The Egyptian Journal of Hospital Medicine (October 2016) Vol. 65, Page 568- 572

Hematological and Biochemical Changes Associated with Ectopic Pregnancy in Jazan Area Saudi Arabia

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ABSTRACT

Objective: Ectopic pregnancy (EP) is an implantation of fertilized ovum outside the intrauterine cavity. Many cases of EP are not associated with a clinical signs at early stages that makes its diagnosis is difficult. The confirmation of EP needs several investigations as ultrasonography and repeated measurements of serum β-hCG levels every 48 hours that make it very expensive and take a long time so, rupture may be occurred that leads to increased maternal morbidity and mortality rates. Thus, the aim of this study was to investigate the alterations of some hematological and biochemical parameters associated with normal and ectopic pregnancy in addition to evaluate their efficacy in early diagnosis of tubal ectopic pregnancy (TEP) among women living in Jazan area, Kingdom of Saudi Arabia.

Subjects and methods: this retrospective study was carried out on 200 women with their ages ranged from 25–37 years old at the Obstetric and Gynecology Department of King Fahd Central Hospital and Sabiya General Hospital during the period between March 2010 and March 2014. The subjects were divided into three groups. Group (1) consists of 69 cases ruptured EP; Group (2) consists of 61 cases non-ruptured by visual examination during surgery and subsequently histopathological examination, where as group (3) consists of 70 women representing the control group having a normal intrauterine pregnancy**.** Hematological and biochemical measurements were done on all groups.

Results: the hematological findings revealed a significant increase in mean platelet volume (MPV), total leukocytic count (WBC) and erythrocyte sedimentation rate (ESR) among TEP patients especially in ruptured cases in comparison with those of normal pregnancy control**. A** significant decrease in hemoglobin (Hb) and packed cell volume (PCV) in TEP cases either ruptured or non-ruptured and a non-significant changes in total erythrocytic count (RBC)**.** The biochemical findings revealed a significant increase in serum creatine kinase (CK) but a significant decrease in serum β-hCG in both ruptured and non-ruptured TEP.

Conclusion: it could be concluded that theWBCs,MPV count and ESR were significantly increased in TEP especially in ruptured cases. The MPV can differentiate between TEP and normal pregnancy but has less clinical significance to differentiate between ruptured and non-ruptured cases. On the other hand, the level of β-hCG is an important indicator of TEP. Moreover, serum CK cannot be used as a tool for diagnosis of TEP but may differentiate between ruptured and non-ruptured cases.

Keywords: Ectopic pregnancy, Hematology, Biochemistry.

INTRODUCTION

Tubal ectopic pregnancy (TEP) is considered one of the most important causes of maternal morbidity and mortality in the first trimester all over the world, particularly when rupture and hemorrhage occur[1]. It is a result of implantation of fertilized ovum outside the intrauterine cavity[2]. The fallopian tube is the most common site for EP, but abdominal and ovarian implantation were also may be occurred[3]. The main cause of EP is still unknown. The incidence of EP among normal women is 1-2% of all pregnancies [4]. The incidence may reach 35- 50% among women with previous salpingitis[5]or pelvic inflammatory disease[6]. The TEP leads to histopathological changes like endothelial damage, inflammation and tissue hypoxia [7].Spontaneous bilateral EP may be recorded [8].

Diagnosis of EP can be done by routine blood tests in addition to ultrasonography when pain or bleeding occurs in early pregnancy[9]. Such tools for diagnosis are still not sufficient to predict ruptured TEP[10]. Serum β-hCGis produced by trophoblasts[11]. Moreover, the level of β-hCG increased when pregnancy occurred and its estimation may help the diagnosis of EP[12]. The increased β-hCG in serum, bile, vitreous, pericardial and cereprospinal fluid may help in diagnosis of EP postmortem [13]. Creatine kinase (CK) is an

Received: 20/9/2016
Accepted: 25/9/2016
DOI : 10.12816/0033765

intracellular enzyme present in brain, striated muscles (cardiac and skeletal) and smooth muscles as it found in fallopian tube [14]. It is reported that serum CK was increased in EP [15]. On the other hand, platelets may play a role in the pathogenesis of EP[16]. **Vagdatli *et al.*[17]** stated that the platelets are associated with endothelial damage. Leukocytosis besides low hemoglobin and hematocrit values may be associated with ruptured tubal EP [18].

The aim of this study was to investigate the alterations of some hematologicaland biochemical parameters associated with normal and ectopic pregnancy in addition to evaluate their efficacy in early diagnosis of TEP among women living in Jazan area, Kingdom of Saudi Arabia.

SUBJECTS AND METHODS

This retrospective study was carried out on 200 women with ages ranged from 25–37 years old at the Obstetric and Gynecology Department of King Fahd Central Hospital and Sabiya General Hospital during the period between March 2010 and March 2014. The study groups were included 130 women with TEP who admitted to the clinic having a positive urine pregnancy test with signs and symptoms suspicious TEP. The main complain was pelvic pain and abnormal vaginal bleeding in some cases. These cases were divided into 3 groups:

- Group (1) consists of 69 cases ruptured EP.
- Group (2) consists of 61 cases non-ruptured by visual examination during surgery and subsequently histo-pathological examination,
- Group (3) consists of 70 women representing the control group having a normal intrauterine pregnancy with similar gestational age as assessed by menstrual dates and confirmed by ultrasound scan.

Collection of samples*:*

Clinical information including age, reproductive history, time without menstruation, time of vaginal bleeding and ultrasound were recorded before collection of samples.

Venous blood samples were obtained by ulnar venous punctures in all women upon admission as soon as the diagnosis was made before any invasive procedure or intramuscular injections. Women with recent trauma, surgery, intramuscular injections or with a history of muscle, heart or liver diseases, hemoglobinopathies, diabetes mellitus, coagulopathies and those with systemic lupus erythematosus were excluded. The blood samples in control group were drawn at the prenatal care clinic. All samples were subjected to hematological and biochemical studies.

Hematological studies:

Complete blood count samples which were drawn into vacutainer tubes containing 0.04 ml of 7.5% K3 salt of EDTA were analyzed within 1 hour after sampling. Hemograms were obtained using an automated Sysmex Kx-21N analyzer according to manufacturer's instructions.

Biochemical studies:

Serum was separated and frozen at -20^{o}C and later used to measure β-hCG level and serum CK. Serum creatine kinase (CK) concentrations were measured by spectrophotometric method on a Technicon DAX System automated analyzer.

A CK kit based on the kinetics of the enzyme (Roche Diagnostics, Germany) and Roche's clinical automated biochemistry analyzer (within-batch variation of 0.5~ 0.6% and between batch variation of .4~1.4%) were used to measure CK concentration.

Serum β-human chorionic gonadotrophin (β-hCG) levels were determined by an automated Chemiluminescent enzyme immunoassay (Immulite 2000 HCG, Diagnostic products Corp., Los Angeles, (A), calibrated against the third International Standard by using a test kit for total β-hCG (Siemens Medical Solutions Diagnostics, USA) and Bayer's ADVIA centaur (within batch variation of 2.1~ 3.9% and between batch variation of 1.7~ 4.3%) were used to measure β-hCG concentration.

Statistical analysis:

Statistical analysis of the obtained data of hematological values and biochemical parameters from all groups was carried out by using analysis of variance (ANOVA) as described by **Victor [19],** followed by multiple range test to indicate the groups which were significantly different at ($P< 0.05$).

RESULTS

In the present investigation,the alterations of some hematological and biochemical parameters associated with normal and ectopic

pregnancy were determined to evaluate their efficacy in early diagnosis of TEP and predict the risk of ruptured tubes.

Hematological findings:

The hematological parameters as shown in table (1) revealed a significant increase in MPV among TEP patients either ruptured or non-ruptured in comparison with those of normal pregnancy control.

The recorded data showed a significant increase in total leukocytic count in ruptured and non- ruptured cases. The leukocytosis provides a clinical importance to differentiate between ruptured and non- ruptured cases as there was a significant difference between the 2 groups.

The present study revealed that there was a significant increase in ESR in TEP patients compared with normal cases of normal pregnancy. There was a significant decrease in Hb and PCV in TEP cases either ruptured or non-ruptured and non-significant changes in total erythrocytic count.

Biochemical findings:

The biochemical parameters as shown in table (2) revealed a significant increase in serum CKspecially in rupturedTEP in comparison with normal pregnancy control. There was a significant decrease in β-hCG in both ruptured and non-ruptured TEP. However, the level of β-hCG in ruptured TEP was significantlyhigher than the non-ruptured.

DISCUSSION

The increase in MPV among TEP patients either ruptured or non-ruptured in comparison with those of normal pregnancy control. This could be attributed to an increase in the function of the platelets. **Jaremo *et al.*[20]** mentioned that there was an increase in the MPV and platelet distribution width to compensate thrombocytopenia associated with normal pregnancy due to dilution state. Such findings are in agreement with that recorded by **Turgut *et al.*[18]**.The obtained data revealed that the mean platelet volume can differentiate between normal pregnancy and TEP but has less clinical significance to differentiate between ruptured and non- ruptured fallopian tubes.

The leukocytosis provides a clinical importance to differentiate between ruptured and non- ruptured cases as there was a significant difference between the 2 groups. The leukocytosis associated with TEP could be attributed to the damage of epithelial lining of fallopian tubes in addition to angiogenesis and the salpingitis, inflammation of fallopian tube. This was supported by **Jia- Rong *et al*.[3]** who studied the pathogenesis of TEP and described similar histopathological changes.

The increase in ESR in TEP patients could be attributed to the severe inflammation of the fallopian tube associated with TEP. On the other hand, the significant decrease in Hb and PCV in TEP cases and non-significant changes in total erythrocytic count either ruptured or non-ruptured are in agreement with **Anna *et al.*[21]**.

The increase in serum CK in ruptured TEP could be attributed to the damage occur in the muscularis of fallopian tube when invaded by trophoblast[22]. On the other hand, the level of β-hCG considered the first and important indicator of EP [23]. The decrease in β-hCG in both ruptured and non-rupured TEP should be considered, as, **Fistouris *et al.*[24]** classified Ep to low and high risk according to the percentage of decline in β-hCG. The increase in the level of β-hCG in ruptured TEP than non-ruptured is in agreement with **Di Marchi *et al.*[25]**. **Qi *et al.*[26]** added that the level of β-hCG depend upon the depth of trophoblast invasion in the wall of the tube**.** Whereas, **Guven *et al.*[4]** reported that the level of β-hCG depend upon the adnexal mass size.

Conclusion, finally it could be concluded that the MPV,WBCs count and ESR were significantly increased in TEP specially in ruptured cases. The mean platelet volume can differentiate between TEP and normal pregnancy but has less clinical significance to differentiate between ruptured and non-ruptured cases. On the other hand, the level of β-hCG is an important indicator of TEP. Moreover,serum CK cannot be used as a tool for diagnosis of EP but may differentiate between ruptured and non-ruptured cases.

REFERENCES

1. Cantwell R, Clutton- Brock T, Cooper G *et al.* (2011): Saving mothers' lives: reviewing maternal deaths to make motherhood safer 2006- 2008. The 18th report of Confidential Enquiries into maternal deaths in the United Kingdom. Br. J. Obstet. Gynaecol., 118 (1) :1- 203.

2. Barnhart KT (2009): Clinical practice. Ectopic pregnancy. N. Engl. J. Med., 361: 379- 387.

3. Jia-Rong Z, Shuang-Di L and Xiao-Ping W (2009): Eutopicorectopic pregnancy: a completion between signals derived from the endometrium and fallopian tube for blastocyst implantation. Placenta, 30: 835- 839.

4. Guven ESG, Dilbaz S, Dilbaz B *et al.* (2006): Serum biochemistry correlates with the size of tubal ectopic pregnancy on sonography. Ultrasound Obstet. Gynecol., 28, 826- 830.

5. Cartwright J, Duncan W, Critchley H and Home A (2009): A serum biomarkers of tubal ectopic pregnancy: Current candidates of future possibilities. Reproduction, 138: 9- 22.

6. Das BB, Ronda J and Trent M (2016): Pelvic inflammatory disease: improving awareness, prevention and treatment. Infect. Drug Resist., 19(9): 191- 197.

7. Hunter R (2002): Tubal ectopic pregnancy: a pathophysiological explanation involving endometeriosis. Hum. Reprod., 17, 1688- 1691.

8. Abi Khalil ED, mufarri SM, Moawad GN and Mufarri IS (2016): Spontaneous bilateral ectopic pregnancy: A case-report. J.Reprod. Med., 61(5-6): 306-308.

9. Sindos M, Togia A, Sergentains T. *et al.* (2009): Ruptured ectopic pregnancy: risk factors for a life- threatening condition. Arch. Gynecol. Obstet., 279: 621- 623.

10. Lai YJ, Lin CH, Hou WC, Hwang KS, Mh YU and Su HY (2016): Pregnancy in non-communicating rudimentary horn of a unicornuate uterus: prerupture diagnosis and management. Taiwan J. Obstet. Gynecol.,55(4): 604-606

11. Mostafa-Gharabaghi P, Abdollahi-Fard S and Mostafa-Gharabaghi M (2011): Is serum creatin kinase a reliable indicator for early diagnosis of ectopic pregnancy? Adv. Environ. Biol., 5(9): 2732- 2735.

12. Derbak A (2016): Ectopic pregnancy in the ultrasound. Case reports. Retrospektive analysis. CeskaGynekol., 81(1): 63-70.

13. Palmiere C, Lesta M, Fanton L, Ventura F, Bonsignore A and Reggiani Bonetti L (2016): Determination of human chorionic gonadotropin in postmortem samples in ectopic pregnancy. J. Forensic Sci., 61(1): 234-7.

14. Soundrarally R, Latha TK, Raghavan S *et al.* (2013): Diagnostic significance of total creatin kinase and its isoform in tubal ectopic pregnancy. J. Obstet. Gynaecol. Res., 39 (12): 1587- 1591.

15. Wazir S, Yasmeen S, Paraveen S *et al.* (2009):Reliability of maternal serum creatinine phosphokinase (CPK) in the diagnosis of ectopic pregnancy. JK Science, 11 (2): 67- 70.

16. Biino G, Portas L, Murgia F *et al.* (2012): A population- based study of an Italian genetic isolate reveals that mean platelet volume is not a risk factor for thrombosis. Thromb. Res., 129; 8-13.

17. Vagdatli E, Gounari E and Lazaridou E (2010): Platelet distribution width: a simple practical and specific marker or activation of coagulation. Hippokratia, 14: 28- 32.

18. Turgut A, Sak ME, Ozler A, Soydinc HE, Karacor T and Gul T (2013): Altration of peripheral blood cells in tubal ectopic pregnancy. Ginekol. Pol. Mar., 84(3):193-196.

19. Victor HD (1976): Statistical and experimental design for behavioral researches. John Wiley and sons Inc. New York, USA.

20. Jaremo P, Lindahl T, Lennmarken C and Forsgren H (2000): The use of platelet density and volume measurements to estimate the severity of pre- eclamsia. Eur. J.Clin.Invest., 30, 1113-1118.

21. Anna K, Pawel B, Krzysztofs S *et al.* (2009): Ectopic pregnancy ruptured- Can it be proved? Ginekol. Pol., 80; 734- 739.

22. Rausch ME and Barnhart KT (2012): Serum biomarkers for detecting ectopic pregnancy. Clin. Obstet. Gynecol., 55(2) 418-423.

23. Greene DN and Grenache DG (2015): Pathology consultation on human chorionic gonadotrophin testing for pregnancy assessment. Am. J.Clin. Pathol.,144 (6): 830-836.

24. Fistouris J, Berqh C and Strandell A (2016): Classification of pregnancies of unknown location according to four different hCG-based protocols. Hum.Reprod., 31

25. DiMarchi JM, Kosasa TS and Hale RW (1989): What is the significance of the human chorionic gonadotropin value in ectopic pregnancy?; Obstet. Gynecol., 74(6): 851-855

26. Qi Y, Wang J, Wang Y, Ai Z. and Teng Y (2012): Peritoneal relative to venous serum biomarker concentrations for diagnosis of ectopic pregnancy. Arch. Gynecol. Obstet. 285(6):1611-1617.

Table (1): Age of the women, gestational age & hematological parameters (mean±SD)

	Ruptured	Non ruptured	Contrl
Age	**25 – 35 years**		
Gestational age	**6 – 10 weeks**		
RBCs (10^6/mm^3)	**3.01±1.3**	**3.37±0.17**	**3.98±1.05**
Hb (g/dl)	**10.2±1.6***	**11.3±1.2***	**12.6±1.7**
PCV (%)	**28.0±3.2***	**30±2.9**	**33±3.3**
MPV (fL)	**9.32±1.8***	**9.60±1.4***	**7.73±1.8**
WBCs (/mm^3)	**15000±01**	**9820±1.9**	**9340±2.5**
ESR (mm)	**36±2.1***	**20±0.5**	**11±2.6**

Mean differences is significant at $P \leq 0.05$

Table (2): Age of the women, gestational age & biochemical parameters (mean±SD)

	Ruptured	Non ruptured	Control
Age	**25 – 35 years**		
Gestational age	**6 – 10 weeks**		
SCK (IU/L)	**104±4.2***	**87.5±51.2**	**60.4±23.8**
β-hCG(mIU/mL)	**2332±1087***	**1425±456***	**4615±981**

Mean differences is significant at $P \leq 0.05$