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Original Research Article

Serum creatine kinase in ectopic pregnancy and its association with tubal rupture: a hospital-based case control study

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ABSTRACT

Background: Ectopic pregnancy (EP) remains an important cause of morbidity in pregnancy and diagnosis may be difficult when clinical findings and ultrasonography are inconclusive. This study evaluated serum creatine kinase (CK) in EP and its relationship with tubal rupture.
Methods: This hospital-based case-control study included 50 women with EP and 50 women with confirmed intrauterine pregnancy (IUP), all at ≤14 weeks of gestation, at Pannadhaya Rajkiya Mahila Chikitsalaya, RNT Medical College, Udaipur. Clinical, risk-factor and ultrasonographic data were recorded and serum CK and β-hCG were measured. Continuous variables were compared using the independent-samples t-test and categorical variables using chi-square/Fisher's exact test, as appropriate.
Results: Mean serum CK was significantly higher in EP than in IUP (112.4±24.6 vs 54.8±16.2 IU/l; p<0.001). CK >100 IU/L occurred in 76% of cases versus 12% of controls. Among EP cases, 32 (64%) were ruptured and 18 (36%) were unruptured. Mean CK was higher in ruptured than unruptured EP (130±18 vs 95±15 IU/l; p<0.001). Mean β-hCG was lower in ruptured than unruptured EP (2800±700 vs 3500±900 mIU/ml; p<0.01). Pelvic inflammatory disease was associated with EP (OR 3.63; p=0.03).
Conclusions: Serum CK was significantly elevated in EP and was higher in ruptured disease. CK may provide adjunctive information regarding ectopic pregnancy and tubal injury, but should be interpreted with clinical assessment, ultrasonography and β-hCG rather than used as a standalone diagnostic test.

Keywords: Ectopic pregnancy, Creatine kinase, Tubal rupture, β-Hcg, Biomarker, Case-control study

INTRODUCTION

Ectopic pregnancy is implantation of a fertilized ovum outside the uterine cavity and remains an important cause of morbidity and mortality during early pregnancy. Most ectopic pregnancies occur in the fallopian tube and delayed diagnosis may result in tubal rupture, hemoperitoneum and hemodynamic instability.[1-3] Clinical presentation may be nonspecific, with abdominal pain and vaginal bleeding occurring in many early-pregnancy conditions. Transvaginal ultrasonography and serial serum β-hCG remain the principal diagnostic tools, but diagnostic uncertainty persists in very early pregnancy and pregnancy of unknown location.[2,4]

Creatine kinase is an intracellular enzyme involved in cellular energy metabolism. Tubal trophoblastic invasion and tissue injury provide a biological rationale for investigating maternal CK as an adjunctive biomarker. Earlier studies have reported higher CK concentrations in ectopic pregnancy, although its diagnostic performance has not been consistent.[5-10]The potential relationship between CK and tubal rupture is clinically relevant because more extensive tubal muscular injury may result in greater enzyme release. The present study therefore

evaluated serum CK in women with ectopic pregnancy compared with women with intrauterine pregnancy and assessed its relationship with rupture and selected clinical characteristics.[9,11]

METHODS

Study design and setting

This was a hospital-based case-control study conducted in the Department of Obstetrics and Gynaecology, Pannadhaya Rajkiya Mahila Chikitsalaya, RNT Medical College, Udaipur, Rajasthan. The thesis states that the study was conducted after Institutional Ethics Committee approval and written informed consent.

Study population

Women with early pregnancy (≤14 weeks) attending outpatient or emergency services were eligible. Cases were women diagnosed with ectopic pregnancy; controls were women with confirmed intrauterine pregnancy and comparable gestational age. 50 cases and 50 controls were included.

Eligibility

Cases were women aged 18-45 years, pregnancy ≤14 weeks, presenting with clinical features such as amenorrhoea, abdominal pain or vaginal bleeding, with ectopic pregnancy confirmed on ultrasonography. Controls were women aged 18-45 years, pregnancy ≤14 weeks, confirmed intrauterine pregnancy on ultrasonography and comparable gestational age. Written informed consent was required. Women with suspected/confirmed heterotopic pregnancy and those with medical conditions likely to elevate CK independently, including major trauma, chest pain, neurological disease or recent multiple intramuscular injections, were excluded.

Sampling and sample size

Convenient sampling was used for cases and controls. The thesis reports a sample-size calculation for comparison of two means, with an expected difference of 30 IU/L, 95% confidence level and 80% power; 39 participants per group were required. After allowing 10% attrition, 43 per group were required and the final sample was rounded to 50 cases and 50 controls.

Data collection

Demographic and obstetric characteristics, period of amenorrhoea, symptoms, examination findings, risk factors, ultrasonographic findings, treatment and outcomes were recorded on a structured proforma. Serum CK and β-hCG were measured according to the study protocol. Ectopic pregnancy was diagnosed based on ultrasonographic assessment in conjunction with the clinical findings. Patients were managed according to institutional protocols using expectant, medical or surgical treatment.

Statistical analysis

Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics for Windows, version 26.0. Continuous variables were expressed as mean±standard deviation and categorical variables as frequencies and percentages. Normality was assessed using the Shapiro–Wilk test. Continuous variables were compared using the independent-samples t-test and categorical variables using chi-square or Fisher's exact test, as appropriate. Odds ratios with 95% confidence intervals were calculated for selected risk factors. A p value <0.05 was considered statistically significant.

RESULTS

A total of 100 participants were included, comprising 50 ectopic pregnancy cases and 50 intrauterine pregnancy controls. Baseline demographic characteristics were broadly comparable between the groups.

Table 1: Baseline characteristics of study participants.

Characteristic	EP (n=50)	IUP (n=50)
Age, mean±SD (years)	28.9±5.4	29.6±5.1
Age 25-30 years, N (%)	18 (36)	20 (40)
Rural residence, N (%)	32 (64)	30 (60)
Literate, N (%)	48 (96)	49 (98)
Primigravida, N (%)	12 (24)	14 (28)
Multigravida, N (%)	38 (76)	36 (72)

EP, ectopic pregnancy; IUP, intrauterine pregnancy; SD, standard deviation.

Among the assessed risk factors, pelvic inflammatory disease was significantly associated with ectopic pregnancy (OR 3.63; p=0.03); other evaluated factors were not statistically significant.

Table 2: Risk factors associated with ectopic pregnancy.

Risk factor	EP N (%)	IUP N (%)	OR	P value
Pelvic inflammatory disease	12 (24)	4 (8)	3.63	0.03
Previous caesarean section	10 (20)	6 (12)	1.83	0.28
Previous ectopic pregnancy	3 (6)	1 (2)	3.13	0.31
Contraceptive failure	8 (16)	2 (4)	4.57	0.092

Continued.

Risk factor	EP N (%)	IUP N (%)	OR	P value
Infertility history	3 (6)	1 (2)	3.13	0.617
Previous tubal surgery	3 (6)	0	—	0.242

OR, odds ratio; EP, ectopic pregnancy; IUP, intrauterine pregnancy.

Abdominal pain and bleeding per vaginum were the predominant presenting symptoms. Abdominal tenderness, cervical motion tenderness, fornicial mass and haemodynamic instability were more frequent among cases; ultrasonography showed an empty uterus, adnexal mass, free pelvic fluid and tubal ring sign in substantial proportions.

Table 3: Key clinical and ultrasonographic findings at presentation.

Finding	EP N (%)	IUP N (%)	P value
Abdominal pain	46 (92)	8 (16)	<0.001
Vaginal bleeding	22 (44)	6 (12)	0.001
Haemodynamic instability	18 (36)	0	0.01
Empty uterus on USG	40 (80)	0	<0.001
Adnexal mass	30 (60)	0	<0.001

USG, ultrasonography; EP, ectopic pregnancy; IUP, intrauterine pregnancy.

Serum CK was significantly higher in ectopic pregnancy than in intrauterine pregnancy (112.4±24.6 vs 54.8±16.2 IU/L; p<0.001), with CK >100 IU/L observed in 76% versus 12%, respectively.

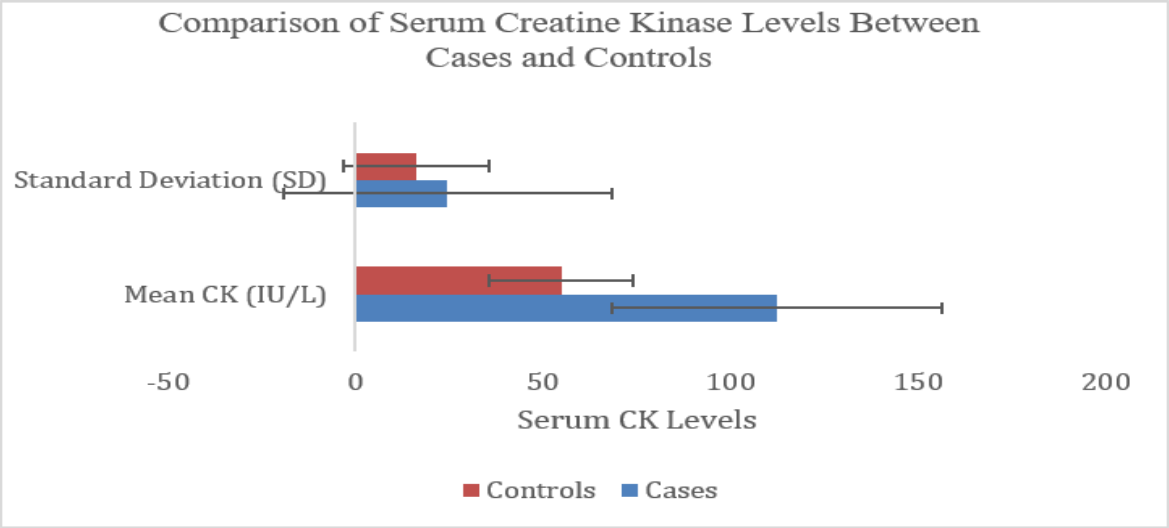

Figure 1: Mean serum creatine kinase levels in ectopic pregnancy cases and intrauterine pregnancy controls. Values are presented as mean+/- SD; p<0.001.

Among ectopic pregnancies, 32 (64%) were ruptured and 18 (36%) were unruptured. Mean CK was significantly higher in ruptured than unruptured ectopic pregnancy (130±18 vs 95±15 IU/l; p<0.001). Mean β-hCG was significantly lower in ruptured than unruptured ectopic pregnancy (2800±700 vs 3500±900 mIU/ml; p<0.01).

Table 4: Serum creatine kinase and β-hCG findings.

Biomarker / comparison	Finding	p
CK >100 IU/L, EP vs IUP	76% vs 12%	<0.001
Mean CK, EP vs IUP	112.4±24.6 vs 54.8±16.2 IU/	<0.001
Mean CK, ruptured vs unruptured EP	130±18 vs 95±15 IU/l	<0.001
Mean β-hCG, ruptured vs unruptured EP	2800±700 vs 3500±900 mIU/ml	<0.01

CK, creatine kinase; β-hCG, beta-human chorionic gonadotropin; EP, ectopic pregnancy; IUP, intrauterine pregnancy. Continuous values are mean±SD

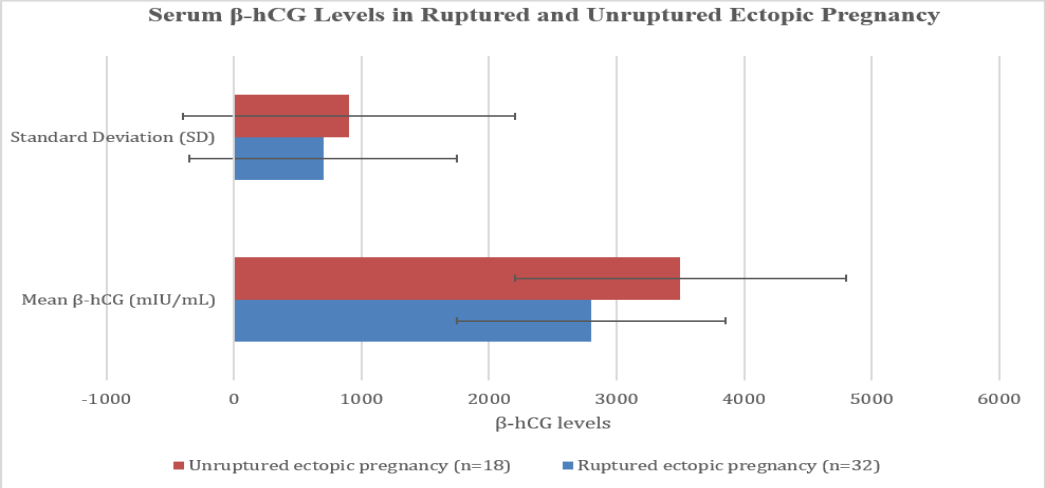

Figure 2: Mean serum β-hCG levels in ruptured and unruptured ectopic pregnancy. Values are presented as mean±SD; p<0.01.

Tubal ectopic pregnancy was the predominant anatomical site (46/50, 92%). Surgical management was most common (68%), followed by medical (24%) and expectant (8%) management. Mean CK was 122±18 IU/l in surgically managed cases, 102±16 IU/l in medically managed cases and 90±12 IU/l in expectantly managed cases.

DISCUSSION

The principal finding was a significant elevation of serum CK in ectopic pregnancy compared with intrauterine pregnancy. The higher CK concentration observed in this study is consistent with earlier reports, although published evidence regarding its diagnostic accuracy has been heterogeneous.[5-10]

CK was also significantly higher in ruptured than unruptured ectopic pregnancy. This finding supports the proposed association between CK release and tubal tissue injury, but does not establish CK as a standalone predictor of rupture.[8,11]

The literature remains insufficient to support CK as an independent diagnostic test because reported sensitivity and specificity vary across studies. Differences in assay methods, timing of sampling, sample size and the proportion of ruptured pregnancies may contribute to the variability.[6,8]

Pelvic inflammatory disease was the only evaluated risk factor significantly associated with ectopic pregnancy in this cohort, consistent with the established biological effect of tubal damage on embryo transport.[12-14]

The clinical and ultrasonographic findings reinforce that biochemical markers should complement, rather than replace, established diagnostic assessment. The lower β-hCG observed in ruptured compared with unruptured ectopic pregnancy should be interpreted cautiously because β-hCG reflects trophoblastic activity and its relationship with rupture is variable.

Strengths include the case-control design, an intrauterine pregnancy control group, systematic clinical and ultrasonographic assessment and evaluation of CK in relation to rupture. Limitations include the small single-centre sample, convenience sampling, single-time-point CK measurement and absence of formal ROC analysis or a validated diagnostic threshold.

Prospective studies with standardized CK measurement, serial sampling and formal diagnostic-accuracy analysis are required to determine whether CK provides clinically meaningful incremental value beyond ultrasonography and β-hCG.

CONCLUSION

Serum CK was significantly elevated in ectopic pregnancy and was higher in ruptured cases. CK may serve as a useful adjunctive biomarker alongside clinical assessment, ultrasonography and β-hCG; however, larger prospective studies are needed to establish its diagnostic and predictive utility.

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