



Reliability of Maternal Serum Creatinine Phosphokinase (CPK) in The Diagnosis of Ectopic Pregnancy

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Abstract

The present study was done to investigate the reliability of maternal serum Creatinine Phosphokinase (CPK) in the diagnosis of ectopic pregnancy. 100 consecutive women with documented tubal pregnancies (Group A) and 50 women with normal intra-uterine pregnancy (Group B) were prospectively studied. Women matched for age, gestational age and parity were included in both groups. Serum CPK levels of both groups were analyzed and plotted. The mean CPK levels in the study group (103 ± 50.3 IU/L) were significantly higher than the mean CPK levels of control group (52.4 ± 10.9 IU/L). The mean CPK levels in the study group showed gradual increment with increase in the gestational age, unlike the control group. The sensitivity and specificity of serum CPK level at 70 IU/L was 95% and 98% respectively. The positive predictive value was 99% and the negative predictive value 90.7% for the diagnosis of tubal pregnancy. Hence, serum CPK levels are significantly higher in women with tubal pregnancy that may or may not have ruptured and are reliable in the diagnosis of a tubal pregnancy.

Key Words

Tubal pregnancy, Creatinine Phosphokinase

Introduction

Based on the histology of the fallopian tube Lavie *et al* (1) put forth a hypothesis, backed by a study, that consequent to early smooth muscle destruction in tubal pregnancy the maternal serum creatinine phosphokinase (CPK) levels should be higher in comparison to those having normal intra-uterine pregnancy. Realizing the impact of such a marker more studies were carried out by many authors to test the hypothesis. Where some authors had similar results (2–7) and supported the hypothesis, others (8–19), based on their results did question and disagree with the diagnostic ability of maternal serum creatine phosphate levels in diagnosing an ectopic pregnancy.

Thus, in view of the conflicting claims by various studies prompted us to evaluate the reliability of maternal serum CPK levels to detect a tubal pregnancy.

Material and Methods

A one year prospective study was conducted at Postgraduate Department of Obstetrics and Gynecology, Lalla Ded Hospital, Government Medical College, Srinagar, Kashmir, in which consecutive patients (Group A; $n = 100$) of documented tubal pregnancy were studied as cases. 50 patients attending the antenatal clinic of the same hospital in the same period, who matched for age, parity and gestational period were taken as controls (Group B; $n = 50$). Since most of the women do not register for antenatal care when they are just overdue, thus a smaller group of controls matching gestational age, maternal age and parity attending the antenatal OPD, (minimally acceptable for statistical analysis) was obtained. Women with history of heart disease, nervous system disease, thyroid disease, renal disease, myopathy, recent trauma and/or recent history of multiple intra-muscular injections were excluded from the study. At

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the time of registration a thorough history was taken and a meticulous physical examination was done. A venous blood sample was collected for serum Creatinine Phosphokinase (CPK) levels followed by routine investigations and ultrasonography (USG) of abdomen, transvaginal ultrasound, laparoscopy and/ or laparotomy where appropriate. CPK levels were determined by Kinetic UV Method-NAC Activated.

Statistical Analysis

Data collected was compiled and analyzed using Microsoft Office Excel 2007 software and Unpaired Students “t” test.

Results

The study group (group A; n=100) comprising of tubal pregnancies were found to have significantly elevated levels of serum creatinine phosphate with mean of 103.3 ± 53.0 IU/L (range 36 – 426 IU/L) in comparison to 52.4 ± 109.0 IU/L (range 34.2 – 86.0 IU/L) in case of Group B as is documented in (Table 1).

Group A was subdivided into two groups ruptured tubal pregnancy (Group A1; n=48), unruptured tubal pregnancy (Group A2; n=52) based on the finding whether the tubal pregnancy was ruptured or not (Table 2) and here again a significant rise of serum CPK levels was documented, with women having ruptured tubal pregnancy.

One patient of unruptured tubal pregnancy was found to have minimal ascites that proved to be of tubercular origin, which could probably be the cause of markedly increased serum CPK levels (426 IU/L) in her. Similarly one patient with bilateral ruptured tubal pregnancy had high serum CPK levels (384 IU/L).

Table 3 depicts the variation of CPK levels with respect to the gestational age in the cases and the control group documenting a gradual increment in levels of serum CPK with increase in gestational age. A similar increment, however, is not noted in the control group.

When all serum creatinine phosphate levels were plotted in the form of scatter diagram in three groups i.e., Ruptured tubal pregnancy (Group A1; n=48), unruptured tubal pregnancy (Group A2; n=52) and normal intra-uterine (Group B; n = 50) the standard deviation and the mean values indicate the significant rise of serum CPK levels in patients of ruptured and unruptured tubal pregnancies in contrast to the serum CPK levels of women with normal intrauterine pregnancy (Fig-1). The sensitivity and specificity of serum CPK level at 70 IU/L

Table 1. Comparison of Serum CPK Levels in Patients with Ectopic Pregnancy (Group A) & Normal Pregnancy (Group B)

CPK levels (IU/L)	Minimum	Maximum	Mean	SD	Median	Results
Group A	36.0	426.0	103.3	53.0	92.0	t = 6.702
Group B	34.2	86.0	52.4	10.9	50.1	p = 0.000 (significant)

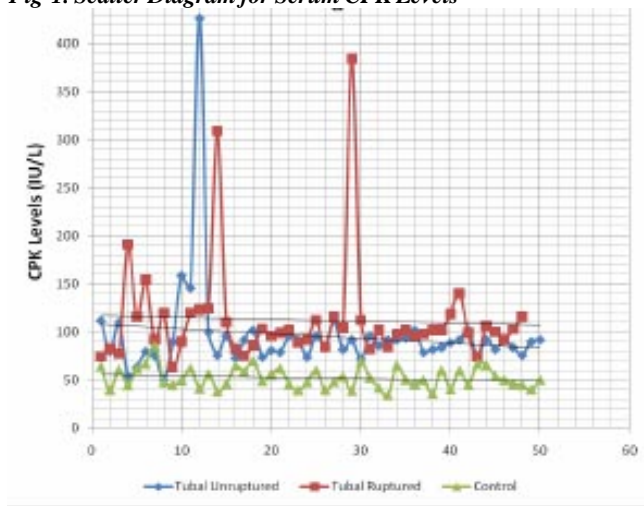
Table 2. Showing Comparison of Serum CPK levels in Patients with Ruptured Ectopic Pregnancy (Group A1) and Patients with Unruptured Ectopic Pregnancy (Group A2)

CPK levels (IU/L)	Minimum	Maximum	Mean	SD	Median	Results
Group A1	63.0	426.0	119.8	70.5	102.5	t = 3.111
Group A2	36.0	384.0	88.6	19.6	89.5	p = 0.002 (significant)

Table 3. Comparison of Serum CPK Levels in Patients with Normal & Ectopic Pregnancy with Respect to the Gestational Age

Gestational age (weeks)	Group	n	CPK levels (IU/L)				
			Minimum	Maximum	Mean	SD	Median
4 – 6	Group A	54	36.0	426.0	100.9	50.1	96.0
	Group B	24	36.2	86.0	54.0	12.2	51.3
7 – 9	Group A	37	63.0	384.0	102.0	53.1	92.0
	Group B	19	34.2	65.4	49.2	7.9	46.2
10 – 12	Group A	9	79.0	309.0	119.8	71.7	100.2
	Group B	7	48.6	67.4	55.8	7.6	53.3

Fig-1. Scatter Diagram for Serum CPK Levels





was 95% and 98% respectively. The positive predictive value was 99% and the negative predictive value 90.7% for the diagnosis of tubal pregnancy.

Discussion

Ectopic pregnancy presents a major health problem for women of child bearing age. It is a result of flaw in the human reproductive physiology that allows the conceptus to implant and mature outside the endometrial cavity, which ultimately ends in death of the fetus.

During the past 25 years, the incidence of ectopic pregnancy has progressively increased while the morbidity and mortality associated with it has decreased, and the treatment options available have progressed from salpingectomy by laparotomy to conservative surgery by laparoscopy and medical therapy. This therapeutic transition from surgical emergency to medical management has been attributed to early diagnosis by the use of sensitive assays for beta-HCG and high definition transabdominal and vaginal ultrasound.

An empty uterus with low serum levels of beta-HCG may be an evidence of tubal pregnancy but may also be consistent with an intra-uterine pregnancy, which is too small to be seen on ultrasound. In attempts to reduce the risk coincident with the time required for serial testing, at a gestational age when ultrasound is indeterminate, a test that distinguishes ectopic from intra-uterine gestation obviously would be of value.

Our results, based on a larger group, clearly points out that serum CPK levels are significantly raised in a tubal pregnancy and that the rise in serum CPK levels documented a gradual increment with increasing gestational age, only to agree with the original hypothesis of Lavie *et al* (1). Also the serum CPK levels were higher in cases of ruptured tubal pregnancies. One important thing that needs to be noted is the high frequency, nearing 50%, of tubal pregnancies reporting when they have already ruptured; thereby pointing out the risk associated with tubal pregnancy and a need, therefore of a marker which is sufficiently accessible and reliable enough to detect tubal pregnancy early. This is more relevant in developing countries where other investigations that have high sensitivity to detect tubal pregnancy like ultrasound (transabdominal / transvaginal) or diagnostic laparoscopy is not available round the clock even in the central hospitals / tertiary centers.

Detection of rising levels of serum CPK is one such marker which has been studied widely for early diagnosis

of ectopic pregnancy. Lavie *et al* (1) studied the role of maternal serum CPK levels as a predictor of tubal pregnancy. In their study of 3 groups of documented tubal pregnancy, spontaneous abortion and normal pregnancy, they found serum CPK levels significantly higher in the tubal pregnancy group than in the other two groups and Chandra *et al* (2) in their study of 20 patients evaluated and endorsed the positive role of serum CPK as a possible marker of tubal pregnancy. Similar results were obtained by Saha *et al* (3) in their comparative study of 20 patients. Develioglu and co-workers (5) conducted a comparative study on 32 cases and their results revealed that serum CPK levels can be taken as an adjuvant tool in ruling out ectopic pregnancy, particularly if it was ruptured ectopic pregnancy. Yet another comparative study by Singh *et al* (6) on 15 patients revealed that CPK levels were higher in tubal pregnancy than normal intra-uterine pregnancy.

Several authors have, however, found conflicting results regarding the reliability of serum CPK levels in the diagnosis of ectopic pregnancy. Qasim *et al* (9) in their study found no significant difference in mean CPK levels in patients with ectopic pregnancy and those with normal intrauterine/abnormal intrauterine pregnancy. Vitoratos *et al* (16) studied 56 patients under 4 groups and found no significant difference in the median CPK levels amongst those with normal intrauterine pregnancy, threatened abortion, symptomatic tubal pregnancy and asymptomatic tubal pregnancy. Plewa *et al* (15) also concluded in his study that although the mean CPK levels are higher amongst the patients of ectopic pregnancy than those with normal intrauterine or threatened abortion, a significant overlap in serum CPK levels makes this marker unreliable for detecting ectopic pregnancy. Most of these studies, however, are based on smaller study groups.

Conclusion

The present study suggest that maternal CPK levels are significantly higher in women with tubal pregnancy and are reliable in the diagnosis of a tubal pregnancy. Hence, it may serve as important adjuvant in diagnosing ectopic pregnancy, particularly if it is ruptured ectopic pregnancy. Early diagnosis followed by prompt and appropriate management would definitely reduce mortality and morbidity associated with the condition thereby also help preserving fertility by adoption of lesser invasive management protocols.



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