Research Article

Correlation of βhCG Levels with Size of Gestational Sac in Patients of Ectopic Pregnancy Presenting to a Tertiary Care Health Facility

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Abstract: The objective of this study was to determine correlation of β- HCG levels with size of gestational sac in patients of ectopic pregnancy presenting to a tertiary care health facility.

Materials & Methods: This descriptive cross-sectional study was carried out in the Department of Obstetrics and Gynecology, district headquarter Hospital, Rawalpindi from Jan 2019 to Jan 2020.

This study involved 100 pregnant women aged between 20-40 years diagnosed of ectopic pregnancy on transvaginal ultrasound. Serum βhCG level was acquired in all these women while the size of gestational sac was measured on transvaginal ultrasound. Outcome variable was correlation between serum βhCG level and size of gestational sac on transvaginal ultrasound which was noted and compared across various subgroups of patients based on age, gestational age, site of ectopic pregnancy and presence/absence of fetal cardiac activity.

Results: The mean age of the patients was 29.3±6.1 years while the mean gestational age was 5.1±1.1 weeks. Serum βhCG level ranged from 1647 mIU/mL to 18378 mIU/mL with a mean of 7968.4±4523.7 mIU/mL while the size of gestational sac on TVS ranged from 17 mm^3 to 45 mm^3 with a mean of 36.40±7.86 mm^3. There was significantly strong positive correlation between serum βhCG and size of gestational sac on TVS (r=0.659; p- value<0.001).

Conclusion: There was significantly strong positive correlation between serum βhCG and size of gestational sac on TVS (r=0.659; p-value<0.001).

Keywords: Correlation, Ectopic pregnancy, Serum βhCG, Gestational sac, Transvaginal ultrasound, Cilia.

INTRODUCTION

Ectopic pregnancy has given challenges to gynecology in its early detection. The implantation of embryo outside the uterine cavity is called ectopic pregnancy. In female with child bearing, ectopic pregnancy has grave adverse effects on maternal health, accounting for 3-4% of pregnancy related deaths [1]. B-HCG levels and transvaginal sonography are used for early detection and exclusion of ectopic pregnancy [2]. In developed world 1-2% of pregnancies are ectopic, however, the incidence is increasing due to pelvic inflammatory disease, smoking and assisted reproductive technique. All over the world about 10% of women with diagnosis of ectopic pregnancy die ultimately. In developed countries, during first trimester, ectopic pregnancy is the leading cause of maternal death and its incidence is expected to increase in future [3, 4]. Transvaginal high definition ultrasound and serial β-HCG levels have revolutionized the assessments of patients with early pregnancy problems [1].

The fallopian tube provides a conducive environment for both the transport of ova and for fertilization to take place. It further facilitates migration of fertilized ovum into the uterine cavity and its implantation. The most common place of ectopic pregnancy is the fallopian tube. Any change in the fallopian tube environment or defective embryo migration may result in ectopic tubal pregnancy [5]. The migration of both ovum and early embryo with in the tube is dependent on coordinated movements of cilia and contraction of tubal smooth muscles. Several intrinsic and extrinsic factors affect this conducive environment like infections, different hormones, toxins and immunological agents. Coordinated ciliary motion is affected by the hormonal changes during different phases of menstrual cycle. Also, cilia may be damaged by the deleterious effects of smoking and infections decreasing ciliary density [5, 6]. When ciliary epithelium of fallopian tube is exposed to nitrous oxide and estradiol, it increases ciliary beating frequency with resultant defective migration of fertilized ovum with in the fallopian tube. The contraction of tubal smooth muscles is also affected by nitrous oxide. During different phases of menstrual cycle, the expression of nitrous oxide varies due to hormonal variations, with possible implications for ectopic and normal pregnancy. Similarly, it has been postulated that pathways and genes responsible for embryo transportation through the tube and implantation in the uterine cavity may be affected by estradiol

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which exerts its effect through estrogen receptors. However, the exact mechanism of ectopic pregnancy is not clear and seems to be multi factorial [7, 8]. Ectopic pregnancy has suboptimal range of serum β-HCG levels [9]. Expeditious diagnosis of ectopic pregnancy by transvaginal ultrasound and serum β-HCG levels can be lifesaving. Ectopic pregnancy is one of the conditions that have expectant, medical and surgical management and early diagnosis allows consideration of medical and conservative management in un-ruptured ones, tubal conserving procedures [10].

The purpose of this study was early diagnosis of ectopic pregnancy which can help in successful medical management of ectopic pregnancy and local data was deficient on literature in this regard.

MATERIAL AND METHODS

This descriptive cross sectional study was carried out in the Department of Obstetrics and Gynecology, district headquarter Hospital, Rawalpindi from Jan 2019 to Jan 2020 after approval from ethical review board of Rawalpindi Medical University. Sample size of 100 cases was calculated with 80% power of test and 5% level of significance while taking expected correlation between βhCG and size of gestational sac to be r=0.252 [11]. Sampling technique used was Non-Probability, Consecutive Sampling. Patients included in the study were aged 20-40 years, gestational Age: ≤ 6 weeks irrespective of parity and confirmed diagnosis of ectopic pregnancy on TVS. Patients excluded from the study were patients with β–HCG sample collection more than 12 hours, patients presenting in shock and massive bleeding, patients with pre- existing adnexal mass, patients with β-HCG secreting tumors, patients with molar pregnancy and patients with heterotrophic pregnancy.

DATA COLLECTION PROCEDURE and ANALYSIS

After approval of my synopsis from institutional ethical research committee, study was conducted in Gynecology department of DHQ and Holy Family hospital. Written informed consent was taken from patients coming to OPD and emergency with suspected ectopic pregnancy by consecutive random sampling. The patient not willing to be part of study was skipped. β-hCG was measured in mIU/mL by standardize laboratory test from Holy Family Hospital [26]. Transvaginal ultrasonography was done by a consultant gynecologist to measure the size of gestational sac of ectopic pregnancy in mm^3. All the information was recorded in structural performa designed from study.

All the collected data was collected from patients and was entered using anonymous codes. Patients name was kept confidential. Data was analyzed through SPSS version 22.0. Master file of the data were only accessible to primary researcher and is kept in password protected files. Numerical variables i.e. age, gestational age, β-HCG level and size of gestational sac have been presented by mean ±SD. Pearson correlation coefficient r has been determined for β-HCG level and size of gestational sac on TVS taking $p \leq 0.05$ as significant. Data has been stratified for age, gestational age, site of ectopic pregnancy and presence of fatal cardiac activity. Post-stratification Pearson correlation coefficient r has been determined for β-HCG level and size of gestational sac on TVS for each stratum taking $p \leq 0.05$ as significant.

RESULTS

The age of the patients ranged from 20 years to 40 years with a mean of 29.3±6.1 years while the gestational age ranged from 2 weeks to 6 weeks with a mean of 5.1±1.1 weeks. It was adnexal in 91 (91.0%) cases and non-adnexal in 9 (9.0%) cases. Fetal cardiac activity was detected in 5 (5.0%) cases as shown in Table **1**. Serum βhCG level ranged from 1647 mIU/mL to 18378 mIU/mL with a mean of 7968.4±4523.7 mIU/mL while the size of gestational sac on TVS ranged from 17 mm^3 to 45 mm^3 with a mean of 36.40±7.86 mm^3. There was significant positive correlation between serum βhCG and size of gestational sac on TVS (r=0.659; p- value<0.001) as shown in Table **2**.

Similar positive correlation was observed across various subgroups of patients based on age, gestational age, site of ectopic pregnancy and fetal cardiac activity status as shown in Table **3**.

Table 1. Demographic Characteristics of Study Sample.

Characteristics	Participants n=100
Age (years)	29.3±6.1
20-29 years	55 (55.0%)
30-40 years	45 (45.0%)
Gestational Age (weeks)	5.1±1.1
<5 weeks	22 (22.0%)
≥5 weeks	
Site of Ectopic Pregnancy	78 (78.0%)
Adnexal	91 (91.0%)
Non-Adnexal	9 (9.0%)
Fetal Cardiac Activity	
Yes	5 (5.0%)
No	95 (95.0%)

Table 2. Means of Serum βhCG (mIU/mL) and Size of Fetal Gestational Sac (mm^3) and Correlation between the Two. n=100.

	mean±sd	**Pearson Correlation (r)**	**P-value**
Serum βhCG (mIU/mL)	7968.4±4523.7	0.659	<0.001*
Size of Gestational Sac (mm^3)	36.40±7.86		

* P-value is significant ≤0.05.

Table 3. Correlation between Means of Serum βhCG (mIU/mL) and Size of Fetal Gestational Sac (mm^3) across various Subgroups. n=100.

Subgroups	**n**	**Size of Gestation Sac (mm^3)**	**Serum βhCG (mIU/mL)**	**Pearson Correlation (r)**	**p-value**
Age					
20-29 years	55	35.24±8.33	7508.1±4592.4	0.653	<0.001*
30-40 years	45	37.82±7.07	8530.9±4424.0	0.657	<0.001*
Gestational Age					
<5 weeks	22	24.68±5.53	4516.6±1786.2	0.654	0.001*
≥5 weeks	78	39.71±4.55	8941.9±4590.9	0.648	<0.001*
Site					
Adnexal	91	36.90±7.60	8088.4±4587.3	0.662	<0.001*
Non- Adnexal	9	31.33±9.12	6754.6±3832.0	0.652	0.057
Cardiac Activity					
Yes	5	38.80±4.76	7025.4±3565.8	0.638	0.247
No	95	36.27±7.98	8017.9±4578.4	0.666	<0.001*

* P-value is significant ≤0.05.

DISCUSSION

Although several risk factors have been discovered, it is still unclear what causes ectopic pregnancies. During first trimester, ectopic pregnancy is the most common life-threatening condition. Outcome of ectopic pregnancy may be variable; it may resolve spontaneously, may result in life threatening hemorrhages or may end up with rupture of fallopian tube. Most of the complications of ectopic implantations occur during early pregnancy when product of conception is non-viable [11]. Due to typical symptomatology of lower abdominal pain and bleeding per vagina, the condition is picked up early. However, at time the diagnosis of ectopic pregnancy may not be that straightforward and required extensive workup [11]. Ectopic pregnancy may be managed successfully by both non invasive and invasive procedures depending on bleeding severity, gestational sac size and size of the fetus. In emergency situation, ultrasonography may help in early diagnosis [12].

However, in challenging diagnostic cases a number of invasive and non-invasive methods may be used with each having its advantages and disadvantages. Recent research is focusing on methods which are accurate, cost effective and which may decrease the false positive rates. Consequently, a lot of research projects are aiming to create biomarkers that would allow for a conclusive diagnosis. Recent studies claimed that serum βhCG level is not only diagnostic but also correlates positively with the size of sac and can be used in management planning of these women. However, the available evidence was limited and contained controversy whereas such locally-published information did not exist, making the current investigation necessary [11, 13, 14]. The purpose of this research was to examine the relationship between β-HCG levels and the size of the gestational sac in women with ectopic pregnancies who presented to a university hospital.

Patients' mean ages were 29.36.1 years, and their mean weeks of gestation were 5.11.1. Similar results were found by Lal *et al.* among women presenting with ectopic pregnancy at Jinnah Postgraduate Medical Center, Karachi (mean age: 29.23.2 years) [15]. Women presenting to the Pakistan Institute of Medical Sciences in Islamabad with an ectopic pregnancy had a mean age of 28.84.8 years, as reported by Mahboob *et al.* [16]. Similar mean age of 30.2±4.3 years and 28.7±3.3 years has been reported by Sudha *et al*. in India and Shrestha et al. in Nepal respectively [17, 18]. Park *et al.* reported comparable mean age of 30.6±4.1 years in Korean women with ectopic pregnancy while Zhang *et al.* observed it to be 30.6±3.9 years in China [19, 20]. Bhattacharya *et al.* observed it to be 27.8±5.7 years in Scotland while Katsikis *et al.* reported it to be 28.1±6.3 years in Greece [21, 22]. Al-Turki *et al.* and Goksedef *et al.* reported similar mean age of 28.9±5.6 years and 29.6±5.6 years in Saudi and Turkish women with ectopic pregnancy respectively [23, 24]. Katsikis *et al.* reported similar mean gestational age of 5.8.±0.9 weeks among women presenting with ectopic pregnancy in Greece while Goksedef *et al.* observed it to be 6.4±1.2 weeks in Turkey [22, 24].

In the present study, ectopic pregnancy was adnexal in 91 (91.0%) cases and non-adnexal in 9 (9.0%) cases. Fetal cardiac activity was detected in 5 (5.0%) cases. Our observation also is in line with that of Park *et al.* who reported adnexal and non-adnexal ectopic pregnancy in 91.5% and 8.5% cases respectively in Korea [19]. A comparable frequency of adnexal (91.7%) and non-adnexal (8.3%) EP has also been reported by Soren *et al.* in Indian women [25]. Saeed *et al.* observed similar distribution of adnexal (93.6%) and non-adnexal (6.4%) EP in women presenting at Dallah Hospital Riyadh. They observed fetal cardiac activity in 4.4% cases in line with the present study [11].

We observed that the mean serum βhCG level was 7968.4±4523.7 mIU/mL while the mean size of gestational sac was 36.40±7.86 mm3 on TVS. Our observation is in line with that of Katsikis *et al.* (8680.9±8821.6 mIU/mL) and Goksedef *et al.* (8735.3±11317.8 mIU/ml) who observed similar mean serum βhCG level among women presenting with EP while Arslan *et al.* (44.1±3.1 mm^3) in Turkey and Mahboob *et al.* (33.5±1.2 mm^3) in Pakistan reported similar mean size of gestational sac on TVS among such women [16, 22, 24, 27].

It was observed that there was significantly strong positive correlation between serum βhCG and size of gestational sac on TVS (r=0.66; p-value<0.001). Similar positive correlation was observed across various subgroups of patients based on age, gestational age, site of ectopic pregnancy and fetal cardiac activity status. Our observation is in line with that of Bree *et al.* who observed similar significantly strong positive correlation between serum βhCG and size of gestational sac on TVS (r=0.82; p-value<0.0001) in American women with ectopic pregnancy [13]. Our results are also comparable to those of Saeed *et al.* who also reported significant positive correlation between serum βhCG and size of gestational sac on TVS (r=0.25; p value<0.0001) in KSA [11]. Gamzu *et al.* reported insignificant correlation however, (r=0.17; p-value>0.05) in Israel [14].

This research is the first of its sort among the local community, and it supplements the few previous literature on the subject. Regardless of patient age, gestational age, site of ectopic pregnancy, or foetal cardiac activity status, a positive correlation was found between serum βhCG and TVS-measured gestational sac size in the current study (r=0.66; p0.001), suggesting a future role for serum βhCG in the risk stratification and management planning of women presenting with ectopic pregnancy.

Our inability to determine whether or not blood βhCG levels correspond with whether or not an ectopic pregnancy has ruptured is a limitation of the current research that might have helped inform future care strategies. Future research should absolutely include such a study.

CONCLUSION

In the present study, there was significantly strong positive correlation between serum βhCG and size of gestational sac on TVS (r=0.659; p- value<0.001) regardless of patient's age, gestational age, site of ectopic pregnancy and fetal cardiac activity status which advocates probable role of serum βhCG level in risk stratification and management planning of women presenting with ectopic pregnancy in future obstetric practice.

AUTHORS' CONTRIBUTION

Sara Malik: Data collection, Data analysis and Result compilation.

Sobia Nawaz: Supervised the whole study.

Masooda Rasheed: Data collection and analysis.

Iqra Nadeem: Data collection and study design.

Sajid Ali Shah: Data analysis.

Falak Nigar: Diagnosis confirmation.

CONFLICT OF INTEREST

Declared none.

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