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Serum Creatinine Kinase – An Alternative Diagnostic Marker In Ruptured Tubal Pregnancy In Women Attending A Tertiary Care Hospital In North India

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Abstract

Introduction: Ectopic pregnancy is the pregnancy outside the uterine cavity with incidence of 1% of pregnancy. Current diagnosis in the hemodynamically stable patient is based on the reliability of 2-D ultrasound (USG) and quantitative levels of β-Human Chorionic Gonadotropin (β-hCG). In tubal pregnancy, the zygote penetrates the tubal epithelium and lies next to the muscular layer as the fallopian tube lacks a sub mucosal layer. This invasion into the muscle causes an increase in muscle cell creatinine kinase (CK) in blood.

Aim and objective: To evaluate the role of serum creatinine kinase (CK) as a biochemical marker in the diagnosis of ruptured tubal pregnancy.

Materials and methods: A prospective study was carried out on 30 women with first trimester pregnancy. Group A (n=15) with features suggestive of ruptured tubal pregnancy formed the study group and group B (n=15) with normal intrauterine pregnancy were taken as controls. CK levels in the two groups were compared.

Results: In tubal pregnancy, the serum CK levels (90.1 ± 31.93 IU/L) were higher than those in normal intrauterine pregnancy (46.3 ± 20.15 IU/L).

Conclusion: Serum CK values appear to be a useful marker in the diagnosis of ruptured tubal pregnancy.

Key words: Ruptured ectopic pregnancy, Serum βhCG, Serum creatinine kinase, Biochemical marker.

Introduction

Ectopic pregnancy is the pregnancy outside the uterine cavity with incidence of 1%. Maternal mortality as a result of ectopic pregnancy is about 2/1000 estimated ectopic pregnancies. The most common site of ectopic pregnancy is tubal (98%) whereas other less common sites involved are abdomen, ovary, cervix and caesarean section scar etc**.** In the last few decades, the incidence of ectopic pregnancy has risen all over the world. Early diagnosis of ectopic pregnancy before its rupture reduces morbidity and mortality, and facilitates proper treatment. Around 50%of women are asymptomatic before tubal rupture and do not have an identifiable risk factors for ectopic pregnancy. In women who are symptomatic, no constellation of history and physical findings can confirm or exclude the diagnosis with a high degree of reliability.

Current diagnosis in the hemodynamically stable patient is based on the reliability of 2-D ultrasound (USG) and quantitative levels of β-hCG. When β-hCG is below 1000 mIU/dL, the woman is suspected to have an early unruptured tubal pregnancy. When USG also is inconclusive, an alternative diagnostic marker becomes desirable. In tubal pregnancy, the zygote penetrates the tubal epithelium and lies next to the muscular layer as the fallopian tube lacks a sub mucosal layer. This invasion into the muscle causes an increase in muscle cell CK in blood. The extent of penetration into the muscle will depend upon the site of implantation. Earlier it was reported that an initial maternal serum CK was predictive of tubal pregnancy in first trimester (1).Subsequently, three other studies were able to reproduce these findings (2-4).Another study found an elevated mean CK level but with questionable clinical utility (5).However, few studies reported no elevation in serum CK in tubal pregnancy (6-9).This apparent discrepancy in data led us to investigate the utility of maternal serum CK in the diagnosis of tubal pregnancy. Transvaginal ultrasound and serial β-hCG determination are currently the most common methods used for diagnosis (10-13).Despite the use of high resolution transvaginal sonography and sensitive assays for β-hCG. It is believed that 40 to 50% of cases are initially misdiagnosed (14). Serum β-hCG measurements can distinguish a normal intrauterine pregnancy (IUP) from a non-viable pregnancy but cannot distinguish arrested IUP from ectopic pregnancy (10,12,15-16).In fact, despite the advances in ultrasound a recent series reported that 48-82% of all patients presenting with abdominal pain and/or vaginal bleeding in the first trimester had an indeterminate ultrasound when the quantitative β-hCG was below 1000mIU/dl. This subgroup of patients in particular cannot be accurately evaluated and may benefit most from a serum marker that is rapidly available and useful in the early diagnosis of tubal pregnancy (17).The lack of a sub mucosal layer in the fallopian tube allows the zygote to penetrate the epithelium and the trophoblast usually invades the muscle layer allowing muscle cell products such as creatine kinase to enter the circulation leading to increased serum CK levels during ectopic pregnancy (18).Keeping in view that early diagnosis is critical for reducing maternal mortality and morbidity and the fact that despite the efficacy of serum β-hCG and vaginal ultrasonography, diagnosis can be uncertain below the discriminative zone of β-hCG and comparing the cost of ultrasonography and serial β-hCG which are expensive diagnostic tools in comparison to CK estimation, led us to study the role of serum CK as an early diagnostic marker for ectopic pregnancy. This study was conducted to see the reliability of maternal serum CK in diagnosis of tubal pregnancy and to look for the clinical and laboratory parameters in these patients. Few studies have evaluated the value of CPK isoenzymes and another study estimated CPK MM levels (5).One of the study demonstrated that decreased CPK MB has a relative ratio with the diagnosis of ectopic pregnancy (19).Blastocyst implantation and invasion in the fallopian tube where there is no sub mucosal layer, results in the damage to the muscular layer of the tube and thus an increase of CPK in the maternal serum seen. This mechanism was first thought to be as an early diagnosis of ectopic pregnancy (1).

Materials and Methods

A prospective study was conducted on 15 women attending the emergency ward with features suggestive of tubal pregnancy (Group A). Fifteen women attending the antenatal clinic matched for age and gestation period and having confirmed intrauterine pregnancy were taken as controls (Group B).Women with a history of heart disease, nervous system disease, thyroid disease and

myopathy were excluded from the study. A thorough history was taken and physical examination was done along with routine blood tests and ultrasonography. Blood samples were taken for serum CK estimation before any invasive procedure. Total serum CK was estimated on Beckman Coulter AU680 multichannel automated analyser. The results were tabulated and expressed as mean ± SD.

Statistical Methods

The recorded data was compiled and entered in a spread sheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean ± SD. Student's independent t-test was employed for comparing continuous variables. A P-value of less than 0.05 was considered statistically significant. All P-values were two tailed.

Results

Table 1: Demographic characteristics

Parameter	Cases [n=15]		Controls [n=15]		P-value
	Mean	SD	Mean	SD	
Maternal Age (years)	26.8	5.63	29.1	4.83	0.239
Gestational Age (weeks)	8.2	3.52	10.7	3.79	0.072

In this study the total number of patients was 30 out of which 15 were controls having normal intrauterine pregnancy and 15 patients were cases having ectopic pregnancy. Maternal age of control group was 29.1±4.83 years and that of cases was 26.8±5.63 years. Estimated gestational age among control group was10.7±3.79 weeks and among cases was 8.2±3.52 weeks. There was no significant difference in maternal age and gestational age between the two groups.

Table 2: Showing serum CK levels in cases and controls

Group	N	Mean	SD	Range	P-value
Cases	15	90.1	31.93	62-164	0.0001*
Controls	15	46.3	20.15	22-89	

Statistically Significant Difference (P-value<0.05)

The mean level of serum creatinine kinase in the two groups is shown in Table 2. The mean creatinine kinase in tubal pregnancy patients was 90.1±31.93 IU/L and that in patients with normal intrauterine pregnancy was 46.3±20.15 IU/L. This increase in serum creatinine kinase level was considerably higher in tubal pregnancy patients (p-value .0001).

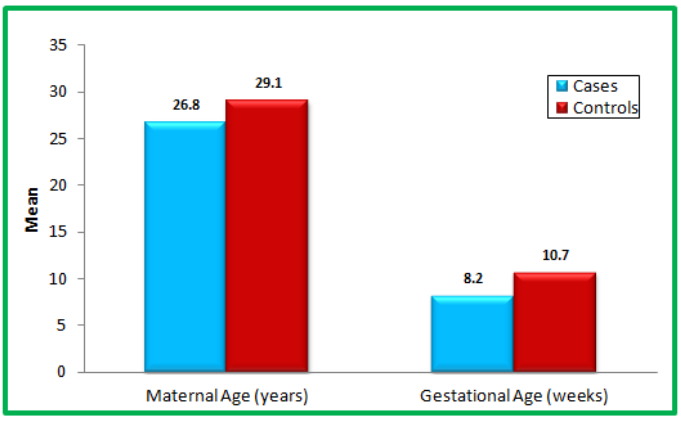

Fig. 1: Demographic characteristics

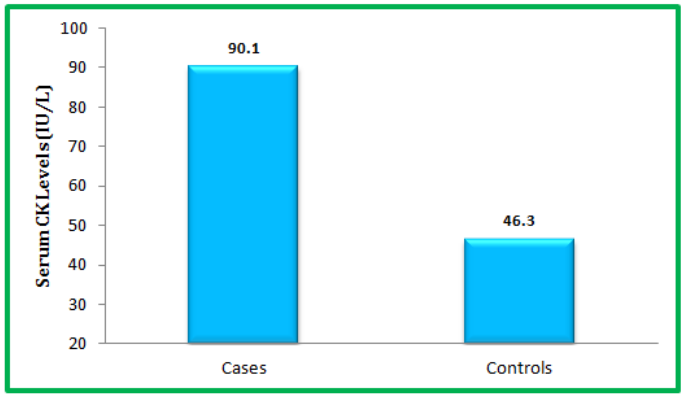

Fig. 2: Showing serum CK levels in cases and controls

Discussion and Conclusion

CK is an intracellular metabolic enzyme which catalyses adenosine triphosphate (ATP) production necessary for the contractile system. A rise in serum CK level is natural in tubal gestation, because the zygote penetrates the tubal

epithelium and lies adjacent to the muscle layer which lacks a sub mucosa. Due to invasion of the muscle layer by trophoblasts, the maternal blood vessels are eroded and blood leaks through the growing trophoblasts and damaged muscle layer giving a rise in muscle cell products like CK. In our study a history of amenorrhea was present in 95%of the cases while cervical movement tenderness and fullness in the posterior fornix were present in 70% and 78% respectively. Hence in cases where the clinical features are misleading and ultrasound is non-conclusive the need for an inexpensive biochemical marker like CK for diagnosis becomes important. We had a mean CK value of 90.1 ± 31.93 IU/L in tubal pregnancy. This was much higher than 46.3 ± 20.15IU/Lin uterine pregnancy (P 0.0001).We often miss the diagnosis of early unruptured ectopic pregnancy as most of us do not advocate the use of ultrasonography as early as 4 weeks post-conception. In our series all the women with ruptured tubal pregnancy had a significant tubal damage and raised values of CK. Thus CK seems to be useful in diagnosing ruptured tubal pregnancy. It is relatively inexpensive when compared to the cost of repeated estimations of βhCG and serum progesterone along with USG. However the study needs to be further validated with large number of cases.

Conflict of interest

It is certified that there was not any conflict of interest.

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