass compressing the right lateral wall of urinary bladder, displacing the bowels to left side. Anteriorly the lesion is adhering with anterior abdominal wall and posteriorly compressing the Inferior Venacava. No enlarged regional lymph nodes noted. The uterus was normal. Her basic blood tests including the tumor markers were within normal limits. A diagnosis of mature ovarian cystic teratoma was made and she was prepared for exploratory laparotomy. She underwent Total Abdominal Hysterectomy with Bilateral Salpingo-ophorectomy. Intraoperative findings included a large multiloculated right ovarian cyst measuring 40x35 cm and weighing 25 kg containing 12 liters of clear serous fluid. (Figures 2 and 3).The outer surface was smooth, with regular margins, cystic consistency and greyish yellow hue. Cut section of the mass showed large amounts of pultaceous material with engulfed hair. The cyst wall showed some amounts of cartilages and teeth.The left ovary had dermoid cyst of ~4x3 cm size. The histopathological report confirmed the diagnosis i.e., mature teratoma. Postoperatively, the patient had an uneventful course in ward and was discharged stable on 9thpost operative day.

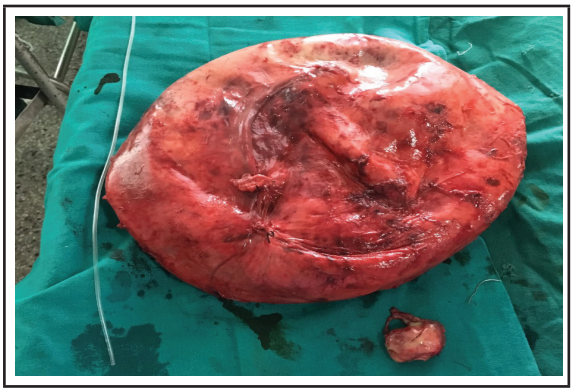

Figure 2- Capsule of the dermoid cyst

Figure 3- Clear serous fluid

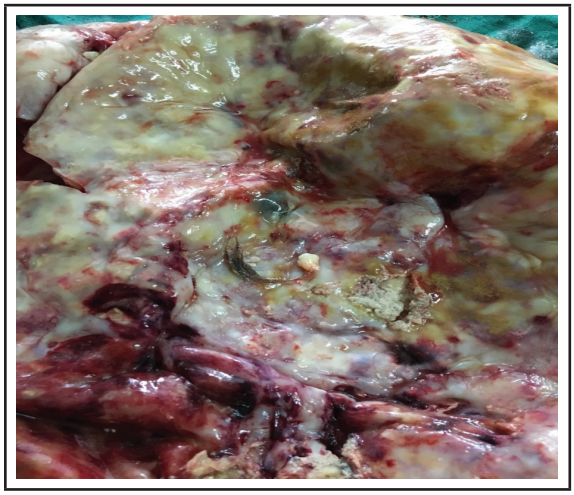

Figure 4- Cyst wall containing hair, teeth, bony and cheesy material

COMMENTS

Dermoid cysts occur mostly during the reproductive years, at ages 20- 40 years. They are bilateral in 10 –13% of cases and so was in our case. The incidence of malignant elements in such teratoma is quite low (approximately 1–2%).[2] They are frequently multi-cystic and contain sebaceous fluid as well as hair, teeth, bone, and skin. Typically, these tumors contain mature tissues of ectodermal (skin, brain), mesodermal (muscle, fat), and endodermal (mucinous or ciliated epithelium) origin.[3] They have a characteristic CT scan appearance with fat/fluid level attenuation and calcification or ossification. The classic sonographic appearance is of a hyperechoic mass termed as a dermoid plug or Rokitansky protuberance. This Rokitansky protuberance is composed of the thickened area of ectodermal tissue from which hair, bone and teeth arise. Pain is usually related to the size of the mass, and ovarian torsion is common.[3]

Mature cystic teratomas grow slowly at an average rate of 1.8 mm each year, prompting some gynecologists

to advocate non-surgical management of smaller (6 cm) tumors. These features were not found in our case. There can be malignant transformation of mature teratoma. Also there are few cases reported in which benign tumor (oftenly mucinous cystadenoma coexist with mature teratoma).[4]

The surgical management of mature cystic teratomas should be directed according to age, desire for future fertility and presence of any concomitant pelvic pathology rather than size or the laterality status. Laparoscopic management of benign dermoid cysts is safe and effective and can therefore be highly recommended.[5] In Our patient as the tumor size was very huge reaching up to xiphisternum, decision of laparotomy and cystectomy was made. This case highlights very atypical features dermoid cysts.

CONCLUSIONS

There are many reported cases of ovarian tumor in perimenopausal women but a huge dermoid cyst is very rare. Timely diagnosis and surgery is the key to management.

CONFLICT OF INTEREST

None

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Identify the methods, apparatus (give the manufacturer's name and address in parentheses), and procedures in sufficient detail to allow other workers to reproduce the results. Give references to established methods, including statistical methods (see below); provide references and brief descriptions for methods that have been published but are not well known; describe new or substantially modified methods, give reasons for using them, and evaluate their limitations. Identify precisely all drugs and chemicals used, including generic name(s), dose(s), and route(s) of administration.

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