Determinants of Ectopic Pregnancy among Pregnant Women Attending Referral Hospitals in Southwestern parts of Oromia Regional State, Southwest Ethiopia: Case control study

A thesis paper to be Submitted to Jimma University, Institute of Health, Department of Biomedical Sciences, in partial fulfillment of the requirements for Masters of Science degree in Clinical Anatomy

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Determinants of Ectopic Pregnancy among Pregnant Women Attending Referral Hospitals in Southwestern parts of Oromia Regional State, Southwest Ethiopia: A multi-centered hospital based case control study.

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Abstract

Background: *Ectopic pregnancy (EP) is abnormal condition in which implantation of the blastocyst occurs outside the endometrium of the uterus. It is gynecological important, particularly in the developing world, because of the associated enormous rate of high morbidity, during the first trimester of pregnancy. A better understanding of its risk factors can help to prevent its prevalence. However, the determinants of ectopic pregnancy are not well understood and few researches conducted in our country were based on secondary data covering small scale area.*

***Objectives*:** *This study aimed to identify determinants of ectopic pregnancy among pregnant women attending referral hospitals in Southwestern part of Oromia regional state, Southwest Ethiopia*.

Methods: *Multi-centered hospital based case control study was employed from June 1 to September 30, 2019. The study was conducted in five referral hospitals in Southwestern part of Oromia regional state, with sample size of 177(59 cases and 118 controls). After confirmed by ultrasound and hCG women with ectopic pregnancy were cases and women who had not diagnosed for ectopic pregnancy were controls. Data were entered by using Epi data version 3.1 and analyzed using SPSS version 23. Descriptive statistics were used to explore the data. All explanatory variables with p -value of <0.25 in bi-variable analysis then entered into multivariable logistic regression. Associated factors were identified at 95% confidence interval (p <0.05). Aggregate results were displayed using frequency tables*.

Results: *From five referral hospitals 177(59 cases and 118 controls), one hundred seventy-four pregnant women (58 EP cases and 116 controls) were participated in the study. History of two or more induced abortions [AOR=3.95:95% CI: 1.22-13.05], at least one previous history of caesarean section [AOR=3.4:95% CI: 1.11-10.94], marital status (being single) [AOR=4.04:95%CI: 1.23-13.21], reporting Prior recurrent STD/STI [AOR=2.25:95%CI: 1.00-5.51], Women reporting prior history of emergency contraceptive pills use [AOR=3.04:95%CI:1.29-7.14] were more likely to have ectopic pregnancy with their respective AOR with 95%C. I*

Conclusion and Recommendation: *It was found that having history of more than two induced abortions during previous pregnancy, marital status (single), recurrent STD/STI, experiencing at least one caesarean section for previous pregnancy and using emergency contraceptives pills use were found to be important determinants of ectopic pregnancy. Hospitals should give emphasis on prevention and early detection of risks of ectopic pregnancy and create awareness in order to reduce the burden of ectopic pregnancy*.

Keywords: *Ectopic pregnancy; Intrauterine pregnancy; pregnant women; Determinants, Southwest Ethiopia.*

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Acronyms

ANC	Ante Natal Care
AOR	Adjusted Odd Ratio
AURH	Ambo University Referral Hospital
B.Sc.	Bachelor of Science
C/S	Cesarean section
CI	Confidence Interval
D/C	Dilatation/Curettage
ECP	Emergency contraceptives pills
EDHS	Ethiopian Demographic Health Survey
EP	Ectopic pregnancy
FMOH	Federal ministry of Health
hCG	Human chorionic gonadotropin
HMIS	Health Management Information System
IEOS	Integrated Emergency Obstetrics & General surgery
IRB	Institutional Ethical Review Board
IUD	Intra Uterine Device
IVF	In-Vitro Fertilization
JU	Jimma University
JUMC	Jimma University Medical Center
km	Kilometer
LSCS	lower segmental Cesarean Section
mIU/Ml	milli-International Units per milliliter
MKRH	Mettu Karl Referral Hospital
MSc	Master of Science
NRH	Nekemte Referral Hospital
OCP	Oral Contraceptives Pills
OPD	Out Patient Department
OR	Odd Ratio
PID	Pelvic Inflammatory Disease
SPSS	Statistical Package for Social Sciences
STD	Sexually Transmitted Disease
U/S	Ultrasound
USA	United State of America
WURH	Wellega University Referral Hospital

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Above all, I would like to thank Almighty God to help me to do this thesis. I would like to express my deepest gratitude to my advisors Mr. Tilahun Alemayehu (M. Sc, Assistant professor of Anatomy), Mr. Getachew Chane (B. Sc, M.Sc), Mrs. Dilab Desta (B.Sc, M.Sc) and Dr. Amenu Diriba (MD. gynecologist and obstetrician) for their constructive comments through the process, I would also thank them for their interest, unreserved guidance and consistent effort made in supervising my thesis work.

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1. Introduction

1.1. Background of the study

Ectopic pregnancy (EP) is abnormal condition in which implantation of the blastocyst occurs outside the endometrium of the uterus. These abnormal sites of implantation in decreasing order of frequency include uterine tube (tubal pregnancy), abdominal cavity or on the mesentery (abdominal pregnancy), and in the ovaries (ovarian pregnancy) (1). It is gynecological importance, particularly in the developing world, because of the high morbidity and mortality associated with it and the enormous threat to life. When ruptured, an ectopic pregnancy is a true medical emergency result in complication. It is one of the leading cause of maternal mortality in the first trimester and accounts for 10%– 15% of all maternal deaths(2).

Figure 1 shows the common sites of ectopic pregnancies ever reported in literature. As shown, the fallopian tube is the most common site of extra-uterine pregnancy, also known as tubal pregnancy, accounting for almost 97.7% of all ectopic gestations, followed by implantation in the abdominal cavity (1.4%), and implantation in the ovaries (0.02%) and in the region of the internal Os, frequently resulting in placenta Previa (0.2%). Almost 80% of the tubal pregnancy occurs in the ampulla, followed by the isthmus (12%), fimbria (5%) and in the narrow portion of the uterine tube (interstitial implantation) [0.2%](3).

Blastocysts that do not implant in the uterine wall are generally unable to develop normally. Ectopic pregnancy cause ruptures of the organ on which they are implanted. Rupture result in severe internal bleeding, shock and death of woman. Fortunately, the ability to early diagnose, monitor, and treat ectopic pregnancy reduces the risk of these life-threatening complications (4). If the fallopian tubes are damaged or abnormal as a result of previous infection or surgery, tumors, or, rarely, due to malformations present since birth, there is an increased risk of ectopic pregnancy (5). Surgery to reconstruct the fallopian tube (to improve a woman's chances of becoming pregnant) can increase the risk of ectopic pregnancy (6).

The etiology of ectopic pregnancy is not well understood however; multiple risk factors have been associated with ectopic pregnancy**,** Pelvic inflammatory disease (PID), puerperal sepsis, post abortion sepsis, appendicitis, and the use of intrauterine contraceptive devices have been identified as sources of pelvic infection and major risk factors (7–9).

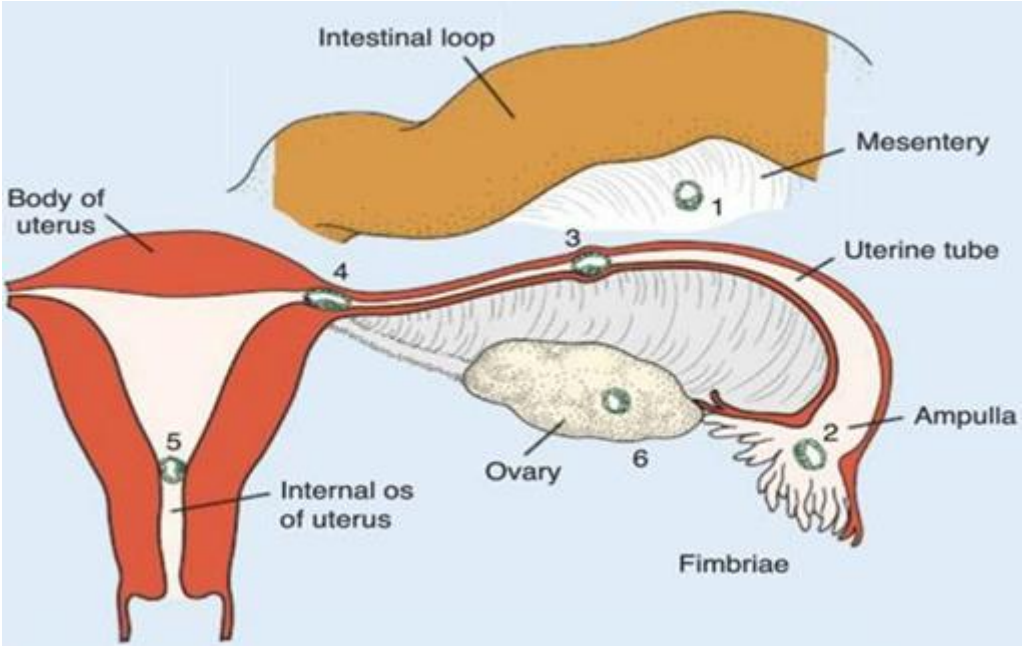


Figure 1: Abnormal implantation sites of the blastocyst

[Adopted from Langman's Medical Embryology: 13 Edition, page 54

Other risk factors are tubal/pelvic surgeries, chromosomally abnormal zygote, use of progesterone-only pills, cigarette smoking, and zygote transfer (assisted reproductive technology), history of previous abortion, previous ectopic pregnancy, history of infertility, and age above 35 years are some of risk factors (7–9). Women with tubal ectopic pregnancy (EP) are increased risk of infertility and tubal EP in future pregnancies. Function of the fallopian tube is to provide the optimal environment for the transport and maturation of gametes and the establishment of pregnancy. Most data suggest that tubal EP stems from both abnormal zygote transport and an alteration in the tubal environment, which enables abnormal implantation to occur(10).

Women who had history of ectopic pregnancy have an increased risk of another ectopic pregnancy (3). The underlying tubal disorder increases the risk of ectopic pregnancy(6). Non-tubal ectopic pregnancy is associated with higher mortality and morbidity than tubal ectopic pregnancy, because they are often difficult to diagnose ectopic pregnancy and tend to present late with sudden rupture. Abdominal/trans- vaginal ultrasound is a useful tool in the diagnosis of ectopic pregnancy. Both the surgical and the medical management exist for the ectopic pregnancy(11).

1.2. Statement of the problem

Ectopic pregnancy is the leading cause of maternal morbidity and mortality Worldwide (4). In developed countries, the prevalence of ectopic pregnancy is approximately 2% in the general population, but as high as 20% in patients who have undergo tubal surgery, previous ectopic pregnancy and STD/STI(12).

Ectopic pregnancy occurs in all races, in all countries and in any socio economic class of women during reproductive years. It is a surgical gynecological emergency and is 10 times, 50 times as dangerous as vaginal delivery and induced abortion respectively(4,13). In previous ectopic the probability of the next intrauterine pregnancy is occurring in 50-80% and the remaining patients will be infertile, which mainly affects young women with low parity who want to become pregnant in the future. The risk of recurrence is increased by 7-15%. Short-term complication of ectopic pregnancy (excessive bleeding, shock) as well as the negative psychological effects on the mother(13).

The rate of ectopic pregnancy has followed an increasing trend during the last three decades throughout the world(14). Ectopic pregnancy remains a leading cause of maternal mortality and morbidity in the first trimester of pregnancy in developing countries(15). The maternal mortality ratio in Ethiopia is one of the highest in sub-Saharan African, 412/100,000 live births(16). Ethiopia is one of the six countries which have contributed to more than 50% of all maternal deaths across the world. Among the causes of maternal

mortality (Hemorrhage, pregnancy induced hypertension, obstructed labor and infection) are common. Ectopic pregnancy is the leading in the first trimester of pregnancy(17).

In spite of different research done on the prevalence of ectopic pregnancy however, the determinants of ectopic pregnancy are not well understood and few researches published in our country were based on secondary data covering small scale area

Ectopic pregnancy is an emergency condition most of the time medical charts of the patients (incomplete information, unreadable patient card, registration book and operation room records and details of socio demographic variables not addressed due to lack of documentation) which leads us to wrong conclusions and major risk factors of ectopic pregnancy are not identified.

The study area has different characteristics cultural, religious, socio-demographic characteristics, sexual behavior, beliefs, contraception usage and practice from other area. Study was aimed to identify risk factors of ectopic pregnancy among pregnant women attending referral hospitals in Southwestern part of Oromia Regional state, Southwest Ethiopia.

1.3. Significance of the study

This study result would worth to detect the potential risk factors of ectopic pregnancy in the study setup which would have further advantages to minimize morbidity and mortality of patients due to ectopic pregnancy.

With regard to the preventable factors associated with ectopic pregnancy in the current population, this study is an important piece of work that could serve as an important source of information to design prevention strategies or to conduct further investigations

2. Literature Review

2.1. Overview of ectopic pregnancy

Ectopic pregnancy is a common obstetric problem in the world. Incidence of the condition varies from one country to others depending on the risk factors predominant in the geographical region. It is an important cause of morbidity and mortality in early pregnancy. The rate of ectopic pregnancy has followed an increasing during the last three decades throughout the world(18).

The studies show the prevalence of ectopic pregnancy has increased in America, so that it has become 6 times as much over the last 25 years(19). This evident increase in the ectopic pregnancy can be due to increase of risk factors in this disease. Despite the continued increase in the prevalence of ectopic pregnancy, the rate of death has declined in developed countries primarily because of earlier diagnosis before tubal rupture(4).

In 1990, a review reported an increase in the incidence of EP from the 1960s until the middle of the 1980s. In this review, the highest EP incidence rates were observed in African countries (between 0.5 and 2.3% of live births) whereas low incidence rates were reported in Asia and the Middle East over the same period: 0.4% of live births between 1964 and 1973 in India and about 0.6% of live births between 1976 and 1982 in Jordan(20). A 3 years' retrospective study in Nigeria shows the prevalence of ectopic pregnancy represented 4.26% of all deliveries, 5.55% of all gynecologic admissions(21). Study was done in Adigrt hospital, Tigray region, Northern Ethiopia indicate the magnitude of ectopic pregnancy among total deliveries and gynecological surgeries was 0.82% and 3.74% respectively. About 57.1%, 9.1% and 16.9% occurs in Ampulla, isthmic and fimbria respectively (22).A Clinical study of Ectopic pregnancies in Bangladesh shows the prevalence of ectopic pregnancy in ampulla(53.2%), isthmus(21.3%) and fimbriae(12.7%)(14).

2.2. Risk factors of ectopic pregnancy

The etiologic factors for ectopic pregnancies includes previous abdominal/pelvic surgery(Salpingectomy), previous ectopic pregnancy, previous genital infections pelvic inflammatory disease, smoking (the risk is increased by number of cigarettes), age (over 30 years), intrauterine device (IUD), Oral Contraceptives(OC) only with progestin, multi-parity, previous abortion (spontaneous or inducted)(11,22–25).

2.2.1. Sociodemographic Factors

Retrospective case control study done in Tehran Iran reveal, the data for socio-demographic characteristics (age and educational level) significantly similar in term of education. There was an association between ectopic pregnancy and age which was disappeared after controlling for the main risk factors(26). Retrospective case control study done in India various significant risk factors for ectopic pregnancy identified, were age above 30 years, low socio-economic status (23). A study done in India out of 86 samples factors with significant association included, age more than 25 years, upper socioeconomic class(27).

In Pakistan risk factors associated with ectopic pregnancy higher age group is at risk for ectopic pregnancy(5). Case-control study of 100 patients and 280 controls was performed in Nigeria, age and socioeconomic status were not risk factors of ectopic pregnancy(28). Retrospective case control study done Nekemte on 99 cases with ectopic pregnancy and 200 controls the identified risk factors were marital status, accordingly, women with single marital status were 10.81 times more likely to develop ectopic pregnancy than married once(24).

2.2.2. Gynecologic Factors

A Clinical retrospective case control study done on ectopic pregnancies in a Tertiary care hospital of Chittagong, Bangladesh shows risk factors of ectopic pregnancy were previous history of tubectomy (2.12%), spontaneous and induced abortion (23.49%), 2.12% had a

history of infertility. Copper-T was inserted in 4.6% cases. 11.9% had a history of D&C, a history of previous ectopic (2.12%) where partial salpingectomy was done, and history of PID (pelvic inflammatory disease) was found in 4.2% of the case(14).

Retrospective case control study done in Tehran Iran shows, there was no statistically significant relation between ectopic pregnancy and prior tubal surgery, tubal pathology, prior abortion, prior infertility, assisted reproductive technology, and oral contraceptive method ($p>0.05$). However, there was a significant association between prior history of ectopic pregnancy, prior history of tubal ligation, use of intrauterine device, and prior abdominal/pelvic surgery with ectopic pregnancy ($p<0.05$). The risk of ectopic pregnancy increased with the use of intrauterine device and tubal ligation, whereas decreased with use of oral contraception(25).

According to case control study done in Turkey the main risk factors for ectopic pregnancy were prior ectopic pregnancy and a history of reproductive system infectious (AOR = 6.8). Other risk factors found to be associated with an increased risk for ectopic pregnancy were, induced conception cycle, current intrauterine device usage. On the contrary, barrier methods were protective from ectopic pregnancy (29).

According to retrospective case control study done in Saudi Arabia the women with ectopic pregnancy had significantly higher frequencies of past PID, previous abortions or its surgical treatment, history of pelvic-abdominal surgery, surgery for previous ectopic pregnancy, and induction of ovulation in the index pregnancy (p values, <0.001, 0.019, 0.024, 0.0147 and 0.001 respectively). On the other hand, women in controls had higher gestational age than those of cases ($6.19 \pm .79$ weeks versus 8.74 ± 1.9) ($p < 0.05$)(30).

Study done in India out of 86 samples 54 were positive for Chlamydia infection women with Chlamydia infection had an increased risk of developing ectopic pregnancy. Among the other risk factors history of pelvic inflammatory disease and history of STD/STI were the most significant with odds of 3.98. History of oral contraceptive use also had a significant risk associated with developing ectopic pregnancy(27).

According to case control study in USA, the risk of EP was associated with previous adnexal surgery, uncertainty of previous pelvic inflammatory disease. Women who had previously used condoms were less likely to have EP during the current cycle (30).

A total of 29 EP cases and 29 controls among IUD users in China were included in study data revealed that history of abdominal or pelvic surgery was associated with risk of EP. However, there was no significant association between the risk of EP and factors including uterus position, first or second time use IUD, period insertion of IUD, shapes of IUD, and copper surface area of IUD(31).

Multi center case control done in China, study revealed that the risk of EP was associated with the traditional risk factors including previous EP, previous Chlamydia trachomatis infection, previous infertility, previous adnexal surgery, previous appendectomy, and previous history of intrauterine devices use (IUDs). Additionally, EP risk was increased following the failure of most contraceptives used in the current cycle including IUDs, oral contraceptive pills levonorgestrel emergency contraception, and female sterilization (32).

A comprehensive analysis based on a large case-control, population-based study in France shown that risk factors were STD/STI; previous pelvic infectious disease and smoking; prior spontaneous abortions, and previous use of an intrauterine device. Prior medical induced abortion was associated with a risk of ectopic pregnancy; no such association was observed for surgical abortion (33).

Case-control study of 100 patients and 280 controls was performed in Nigeria shows that history of induced abortions, pelvic inflammatory disease, sexually transmitted disease (STD), miscarriage, and pelvic surgery significantly increased the risk of ectopic pregnancy. Induced abortion and STD/STD increased the risk 14-fold and nine-fold, respectively. Previous use of intrauterine contraceptive device increased the risk almost four-fold , whereas the use of condoms was protective (28).

2.2.3. Obstetric factors

A Clinical retrospective case control study done on ectopic pregnancies in a tertiary care hospital of Chittagong, Bangladesh shows risk factors of ectopic pregnancy 4.3% had a history of previous Lower Segmental Cesarean section (LSCS)(14).

Among a total of 225 cases and 375 controls study done in Turkey the main risk factors for ectopic pregnancy prior caesarean section (29).

A total of 29 EP cases and 29 controls among IUD users in China were included in study. Data revealed two pregnancies and three or more pregnancies had a significant higher risk of EP compared with one pregnancy (31). In Pakistan risk factors associated to ectopic pregnancy, past history of miscarriages and parities parity (26). Case-control study of 100 patients and 280 controls was performed in Nigeria, age, marital status, socioeconomic status, and parity were not the significant risk factors for ectopic pregnancy(28).

2.2.4. Behavioral factors

From total of 225 cases and 375 controls study done in Turkey the main risk factors for ectopic pregnancy was cigarette smoking at the time of conception with (28). Retrospective case control study was done in India while no significant association was seen with smoking(23). A comprehensive analysis based on a large case-control, population-based study in France shown for >20 cigarettes/day vs women who had never smoked)(28).

2.3. Conceptual framework

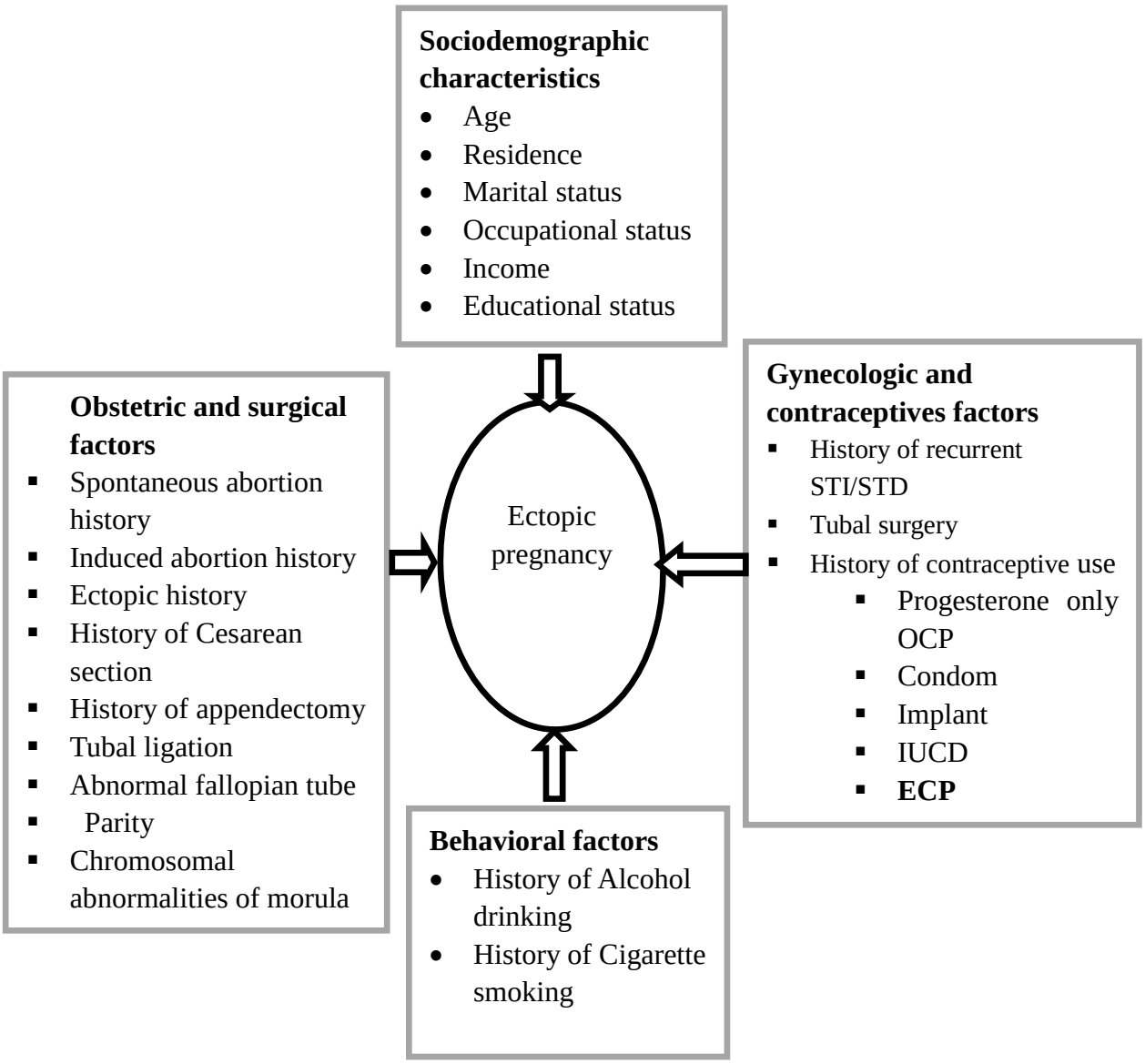


Figure 2: Conceptual frame work adapted by reviewing different literatures

3. Objectives

3.1. General Objective

- To identify determinants of ectopic pregnancy among pregnant women attending referral hospitals in Southwestern parts of Oromia Regional State, Southwest Ethiopia, 2019.

3.2. Specific Objectives

- To assess the common sites of ectopic pregnancy in the current population.
- To identify the factors associated with ectopic pregnancy.

4. Methods and Subjects

4.1. Study areas and period

The study was conducted in five referral hospitals found in Southwestern part of Oromia regional state, Southwest Ethiopia. These include Jimma university Medical hospital (JUMC), Wellega university referral hospita1 (WURH), Nekemte Referral hospital (NRH), Ambo university referral hospital (AURH) and Mettu karl referral hospital (MKRH). They are located at 352 km, 331 km, 331 km, 115 km and 600 km far from the capital city, Addis Ababa respectively. All hospitals are teaching and referral hospital that gave general and specialized clinical services including ANC, family planning, delivery service& treatment obstetric complications are some of the services provided in gynecologic and obstetric ward. These services have been delivered by senior midwifes, gynecologists/obstetricians. Study was from June 1, to September 30, 2019.

4.2. Study Design

Multi centered hospital based case- control study design was conducted.

4.3. Population

4.3.1. Source population

All pregnant women attending Gynecology and Obstetrics department of JUMC, WURH, NRH, AURH and MKRH during the four-month study period were source population.

4.3.2. Study population

For cases: All pregnant women who had been confirmed by ultrasound and hCG to have EP in the inpatient department of gynecology and obstetrics of each hospital were recruited.

For controls: Controls were sampled pregnant women confirmed by ultrasound and hCG to have intra uterine pregnancy at the prenatal clinic in department of gynecology and obstetrics of each hospital.

4.4. Eligibility criteria

4.4.1. Inclusion criteria

For cases: admitted women who had been confirmed by ultrasound and hCG to have EP in the inpatient department of gynecology and obstetrics of each hospital.

For controls: Controls were sampled pregnant women confirmed by ultrasound and hCG to have intra uterine pregnancy at the prenatal clinic in department of gynecology and obstetrics of each hospital.

4.4.2. Exclusion criteria

For both cases and controls

Women with serious medical conditions and couldn't give consent were excluded from the study.

Case Definition /ascertainment of cases

Case: Pregnant women diagnosed by hCG and ultrasound to have ectopic pregnancy confirmed by Obstetrician/gynecologist(33).

Control: Pregnant women diagnosed by hCG and ultrasound to have intrauterine pregnancy confirmed by Obstetrician/gynecologist (33).

4.5. Sample size and sampling procedure

4.5.1. Sample size determination

The required sample size was determined by using Epi-info version 7 statistical software for case-control study design. Results from similar studies were used to approximate the sample size in different potential risk factors of ectopic pregnancy. In a study report from India, by khedar and Mital (23) in 2016, prior tubal surgery was significant risk factor for ectopic pregnancy. A case control study in west Ethiopia at Nekemte hospital, by Kebede and Dessie (24) in 2018, marital status was a significant risk factor for ectopic pregnancy. Similarly, case control study done in Turkey Ankara, by Karear. A (29) in 2016, previous history of ectopic pregnancy was a significant risk factors for ectopic pregnancy. Using these reports as starting point, similar assumptions

- **P_1**: proportion among cases and p_2: proportion of among controls
- **AOR:** Adjusted odds ratio
- At 95% (**Zα/2** = 1.96) level of confidence, Power of study=80%
- Ratio of cases to controls = 1:2

Table 1: Sample size determination by Epi-info version 7 statistical software in Southwestern, Oromia regional state, Southwest Ethiopia, 2019.

Exposure variables	Proportion ion among cases	Proportion on among controls	AOR	Sample size		Final Sample Adding 10% nonresponse
				Cases	Controls	
Pervious History of ectopic pregnancy	9.7	1.3	13.1	53	106	177
Single marital status	25	3	10.8	32	64	105
Pervious tubal surgery	44	3	14	25	50	84

From the above three significant risk factors of ectopic pregnancy, previous history of ectopic pregnancy gives large sample size so which is 59 cases and 118 controls. With total of 177study participants.

4.5.2. Sampling technique and procedures

JUMC, WURH, NRH, AURH and MKRH were purposely selected because these hospitals are the largest teaching and referral hospitals that provides maternal health service. During the study period, all women who had been diagnosed with EP in the department of gynecology and obstetrics of each hospital were recruited in the case group (EP group). Women with an intrauterine pregnancy (IUP) of the same department assigned as controls IUP) with 1:2 ratio.

Sample size was split between the five hospitals proportional to their pregnant women caseload. According to the 2018 G.C HMIS report.

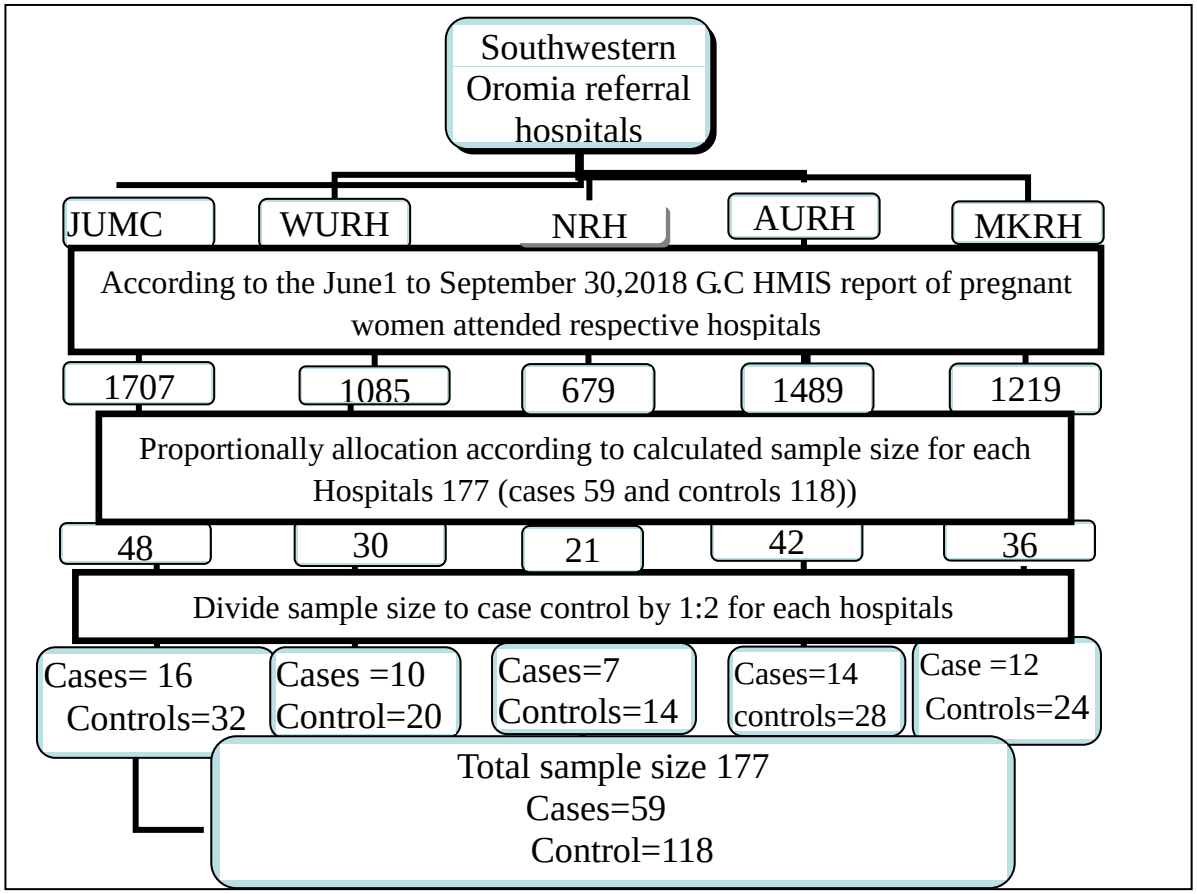


Figure 3: Schematic presentation of sampling procedure, 2019.

4.5.3. Data collection tool and procedure

Urine human chorionic gonadotropic test

Specimens were collected in a clean, dry, plastic container. The procedure was done as guideline by dispensing three drops of specimen into the round sample wait for red lines to appear read results after. The procedure was done by professional laboratory technologist according to guideline(34).

Ultrasound procedure

Transabdominal ultrasound was used to diagnose confirm state of pregnancy. The procedure was done by obstetrics and gynecologist according to guideline(35). Client lied down on an examination table or bed. Gel is applied to abdomen (to provide better contact between skin and the scanner) and the sonographer moved the scanner in various positions. Pictures are sent instantly to a nearby monitor (35).

A semi-structured questionnaire was developed and modified in local context based on reviewing relevant literatures(1,4,9,11,14,19,21,22,24,32,36–40).The questionnaire was prepared initially in English and then translated into Afan Oromo and Amharic language and back to English by 2-independent translator to assure its consistency. Before the actual data collection, the checklist was pre-tested on 5% of pregnant women in Shenen Gibe hospital. Then, necessary correction was made based on the result of the pre-test of the instrument. Then data was collected by Afan Oromo and Amharic version. Five (midwife, medical doctors, laboratory technologists and supervisors) participate in diagnosing the case and control and collecting the Data. Data collectors trained on their specific responsibility, overviews regarding the study objectives. Principal investigator coordinated them supervise daily was checked the consistency, clarity and completeness of the collected questionnaires.

4.6. Variables

4.6.1. Dependent variable

Ectopic pregnancy

4.6.2. Independent variables

Socio-demographic characteristics

- Age
- Marital status
- Religion
- Address
- Ethnicity
- Educational status
- Occupation
- Income

Obstetric/surgical, Gynecologic/contraceptives and behavioral factors

- Habits (Alcohol drinking, cigarette smoking)
- Gravidity
- Abortion history
- History Ectopic pregnancy
- History of STI /STD
- chromosomal abnormalities of morula
- tubal abnormalities
- History of contraceptive use (condom, ECP, IUCD, OCP
- Tubal ligation
- History of appendectomy
- History of tuba surgery
- History of cesarean section

4.7. Operational definitions

Alcohol consumption: occasional drinker mother who had history of alcohol consumption any form (5-15 drinks/month), **nondrinker** (1-4drinks/month

Cigarette smoking: **Occasional smoker: c**igarette smoking more than 4 times a week but an average of less than one cigarette per day, **Nonsmoker pregnant** women who had never take cigarette. **ECP, OCP only progesterone family planning use:** If women used this type of family planning, during the cycle of conception and failed to protect current pregnancy.

Recurrent STD/STI: Infections established by means of sexual contact occurs more than two times for the last 6 months.

4.8. Data processing and analysis

Collected data were rechecked for completeness, consistency and coded before data entry. Data were entered using Epi data version 3.1 and data from five hospitals were merged together then exported to Statistical Package for Social Science (SPSS) version 23 for analysis. Descriptive analysis was conducted to explore the data and present some variables.

Bi-variable binary logistic regression analysis was executed to select candidate variable for multivariable binary logistic regression to identify the predictors. Variables with p-value of less than 0.25 was selected for multivariable logistic regression. Odds ratio (OR) and 95% confidence intervals (CI) were used to describe the association between ectopic pregnancy and potential risk factors. Variables with a p-value <0.05 in multi-variable analysis was considered as significant risk factor for ectopic pregnancy.

4.9. Data quality assurance

Urine sample collection was done through standardized, and sterile technique by professional laboratory technologists, ultrasound was calibrated before the procedure.

The diagnosis and location of pregnancy were confirmed by transabdominal ultrasonography combined to the hCG was used to confirm EP. All women who had been diagnosed with EP in the department of gynecology of each hospital were recruited in the case group (EP) and women with intra uterine at the same department recruited in the control group (IUP).

Data quality was ensured during data collection, coding, entry and analysis. During data collection adequate training and follow up was provided to data collectors and supervisors. Incomplete checklists were returned back to the data collector for completion. Codes were given to the questionnaires and during the data collection so that any identified errors was traced back using the codes. Urine sample collection was done by professional laboratory technologist and Ultrasound was done by gynecologist and obstetrics specialist.

4.10. Ethical consideration

Ethical approval or clearance letter RPSCMF/0132/19 was obtained from institutional review board (IRB) of Institute of Health, Jimma University. Permission letter (Formal letter of cooperation) was written to respective hospitals administration office, and the study was commencing after receiving formal permission from them. Anonymity of the participants was kept by informing them that their name and personal identifiers are not to be written on the questionnaire and verbal informed consent was obtained from each study subject. Participants was told that they have full right to participate or refuse participation in the study and the right to stop in the meantime while interviewing questioners if not feeling comfortable, keeping in mind the rationale of the study and benefit of his/her response. The results of the patient were announced to the patients and linked to respected ward for further diagnosis and management.

4.11. Dissemination of results

The findings of this study will be presented in public defense and submitted as M. Sc thesis to Jimma university department of Biomedical sciences, Anatomy unit. Then it will be disseminated to Jimma university research unit and communicated to the local Health planners and other relevant stakeholders such as administration of each hospitals and Ministry of Health. Finally, the findings will be disseminated through publications and may be presented in scientific conferences and workshops.

5. Results

5.1. Socio-demographic characteristics

In this prospective case control study conducted over four-months from June 1 to September 30, 2019 at five government referral hospitals found in Southwestern part Oromia, Ethiopia. These hospitals were Jimma University Medical Center (JUMC), Wellega University Referral Hospital (WURH), Nekemte Referral Hospital (NRH), Ambo University Referral Hospital (AURH) and Mettu Karl Referral Hospital (MKRH). From a total of 177(59 cases and 118 controls), 174 pregnant women; 58 Cases (EP) and 116 Controls (IUP) were participated. The cases were aged between 18 and 43 years with a mean age of 26 (±5.54) years and a median of cases 26 years, while the controls are between 18 and 39 years, mean = 26 (±4.87) and median of controls 26 years (**Table 2)**

Table 2: The number of cases and controls of pregnant women enrolled into the study at the study hospitals, Southwest Ethiopia, June—September 2019

Study Hospitals	Number of pregnant women available during the study period	Cases Number	Controls number
JUMC	1642	15	30
AURH	1343	13	26
WURH	985	10	20
NRH	600	8	16
MKRH	1120	12	24
Total	5690	58	116

Key: JUMC- Jimma university medical center, **AURH-** Ambo university referral hospital**,** **WURH-** Wellega university referral hospital**, NRH-** Nekemte Referral hospital, **MKRH-** Metu keral referral hospital

Almost two-third (63.8%) of cases and 79(68.1%) of controls were aged between 21 and 30 years. Eighteen (31%) cases and 39(33 %) of controls were orthodox in religion and 37(63.8%) of cases and 79(68.1%) of controls were Oromo by their ethnicity and thirty-seven

(63.8%) cases and 95(81.9%) of controls were married. About 18(31%) cases and 46(39.7%) controls were house wives in occupation **(Table 3).**

Table 3: Socio-demographic characteristics of EP cases and non-EP controls at referral hospitals in south western part of Oromia region, Southwest Ethiopia, 2019

Characteristics	Category	Cases (N=58) n(%)	Controls (N=116 n(%)
Age in year	<=20	10 (17.2%)	14 (12.1%)
	21-30	37 (63.8%)	79 (68.1%)
	>=30	11 (18.9%)	23 (19.8)
Residence	Urban	27 (46.6%)	54 (46.6%)
	Rural	31 (53.4%)	62 (53.4%)
Religion	Orthodox	18 (31.0%)	39 (33.6%)
	Muslim	15 (25.8%)	29 (25.0%)
	Protestant	20 (34.4%)	33 (28.4%)
	others	5 (8.6%)	15 (12.9%)
Ethnicity	Oromo	37 (63.8%)	79 (68.1%)
	Amhara	11 (18.9%)	24 (20.7%)
	Dawuro	5 (8.6%)	7 (6.0%)
	Guragie	5 (8.6%)	6 (5.2%)
Marital status of respondent	Single	9 (15.5%)	7 (6.0%)
	Married	37 (63.8%)	95 (81.9%)
	Others	12 (13.7%)	14 (12.08%)
Educational status	Can't read &write	6 (10.3%)	5 (4.3%)
	Read &write only	10 (17.2%)	17 (14.7%)
	Grade 1-8	18 (31.0%)	48 (41.4%)
	Grade 9-12	15 (25.8%)	32 (27.3%)
	Diploma and above	9 (15.5%)	14 (12.1%)
Occupational status of respondent	Housewife	18 (31.0%)	46 (39.7%)
	Farmer	13 (22.4%)	22 (18.9%)
	Gov't employee	9 (15.5%)	25 (21.6%)
	NGO	5 (8.6%)	6 (5.2%)
	Merchant	6 (10.3%)	6 (5.2%)
	Laborer	7 (12.1%)	11 (9.5%)
Income in ETB	<1000	18 (31.0%)	24 (20.6%)
	1001-2000	12 (20.7%)	23 (19.8%)
	2001-3000	15 (25.7%)	26 (22.4%)
	3001-4000	6 (10.3%)	24 (20.6%)
	>4001	7 (12.1%)	19 (16.4%)

Key- Others divorced and widowed

Only one case (1.7%) and two controls (1.7%) had occasional history of cigarette smoking and only 18(31.1%) cases and 34(29.3%) controls history of occasionally alcohol consumption before current pregnancy **(Table 4).**

Table 4: Behavioral characteristics of cases and controls in Southwestern referral hospitals in Oromia regional state, Southwest Ethiopia, 2019(N=174)

Habits	Category	Cases (N=58, N(%)	Controls(N=116,N(%)
History of cigarette	Non smoker	57 (98.2%)	114 (98.3%)
	Occasional smoker	1 (1.7%)	2 (1.7%)
History of alcohol d	Non drinker	40 (68.9%)	82 (70.7%)
	Occasional drinker	18 (31.1%)	34 (29.3%)

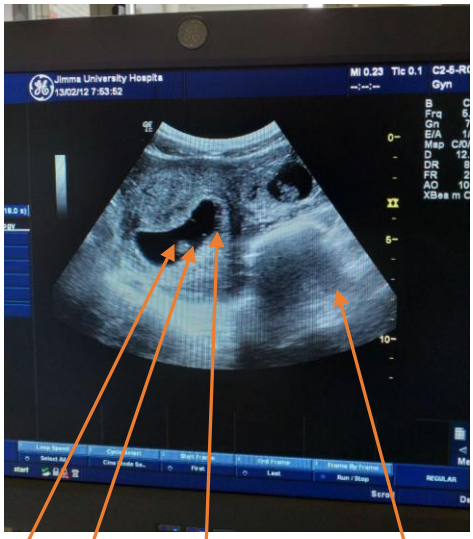
5.2. Site of Ectopic pregnancy

From the various sites of ectopic pregnancy, in this study, almost all of EP cases 56 (96.5%) had tubal ectopic pregnancy; of them 52 (92.8%) were ampulla, 2 (3.5%) isthmic, one case (1.7%) fimbria and 1(1.7%) were interstitium. One case (1.7%) had ovarian ectopic pregnancy, while another woman (1.7%) was diagnosed with abdominal ectopic pregnancy.

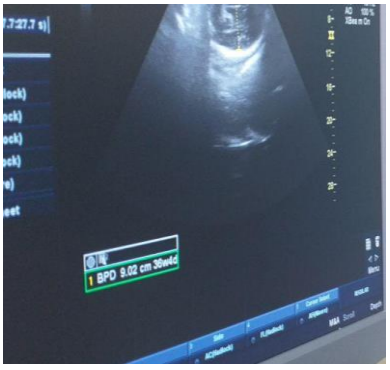
Figure 4 shows the sonographic taken from 30 years old pregnant women as shown (figure c and d), the normal sonographic finding there is gestational sac, fetal pole and yolk sack observed in the uterus, but in sonographic finding in (figure a and b) gestational sac, yolk sac, fetal pole did not observed in the uterus and the uterus was empty.

a

b



a. abdominal pregnancy in right view



c) Normal intrauterine in the right view d) normal in the left view

Figure 4: Ultra sound finding of ectopic pregnancy southwestern, referral hospitals, Oromia regional state, Southwest Ethiopia,2019.

5.3. Obstetrics and surgical history of cases and controls.

Obstetrics and surgical history of the cases and controls is given in (**Table 5).** As indicated in the Table, three of the cases (5.1%) and another three women in the control group (2.6%) had prior history of ectopic pregnancy. Seven women in each of the study groups (12.0% of the cases and 6.0% of the controls) had more than two prior history of spontaneous abortion. Similarly, 8 (13.8%) cases and 6 (5.1%) controls reported two or more prior history of induced abortion. This study shows that 10(17.2%) of cases and 6(5.1%) controls had caesarean section before current pregnancy. Eleven (18.1%) of cases and 6(5.2%) controls had at least one tubal pregnancy before current pregnancy for any reason **(Table 5).**

Table 5: Obstetrics and surgical history of cases and controls in Southwestern referral hospitals in Oromia regional state, Southwest Ethiopia, 2019(N=174).

Characteristics **(N=174).**	Category	Cases (N=58) n(%)	Controls (N=116, N(%)
Prior history of ectopic pregnancy	Yes	3 (5.1%)	3 (2.6%)
	No	55 (94.8%)	113 (97.4%)
Prior history of spontaneous abortion	0	42 (72.4%)	97 (83.6%)
	1	9 (15.5%)	12 (10.3%)
	>=2	7 (12.0%)	7 (6.0%)
Prior history of Induced abortion	0	40 (68.9%)	96 (82.8%)
	1	10 (17.2%)	14 (12.1%)
	>=2	8 (13.8%)	6 (5.1%)
Prior history of caesarean section	Yes	10 (17.2%)	6 (5.1%)
	No	48 (82.7%)	110 (94.8%)
Prior history of appendectomy	Yes	1 (1.7%)	4 (3.4%)
	No	57 (98.3%)	112 (96.6%)
Prior history of tubal surgery	Yes	11 (18.9%)	6 (5.2%)
	No	47 (81.1%)	110 (94.8%)
Prior history of tubal ligation	Yes	5 (8.6%)	5 (4.3%)
	No	53 (91.4%)	111 (95.7%)
Parity	0	19 (32.7%)	43 (37.1%)
	1	22 (37.9%)	48 (41.3%)
	>=2	17 (29.3%)	25 (21.6%)

5.4 Gynecologic and contraceptive history of cases and controls

Practice of contraceptive methods of the study subjects is given in table 6. About 36.2% (21/58) of the cases and 16 (13.7%) controls had prior history of recurrent STD/STI. Majority 42 (72.4%) of the cases and 92 (79.3%) controls had prior history of oral contraceptives use. Only 6 (10.3%) cases and 15(12.9%) controls had history of IUCD use. Twenty (34.4%) cases and 18 (10.8%) controls reported practice of emergency contraceptives pills use before the current conception **(Table 6).**

Table 6: Gynecologic and contraceptive history of cases and controls in Southwestern referral hospitals in Oromia regional state, Southwest Ethiopia, 2019(N=174).

Characteristics	Category	Cases (N=58), n(%)	Controls (N=116), n(%)
Prior recurrent STD/STI	Yes	21 (36.2%)	16 (13.7%)
	No	37 (63.7%)	100 (86.2%)
Prior history condom usage	Yes	16 (27.5%)	28 (33.6%)
	No	42 (72.4%)	88 (75.8%)
Prior history of IUCD usage	Yes	6 (10.3%)	15 (12.9%)
	No	52(89.7%)	101 (87.1%)
Prior history of OCP	Yes	42 (72.4%)	92 (79.3%)
	No	16 (27.6%)	24 (20.7)
Prior history of Injectable	Yes	25 (43.1%)	50 (43.1%)
	No	33 (56.9%)	66 (56.9%
Prior history of implant use	Yes	15 (25.9%)	34 (29.3%)
	No	43 (74.1%)	82 (70.7%)
Prior history of emergency pills	Yes	20 (34.4%)	18 (10.8%)
	No	38 (65.6%)	98 (84.5%)

5.5. Factors associated with ectopic pregnancy

In bivariate analyses conducted to identify candidate variable for multi logistic regressions. A total of 25 individual variables comprising socio-demographic, gynecologic/contraceptives, obstetric /surgical and behavioral factors were evaluated. Among these, seven variables had candidate for multilogistic regression at a p-value less than 0.25. These variables were: marital status, prior history of having more than two induced abortions, prior history of tubal

surgery, prior history of caesarean section, prior history of tubal ligation, history of recurrent STD/STI and history of using emergency contraceptives. For multivariable logistic regression analysis, seven variables were candidates (p<0.25was considered) **(Table 7).**

5.6. Independent Predictors of Ectopic pregnancy

Multivariable analysis was used to identify independent predictors of ectopic pregnancy. All variables with p-value <0.25 in bivariate logistic regression analysis were entered and further examined in multivariable analysis to see their relative effects on occurrence of ectopic pregnancy. In multivariable logistic regression analysis, the model was tested for existence of multicollinearity (VIF=1.001) and this result indicate that there was no multicollinearity and the model was fit and five variables were independently associated (significant at p<0.05) with ectopic pregnancy.

Odds of having at least one caesarean section for previous pregnancy were about 3.4 times more likely to have ectopic pregnancy when compared to pregnant women who didn't experience caesarean section [AOR=3.4:95%CI:1.14-10.94]. Women who had history of more than two induced abortions before present pregnancy were 3.95 times more likely to have ectopic pregnancy when compared to those who did not undergo induced abortion [AOR= 3.95:5%CI:1.22-13.05]. Single women were 4.04 times more likely to have ectopic pregnancy than married women [AOR = 4.04:95%CI:1.23-13.2]. women who had Prior history of recurrent STD/STI were nearly 2.35 times more likely to have ectopic pregnancy compared with counterpart. [AOR=2.35:95%CI: 1.0-5.51] Additionally, women who had used emergency contraceptive pills were 3.04 times more likely to have ectopic pregnancy when compared to non user [AOR=3.04:95% CI: 1.29-7.14] **(Table 7).**

Table 7: Bivariate and multivariate logistic regression of factors associated with ectopic pregnancy: Southwestern referral hospital, Oromia regional state, Southwest Ethiopia, 2019(N=174).

Variables		Status of ectopic pregnancy		COR (95% C.I)	AOR (95% C.I) P value
		Cases (N=58 Number %)	Controls (N=116) Number %)		
Marital status of respondent	Single	9 (15.5%)	7 (6.0%)	3.31[1.14-9.51]	**4.04**[1.23:13.24] **0.02***
	Married	37 (63.8%)	95 (81.9%)	1	
	Others	12 (13.7%)	14 (12.08%)	2.2[0.93-5.1]	2.0[0.75-5.36]0.16
Prior history of induced abortion	0	40 (68.9%)	96 (82.8%)	1	
	1	10 (17.2%)	14 (12.1%)	1.71[0.70-4.18]	1.9[0.71-545] 0.19
	>=2	8 (13.8%)	6 (5.1%)	3.2[1.04-9.81]	**3.95**[1.22-13.05] **0.024***
Previous history of caesarean section	Yes	10 (17.2%)	6 (5.1%)	3.82[1.49-12.22]	**3.4**[1.14-10.94] **0.032***
	No	48 (82.7%)	110 (94.8%)	1	
Prior history of tubal surgery	Yes	11 (18.9%)	6 (5.2%)	4.3[1.49-12.28]	**2.85**[0.90-9.03] **0.074***
	No	47 (81.1%)	110 (94.8%)	1	
Tubal ligation	Yes	5 (8.6%)	5 (4.3%)	2.09[0.67-10.14]	1.08[0.21-5.39) 092
	No	53 (91.4%)	111 (95.7%)	1	
Prior recurrent STD/STI	Yes	21(36.2%)	16 (13.7%)	3.55[1.67-7.52]	**2.35**[1.0-5.51] **0.049***
	No	37 (63.7%)	100 (86.2%)	1	
Prior history of emergency contraceptives pills	Yes	20 (34.4%)	18 (10.8%)	2.86[1.36-5.99]	**3.04**[1.29-7.14] **0.01***
	No	38 (65.6%)	98 (84.5%)	1	

Key-Reference =1, *value statistically significant (P-value< 0.05) **AOR-** Adjusted Odds ratio **COR-** Crude odds ratio, **CI**-Confidence interval

Hosmer Lemshow test=0.46-0.57

6. Discussion

This was multicentered hospital based case control study which was aimed to identify determinants of ectopic pregnancy among pregnant women attending referral hospitals in Southwestern parts of Oromia regional state, Southwest Ethiopia. According to the current finding almost all cases had tubal ectopic pregnancy, one case (1.7%) had ovarian ectopic pregnancies and another one (1.7%) had abdominal ectopic pregnancy. This finding was consistent with study done in Ghana, west Africa and Iran(13,25,41).

Pregnant women who were single independent predictors of ectopic pregnancy. A similar association was reported in studies done in Turkey, west Ethiopia Nekemte (24,43). The association between become single and ectopic pregnancy infection could be explained by the fact that single women engaged in multiple sexual partners following successive infection, ascending infection result in adhesions, impede the morula retention of movement causing implantation in the tube and other site.

Having more than two times history of induced abortion found was statistically significant relation with ectopic pregnancy. This finding was supported by study done in Nepal, India, Tigray Ethiopia, Turkey and Saudi Arabia (1,22,23,30,44). The association might be explained by most abortion are illegal different countries and usually performed in poor aseptic conditions. Thus, increasing post-abortion sepsis risk and subsequent PID.

Women who had prior history of recurrent STD/STI were significantly associated with ectopic pregnancy. This finding was similar to study done in Pakistan, Nepal, India, France, China, Saudi Arabia, Uganda and USA (1,5,11,25,30,32,45,46). The association between STD/STI and ectopic pregnancy might be successive infection, ascending infection result in salphingitis leads to tubal dysfunction, decrease cilia density, ciliary beat this result in retention of morula in the fallopian tube and implantation of blastocyst in the fallopian tube and other site.

Women having at least one caesarean section for previous pregnancy were independently associated with ectopic pregnancy. The study supported by study done in done in Turkey, France (29,45). Underlying mechanism of association between previous caesarean section and occurrence of ectopic pregnancy is might be due to increased pelvic infection and adhesion after caesarean section which disturb the micro environment of the tube and implantation of blastocyst in the tube.

In present study, women who had used emergency contraceptive pills during the cycle of conception were statistical significant with ectopic pregnancy. A similar association was reported in Nepal, china (11,32) The association between emergency contraceptive pills and ectopic pregnancy explained by higher levels of progesterone could alter ciliary beat function and smooth muscles contractility of fallopian tubes and the high serum peak of ECP observed after an administration of a single dose of ECP could possibly result in a tubal motility decline; thus, increasing the risk of EP(44) Thereby, if ECP is taken at a time when it is ineffective in preventing pregnancy, the plasma concentration of ECP might still remain high during the time of blastocyst-tubal transport due to its half-life of 24h; therefore, the chance of blastocyst-tubal implantation increases with declined tubal motility.

I did not find any association between appendectomy, prior use of IUCD, cigarette smoking, alcohol drinking and previous history of ectopic pregnancy, previous tubal surgery with present study, Probably the number of the studied participants was too small.

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Strength of the study

- Multi-centered hospital based prospective case control study.

Limitation of the study

- Due to small number of cases obtained from individual study hospitals, this study did not compare among the five hospitals with regard to risk factors of EP.
- Since this study assesses history of exposure retrospectively, it may be prone to recall and selection bias by nature during data collection time.
- Due to resource, for asymptomatic STD/STI the serology test was not done, it was based on history.
- Genetic cause of ectopic pregnancy (chromosomal abnormality of the zygote) was not assessed.

7. Conclusion and recommendations

7.1. Conclusion

Based on the finding of this study, almost all EP had tubal ectopic pregnancy. Most of tubal ectopic pregnancy occurs in the ampulla. It was found that having history of more than two induced abortions during previous pregnancy, marital status (single), experiencing at least one caesarean section for previous pregnancy, prior history of STD/STI and using emergency contraceptives pills during the cycle of conception were found important determinants of ectopic pregnancy in the study population.

7.2. Recommendation

Based on the study findings the following recommendations are forwarded:

1. For hospitals (JUMC, WURH, AURH, MKRH, NRH)

- Women with history of previous induced abortion and previous caesarean section STD/STI should be followed up carefully, even in the absence of symptoms should always be counselled about the possibility of ectopic pregnancy and the associated risks.
- Promote screening and treatment for STD/STI should strictly be done by involving medical staffs to prevent the risk factors of ectopic pregnancy.
- Mobilize health professionals to give health information to mothers about risk factors of ectopic pregnancy.
- Counsel the women to use other method of family planning and teach emergency contraceptives pills as risk factors for ectopic pregnancy.

2. For FMOH, Zonal and woreda health office should

- Strengthening quality ANC for early screening and interventions of risk factors for ectopic pregnancy so that decrease the cesarean section and STD/STI.

3. For researchers

- It is needed to explore the determinants of ectopic pregnancy in country based by using trans-vaginal ultrasound that used to detect the pregnancy as early as possible.
- The researchers should do serology test for STD/STI.
- Also assess the genetic cause of ectopic pregnancy (chromosomal abnormality of the zygote.
- Include large scale area and long period of time to compare the risk factor in different setting.

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Annex I. Participant consent form

Hello. My name is _____. I am data collector on research working on Determinants of Ectopic Pregnancy among Pregnant Women Attending Southwestern Oromia Referral Hospitals, Oromia Region, Southwest Ethiopia. The information that we collect will help policy makers, and other stakeholders to plan and intervene on ectopic pregnancy. The questions usually take about 15 to 20 minutes. All of the answers you give will be kept confidential and will not be shared with anyone. If I ask you any question you don't want to answer, just let me know and I will go on to the next question or you can stop the interview at any time. In case you need more information about the survey, you may contact the principal investigator whose number written on the bottom of the consent paper.

Voluntary participation

Your participation in this study is voluntary. It is up to you to decide whether or not to take part in this study. If you decide to take part in this study, you will be asked to sign a consent form. After you sign the consent form, you are still free to withdraw at any time and without giving a reason. Withdrawing from this study will not affect the relationship you have, if any, with the researcher. If you withdraw from the study before data collection is completed, your data will be returned to you or destroyed.

Consent

I have read and I understand the provided information and have had the opportunity to ask questions. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason and without cost. I understand that I will be given a copy of this consent form. I voluntarily agree to take part in this study.

Date of interview……. Signature ----------

interviewer name……. Code ----------

Urge Gerema

Tel no: +251910953298 Thank you for your participation!!

Annex II. English Versions Questionnaire

Part I Socio-demographic characteristics of the respondents.

Code	Variable	Response	Remark/note
101	state of pregnancy	0. IUP 1. Ectopic pregnancy	
102	If **Qno 1** is Ectopic pregnancy where is the site of pregnancy?	1. Tubal 2. Abdominal 3. Ovarian 4. Cervix 5. Other specify----------	
103	If Qno2 is tubal where is the site	1. ampulla 2. isthmus 3. fimbrie 4. corneal	
104	Age	----------in years	
105	Residence	1. Urban 2. Rural	
106	Marital status	1. Single 2. Married 3. Widowed 4. Divorced	
107	Educational level	1. Illiterate 2. Read and Write 3. 1-8t^{h} grade 4. 9-12th grade 5. College or University	
108	Occupation	1. Housewife	

		2. Farmer 3. Government employee 4. Non- government employee 5. Merchant 6. Daily laborer	
109	Ethnicity	1. Oromo 2. Amhara 3. Dawuro 4. Guraghe 5. Other/ specify----------	
110	Religion	1. Orthodox 2. Muslim 3. protestant 4. Other/ specify	
111	Monthly average income in ETB	----------	

Part II Past Obstetrics and surgical History

Code	Variable	Response	Skip
112	Do you have Pervious history of Ectopic pregnancy?	0. No 1. Yes	
113	Pervious history of spontaneous abortion?	1. 0 2. 1 3. 2 and above	
114	Previous history of induced abortion	1. 0 1. 1 2. 2 and above	
115	Previous history of appendectomy	0. No 1. Yes	
116	Previous history of tubal surgery	0. No 1. Yes	
117	Previous history of tubal ligation	0. No 1. Yes	

118	Previous history of caesarean section	0. No 1. Yes	
119	Parity	1. 0 1. 1 2. 2 and above	
120	Pervious history of recurrent STI/STD	0. No 1. Yes	
121	History of infertility	0. No 1. Yes	
122	History of condom use	0. No 1. Yes	
123	History of IUCD use	0. No 1. Yes	
124	History of OCP use	0. No 1. Yes	
125	History of injectable contraceptive use	0. No 1. Yes	
126	History of implant(implant + Jeddelle)	0. No 1. Yes	

Part IV Behavioral History

127	Cigarettes smoking	1. non smoker 2. occasional smokers 3. regular smokers	
128	If Yes to **124** how long ago did you start smoking?	----------years	
129	If yes to **124**, how often were you smoking?	1. Daily 2. Once a week 3. 3 times per week 4. Once a month	
130	How many cigarettes do you smoke each day/week on average?	----------numbers of cigarette	
	Alcohol status		

130	Do you have a History of alcohol drinking?	1.Yes 2. No	
131	If Yes to Q128 How often do you have a drink containing alcohol?	1 Never 2. Less than monthly 3. 2-4 times a month 4. 2-3 times a week 5. 4/more times a week	
	Alcohol status		
133	History of alcohol drink containing alcohol?	1 Never 2. Less than monthly 3. 2-4 times a month 4. 2-3 times a week 5. 4/more times a week	

Part V HCG and ultrasound measurement

1. HCG----------(mIU/mL) milli-international units per milliliter (positive or Negative)
2. Result of Ultrasound
    a. Tubal ectopic pregnancy
    b. Abdominal
    c. Ovarian pregnancy
    d. Cervical pregnancy
    e. Intrauterine pregnancy
    f. Heterotrophic pregnancy

3. Is there tubal abnormalities a yes
    b miti

Annex III. Afaan Oromo Version Questionnaire

Gaffiillee: Afaan Oromo version

Uunkaa 1: Waliigaltee

Harka fuune! Maqaan koo ----------jedhama. Qorannoo saayinsawaa barataa digirii lammataa Urgee Garramaattin Yuunvarsiitii Jimmaatti Inistituutii saayinsii fayyaatti muummee baayoomedikaalaatti geggeeffamuuf odeeffannoo funaana. Qorannoon saayinsawaa kunis Sababootaa ulfaa gadameessaan alaatti uumaamuuf sababaa tahaan dubartoota ulfaa keessaatti addaa baasuu irratti kan geggeeffamuudha. kanaafuu, namoota qoarannoo kana irratti hirmaachuu danda'an keessaa isa tokko waan taatanif akka irratti hirmaattan kabajaan isin gaafanna. Hirmaannan keessan fedhii keessan irratti kan hundaa'e yoo ta'u, hirmaachuu dhabuun keessan tajaajila nu biraaa argattan irratti rakkoo tokkoyyuu hin qabu. Qoranannon kun rakkoo qaamaas ta'ee kan xiinsammuu kan hin geechifne akkasumas baasii kan isin hin baasisne ta'uu isin hubachiisna. Qorannichi sababootaa ulfaa gadameessaan alaatti umaamaanif sabaabaa tahaan addaa baasuun rakkichi garaa fulduraa akka hin umaamnee fi yoo ummamee osoo rakko guddaaf hin saxileef gargaaraa. Qorannicha irratti hirmaachuf fedhii qabaattan gaafiifi deebii kan isiniif goonu akkasumas qorannoo ulfaa finca'aan keessaan fudhachuun fi meeshaa ulfaa sirritti addaa baasuu ultrasound kan jedhaamuun kan godhaamuudha. Migi qorannicha irratti hirmaachuu dhiisuu keessanii kan eeggame yoo ta'u, erga eegaltaniis adda kutuuf mirga guutuu kan qabdan akkasumas waan isinii hin galle gaafachuufillee mirga guutuuu qabdu. Odeeffannoon isinirraa fi kaardii keesssan irraa fudhatame iccitiin kan turuudha. Irrati hirmaachuuf fedhii qabduu? Yoo maamilli itti walii gale gaafiifi deebiin akkasumas qorannoole bira itti fufa.

Ani……. waa'ee qorannichaa odeeffannoo ga'aa kanan argadhe yoo ta'u qorannicha irratti hirmaachuuf walii galee jira.

Maqaa hirmaataa ……. Mallatoo hirmaataa …… guyyaa…….

Maqaa nama odeeffannoo funaanuu---------- mallattoo -----guyyaa-------

Maqaa hordofaa ----------mallattoo ----------guyyaa ----------

Galatooma!

Kutaa I: Gaaffilee waa'ee hawaasummaafi dinagdee

kood ii	Gaaffii	Deebii	Irraa daarbii
101	Idoo ulfii itti umamee	0 gadameessaa keessaatti 1 gadamessaan ala	
102	Gadameesssan ala yoo tahee essaati?	1 ujummoo gadameessaa 2 garaa keessaa 3 ovaarii 4 qarqaaraa gadamessa 5 kan biro adda baasi	
103	Yoo ujummoo gadameessaa yoo tahee essaati	1 ampullaa ujjummoo gadameessa 2 isthumsii ujummoo gadamesssa 3 fimbrie ujummoo gadameessaa 4 courna ujummoo gadameessaa	
104	Umrii	----------waggaadhan	
105	Teessoo	1. Magaalaa 2. Badiyaa	
106	Haala ga'eelaa	1 Kan hin fuunee 2 Kan kan heerumtee 3 Kan dhirsii irra du'ee 4 Kan wal hiikaan	
107	Sadaarkaa barumsaa	1 Kan hin baranee 2 Dubisuu fi bareesssuu kan danda'uu 3 Kutaa 1-6ffaa 4 Kutaa 7-12fffa 5 Kolleejii ykn university	
108	Gosaa hojii	1 Qotee bulaa	

		2 Haadhaa manaa 3 Hojeetuu mootuummaa 4 Hojii miti motummaa 5 Hojii guuyyaa	
		6 Kan birro addaa baasi	
109	Gosa	1. Oromoo 2. Amhaaraa 3. Guraagee 4. kan biro addaa baasi------	
110	Amantaa	1. Orthodooxsii 2. musiliimaa 3. proteestaantii 4. kan biroo adda baasi	
111	Gaalii ji'aa qarshii	----------	

Part II haalaa wal hormaataa waaliin waal qabaataan

Koodii	Gaaffii	Deebbii	Irraa darbii
1112	Kanaan duraa ulfaa gadameessaan alaa si mudaatee beekaa?	0 eeyyen 1 lakki	
113	Daa'immni osoo torbaan 28 hin gahiin ofumaa sirraa ba'ee beeekaa?	1. 0 2. 1 2. 2 fi isaa oli	
111	Daa'immni osoo torbaan 28 ofii kee baastee jirtaa?	1. 0 2. 1 2. 2 fi isaa oli	

112	Operationii isaa marimaani taatee beektaa	0. eyyee 1. mitti	
113	Kanaan duraa dahumsaa dadhabdee opitashiinii taatee beektaa?	0. eeyyen 1. lakki	

114	Ujummoo gadameessaa irratti opirationii taatee beektaa?	0. eyyee 1. mitti	
115	Kanan duraa dhukkubaa saalaa qabdaa turtee?	0. eeyyee 1. lakki	
116	Kanan duraa ujummo gadameessaa gudufitee turtee?	0. Eeyye 2. mitti	
117	Ijoollee meeqaa deessee?	1. 0 2. 1 3. 2 fi isa oli	
118	Codoomii fayyadatee beektaa?	0. eeyye 1. mitti	
119	Kiniinii qusaanaa kan guyyaa guyyan fudhataan fayyadamtee beekta?	0. eeyye 1. mitti	
119	Implantti qusaanaa kan waggaa sadi/shani fudhatee beektaa?	0. Eeyyee 1. Miti	
120	Qusaanaa isaa gadameessaa keessaa tahuu fudhatee beektaa?	0. eeyye 1. mitti	
121	Quusaanaa isaa sa’aati 72 ergaa wal qunnammti goote fudhatee?	0. Eeyye 1. Mitti	
122	Qusaanaa isaa lilmoo waagaa sadi fudhatee beekta?	0. Eeyye 1. Miti	

Part III waantootaa Amaalaa yookiin Araadaan waal qabaataan

124	Sigaaraa xuutaa beektaa?	1.eeyyee 2. lakki	
125	Yoo G**124** eeeyyen tahe? Hangaamiif sigaara tutee?	----------waggaadhan	
126	YooG124 eeyyen ta'eee hangaam faayadaamta?	1.Guyyaa Guyyaadhan 2. Torbaniti al tokko 3. Torbaanitti al lama 4. Ji'atti al tokko	
127	Yoo G124 eyyee jeetee sigaaraa meeqaa fayyadamta guuyyaatti/torbaanitti?	----------lakkoofsaan	
	Alcohol status		
128	Alkooli ni dhugaa turtee??	1.eeyye 2. lakki	
129	Yoo G128 eeyeen yoo tahee hangaam hangaam fayaadamtaa	1. Ji'atti yeroo toko 2. Ji'tti yeroo 2-4 3. Torbanitti yeroo 2-3 4. Torbanitti yeroo 4 oli	

Part V Qoraannaa fincaa'anii fi ultraasoundii

1. Bu'aa HCG----------(mIU/mL) milli-international units per milliliter (positive or Negative)
2. Bu'aa Ultrasound a Ulfaa Ujjummoo gadaameessaa keessaa

   b. Ulfaa garaa keessaatti umaammuu

   c..Ulfa ovaarii keessaatti uumaamu

   d. Ulfaa gadaameessaa keesssaatti uumaamu

   e. Ulfaa gadaameessaa fi gadameessaa keessaati uumaamu kan biro yoo jiraatee addaa baasi

Annex IV material used for diagnosis

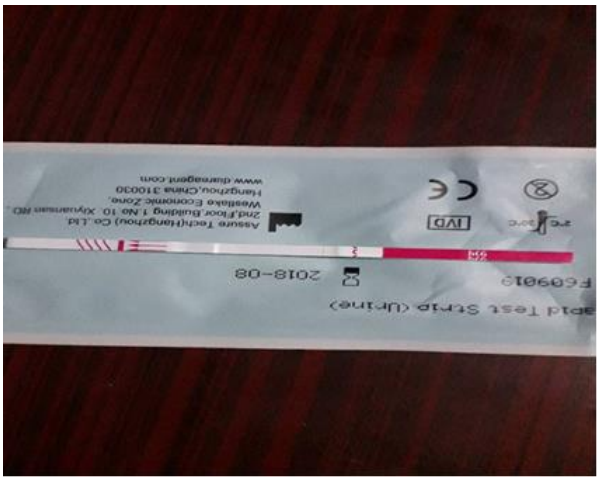

Figure 5: hCG kit

Model of U/S LOG8QCS Premium

Figure 6: Ultrasound

Annex IV. Bivariate analysis result of cases and controls for determinants of ectopic pregnancy in Southwestern Oromia regional state, Southwest Ethiopia. 2019(n=174)

A. Bivariate analysis of socio demographic and economic characteristics

Characteristics	Category	Cases (N=58) n(%)	Controls (N=116 n(%)	COR/95%C.I	P value
Age in year	<=20	10 (17.2%)	14 (12.1%)	1	
	21-30	37 (63.8%)	79 (68.1%)	0.65[0.26-9.1.61]	0.35
	>=30	11 (18.9%)	23 (19.8)	0.67[0.22-1.97]	0.7
Residence	Urban	27 (46.6%)	54 (46.6%)	1	
	Rural	31 (53.4%)	62 (53.4%)	1.00[0.53-1.88]	1.00
Religion	Orthodox	18 (31.0%)	39 (33.6%)	1	
	Muslim	15 (25.8%)	29 (25.0%)	1.12[0.48-2.56]	0.79
	Protestant	20 (34.4%)	33 (28.4%)	1.31[0.59-2.88]	0.49
	others	5 (8.6%)	15 (12.9%)	0.72[0.22-2.29]	0.58
Ethnicity	Oromo	37 (63.8%)	79 (68.1%)	1	
	Amhara	11 (18.9%)	24 (20.7%)	0.97[0.43-2.20]	0.95
	Dawuro	5 (8.6%)	7 (6.0%)	1.52[0.45-5.12]	0.52
	Guragie	5 (8.6%)	6 (5.2%)	1.77 [0.50-5.2]	0.36
Marital status of respondent	Single	9 (15.5%)	7 (6.0%)	3.31[1.14-9.51]	0.07
	Married	37 (63.8%)	95 (81.9%)	1	
	Others	12 (13.7%)	14 (12.08%)	2.2[0.93-5.1]	0.02
Educational status	Can't read &write	6 (10.3%)	5 (4.3%)	1.86[0.43-7.90]	0.4
	Read &write only	10 (17.2%)	17 (14.7%)	0.96[0.29-2.87]	0.97
	Grade 1-8	18 (31.0%)	48 (41.4%)	0.58[0.21-1.58]	0.28
	Grade 9-12	15 (25.8%)	32 (27.3%)	0.72[0.25-2.05]	0.55
	Diploma and above	9 (15.5%)	14 (12.1%)	1	
Occupational status of respondent	Housewife	18 (31.0%)	46 (39.7%)	2.31[0.56-9.4]	0.26
	Farmer	13 (22.4%)	22 (18.9%)	1.08 [0.42-2.77]	0.86
	Gov't employee	9 (15.5%)	25 (21.6%)	1	
	NGO	5 (8.6%)	6 (5.2%)	2.77[0.71-1.8]	0.27
	Merchant	6 (10.3%)	6 (5.2%)	1.72.31[0.52-5.9]	0.35
	Laborer	7 (12.1%)	11 (9.5%)	1.64[0.0.58-4.57]	0.34
Income in ETB	<1000	18 (31.0%)	24 (20.6%)	2.0[0.7-50]	0.28
	1001-2000	12 (20.7%)	23 (19.8%)	1.4[0.46-4.30]	0.54
	2001-3000	15 (25.7%)	26 (22.4%)	1.56[0.53-4.56]	0.41

	3001-4000	6 (10.3%)	24 (20.6%)	0.672.31[0.67-2.38]	0.54
	>4001	7 (12.1%)	19 (16.4%)	1	

B. Bivariate analysis result for Behavioral factors

Habits	Category	Cases (N=58, N(%)	Controls(N=116,N(%)	COR/95%C.I	P value
History o smoking	Non smoker	57 (98.2%)	114 (98.3%)	1	
	Occasional smoker	1 (1.7%)	2 (1.7%)	1.00[0.0.08-11.8]	0.63
History o drinking	Non drinker	40 (68.9%)	82 (70.7%)	1	
	Occasional drinker	18 (31.1%)	34 (29.3%)	1.08[0.0.54-2.15]	0.81

C. Bivariate analysis for Obstetrics and surgical risk factors

Characteristics **(N=174).**	Categor y	Cases (N=58) n(%)	Controls (N=116, N(%)	COR/95%C.I	P value
Prior history of ectopic pregnancy	Yes	3 (5.1%)	3 (2.6%)	2.05[0.0.4-0.38]	0.38
	No	55 (94.8%)	113 (97.4%)	1	
Prior history of spontaneous abortion	0	42 (72.4%)	97 (83.6%)	1	
	1	9 (15.5%)	12 (10.3%)	1.70[0.0.67-4.21]	0.27
	>=2	7 (12.0%)	7 (6.0%)	2.31[0.76-6.7]	0.26
Prior history of Induced abortion	0	40 (68.9%)	96 (82.8%)	1	
	1	10 (17.2%)	14 (12.1%)	1.71[0.70-4.18]	0.23
	>=2	8 (13.8%)	6 (5.1%)	3.2[1.04-9.81]	0.042
Prior history of caesarean section	Yes	10 (17.2%)	6 (5.1%)	3.82[1.42-12.22]	0.007
	No	48 (82.7%)	110 (94.8%)	1	
Prior history of appendectomy	Yes	1 (1.7%)	4 (3.4%)	0.49[0.054-4.90]	0.52
	No	57	112 (96.6%)		1

		(98.3%)			
Prior history of tubal surgery	Yes	11 (18.9%)	6 (5.2%)	4.31[1.49-12.2]	0.007
	No	47 (81.1%)	110 (94.8%)	1	
Prior history of tubal ligation	Yes	5 (8.6%)	5 (4.3%)	2.09[0.67-10.14]	0.16
	No	53 (91.4%)	111 (95.7%)	1	
Parity	0	19 (32.7%)	43 (37.1%)	1	
	1	22 (37.9%)	48 (41.3%)	1.03[0.0.49-2.17]	0.92
	>=2	17 (29.3%)	25 (21.6%)	1.53[0.67-3.49]	0.32

D. Gynecologic and contraceptives

Characteristics	Category	Cases (N=58), n(%)	Controls (N=116), n(%)	COR/95%C.I	P value
Prior recurrent STD/STI	Yes	21 (36.2%)	16 (13.7%)	3.55[1.67-5.21]	0.001
	No	37 (63.7%)	100 (86.2%)	1	
Prior history condom usage	Yes	16 (27.5%)	28 (33.6%)	0.8[0.40-1.70]	0.62
	No	42 (72.4%)	88 (75.8%)	1	
Prior history of IUCD usage	Yes	6 (10.3%)	15 (12.9%)	0.77[0.28-2.11]	0.61
	No	52(89.7%)	101 (87.1%)	1	
Prior history of OCP	Yes	42 (72.4%)	92 (79.3%)	0.61[0..33-1.42]	0.31
	No	16 (27.6%)	24 (20.7)	1	
Prior history of Injectable	Yes	25 (43.1%)	50 (43.1%)	1.0[0.52-1.8]	1.00
	No	33 (56.9%)	66 (56.9%	1	
Prior history of implant use	Yes	15 (25.9%)	34 (29.3%)	0.84[0.0.41-1.71]	0.63
	No	43 (74.1%)	82 (70.7%)	1	
Prior history of emergency pills	Yes	20 (34.4%)	18 (10.8%)	2.86[1.36-5.66]	0.005
	No	38 (65.6%)	98 (84.5%)	1	

Declaration

This is to certify that the thesis entitled: "Determinants of ectopic pregnancy among pregnant women attending referral hospitals in Southwestern parts of Oromia regional state, Southwest Ethiopia: A multi-centered hospital based case control study is prepared by Urge Gerema and submitted in partial fulfillment of the requirements for Masters of Science degree in Clinical Anatomy complies with regulation of Jimma university and meets the accepted standards with respect to originality and quality.

Signed by the Examining Committee:

Principal Investigator: - Urge Gerema Signature…… Date……

Advisors' Name Signature Date

1. Mr. Tilahun Alemayehu (BSc, MSc, Assistant Professor) ---------- ----------
2. Mr. Getachew Chane (BSc. MSc) ---------- ----------
3. Mrs. Dilab Desta (BSc, MSc ---------- ----------
4. Dr. Amenu Diriba (MD. Obstetrician and gynecologist) ---------- ----------

Examiner

Mr Asfaw Gerbi (BSc, MSc, Assistant Professor) signature ------ date ----------