Correlation between Packed Cell Volume and Concentration of Clotting Factors FI, FVII, and FVIII in Smokers Polycythemic males in Babylon Province

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Abstract

Smoking represents a worldwide problem and affects various body functions. The present study was conducted to evaluate the available concentration of some clotting factors in smokers polycythemic male patients. A total number of subjects was 120, 80 smokers males were affected with polycythemia and the remainders 40 males were healthy and served as a control group. The polycythemic patients were subdivided into two groups according to their ages (first group ranged between 30-40 years old and the second group ranged between 41-50 years old). PCV, clotting factor (FI, FVII and FVIII) were detected. The results of present study indicated that the levels of prothrombin time (PT) and activated partial thromboplastine time (APTT) were significantly increased ($p< 0.05$) in both groups of polycythemia in comparison with control group. Regarding concentration of fibrinogen factor (FI) and serum prothrombin conversion accelerator factor (FVII) were elevated ($P< 0.05$) in both groups and pointed out a positive correlation ($r = 0.437$, $r = 0.378$, respectively) with packed cell volume (PCV) when compared with those of control group. On the other hand, concentration of antihemophilic factor (FVIII) recorded a significant fall ($p< 0.05$) in both tested groups and indicated a low correlation ($r = 0.292$). The possible explanation to the changes mentioned above is based on the fact that confirm smoking is a dangerous material containing different toxic substances that affect the vital organs of the body and induce abnormalities of hemostatic mechanism.
Key words: Polycythemia, clotting factors, smoking

الخلاصة

يمثل التدخين مشكلة عالمية واسعة الانتشار من خلال تأثيراته على مختلف وظائف الجسم. صممت الدراسة الحالية لتقييم تراكيز بعض عوامل التخثر لدى الرجال المدخنين و المصابين بحالة فرط كريات الدم الحمر. شملت الدراسة 120 رجلاً, 80 منهم كانوا مدخنين ومصابين بفرط الكريات الحمر في حين كان العدد المتبقي 40 رجلاً هم اصحاء غير مصابين. قسم الاشخاص المصابين طبقا لأعمارهم الى فئتين عمريتين, الفئة الاولى تراوحت بين 30–40 سنة والفئة الثانية تراوحت بين 41–50 سنة. أظهرت نتائج الدراسة ارتفاعا معنويا ($p< 0.05$) في قيم كل من زمن البروثرومبين PT وزمن الثرومبوبلاستين المفعل جزئيا APTT في كلا الفئتين عند مقارنتها مع الاشخاص الاصحاء. وبخصوص تراكيز عوامل التخثر فقد لوحظ حصول ارتفاع معنوي ($p<0.05$) في قيم كل من الفايبرينوجين (FI) وقيم عامل مسرع تحويل البروثرومبين (FVII) في كلا المجموعتين وقد حققا ارتباطا موجبا مع قيم حجم الخلايا المضغوط (PCV) ($r = 0.437$, $r = 0.376$) على التوالي. في حين لوحظ حصول انخفاض معنوي في قيم العامل المضاد للنزف (FVIII) لدى كلا الفئتين وحقق ارتباطا مع حجم الخلايا المضغوط مقداره ($r = 0.292$). ان التغيرات الموضحة في اعلاه يمكن ان تعزى بصورة رئيسة الى ان للتدخين تأثيرات ضارة على الجسم لاحتوائه على مواد ذات سمية عالية والتي بدورها تؤثر على الاعضاء الحيوية للجسم مؤدية الى حصول اضطرابات وظيفية خاصة في عمليات الاتزان الدموي.
الكلمات المفتاحية: فرط الكريات الحمر, عوامل التخثر, التدخين

Introduction

Polycythemia is considered as a heightening in packed red cell volume resulted from various pathological states and stimulaters that may or may not be related with a rise in red cell mass (RCM) (Pearson and Messinezy, 1996). A cigarette smoker become exposed to a number of toxic substances such as nicotine, oxidative stress, carbon monoxide and various amount of gaseous products (Gitte, 2011). In fact,

tobacco cigarette smoking has been identified as one of the major death causes (Kumar *et al.,* 2009). It is familiar that smokers have higher risk factor for hypertension, cardiovascular events, strock , inflammation, clotting disorder, and respiratory disease (Tiel *et al.,* 2002 ; Abel *et al*., 2005).

Many coagulation protein elements are involved in reaction steps that produce the hemostatic process. Absence in any of the coagulator protein elements can lead to continuous bleeding. (Ogedegbe, 2002). Hemostasis is commonly managed by three essential components particularly, the vascular wall, platelets, and the coagulation factors (Kumar *et al*., 2005). Few studies are available on alteration in hemostasis of smoker humans, especially in plasmatic hemostasis. Some of laboratory indices of hemostasis processes are believed to be affected by smoking. There are several reports showing markers of suppressed fibrinolysis by drop tissue – type plasminogen activator and regulated up plasminogen activator inhibitor – 1 concentration. Moreover, heightened fibrinogen concentration and suppressed amounts of protein C and activated protein C have been explained. These alterations can be returned to endothelial injured and then inflammatory process (Yanbaeva *et al*., 2007; Al-Sweedan *et al*., 2010).

Methods and Materials

Subjects of study:

The present study was carried out throughout the period ranged between October 2014 to August 2015, in blood bank of Babylon and laboratories of college of sciences for women in Babylon university. The total number of subjects was (120) : polycythemic smoking patients for a period at least 5 years ago and healthy men. Eighty (80) men were smokers and affected with polycythemia and those have PCV more than 50%. The remaining number (40) were normal healthy men and non-smokers. The smoker polycythemic males were consequently subdivided according to their ages into two groups (First group was 30-40 years old and the second group was 41-50 years old). All subjects of the study were free from other chronic diseases such as diabetes mellitus, thyroid disorders, cardiovascular disease, and renal disturbance. These data were obtained by questioner. All patients attend to blood bank to perform phlebotomy to normalize PCV. The ages of healthy subjects were ranged between 20-50 years old.

Coagulation factors assay

1- Prothrombin time (PT), partial thromboplastin time (PTT) and fibrinogen concentration were determined according to the procedure of the kits of (BioLabo SA, France).

2- Factor VII, factor FVIII concentrations were determined according to the procedure of the kits of (Elabscience Biotechnology)

Statistical analysis

All values were expressed as means ± stander deviation (S.D). The data has been analyzed by using computer SPSS program. Student′s t-test has been used to examine the differences among different groups and $p< 0.05$ was used as lowest significant limit (Daniel, 1999).

The results

1: Packed cell volume (PCV)

The results of PCV in (table 1) point out a significant elevation ($p< 0.05$) in both tested groups of polycythemia (53.65 ± 2.49, 52.33 ± 2.99 %, respectively), in compare with control group (44.94 ± 1.1 %).

2: Prothrombin time (PT)

The results of PT explained in (table 1) show a significantly increase ($p< 0.05$) in both groups of smokers males affected with polycythemia (15.41± 1.88, 15.23 ± 1.45 second, respectively),), in compare with control group (13.23 ± 0.42 second).

3: Activated partial thromboplastin time (APTT)

There is a significant elevation ($P< 0.05$) in APTT values for two groups of smokers' polycythemia (23.15 ± 1.15, 22.89 ± 1.06 second, respectively) as shown in (table 1),), in compare with control group (20.42 ± 0.66 second).

4: Fibrinogen concentration (FI)

The results of fibrinogen concentration illustrated in (table 1) show a significant increase ($p< 0.05$) in the first and second group of polycythemic smokers (324.88 ± 40.25, 351.74 ± 41.52 mg/L, respectively), in compare with control group (277.4 ± 33.98 mg/L). The results of correlation between values of PCV and FI which have been shown in figure (1) revealed a positive correlation ($r= 0.437$).

Table 1: Means of packed cell volume (PCV %), prothrombin time (PT second), activated partial thromboplastin time (APTT second), fibrinogen concentration (mg/L)) of healthy control group and two groups of smoker males suffering from polycythemia.

Groups / Parameters	Healthy control group n = 40	Smokers' polycythemic groups n = 40	
	20-30 years	(First group) 30-40 years	(Second group) 41-50 years
PCV (%)	44.94 ± 1.1	53.65* ± 2.49	52.33* ± 2.99
PT (second)	13.23 ± 0.42	15.41* ± 1.88	15.23* ± 1.45
PTT (second)	20.42 ± 0.66	23.15* ±1.15	22.89* ± 1.06
Fibrinogen(mg/L)	277.4 ± 33.98	324.88* ± 40.25	351.74* ± 41.52

-Values are mean ± SD

- Means with asterisk * are significantly different at $p < 0.05$

- n = number of males in one group

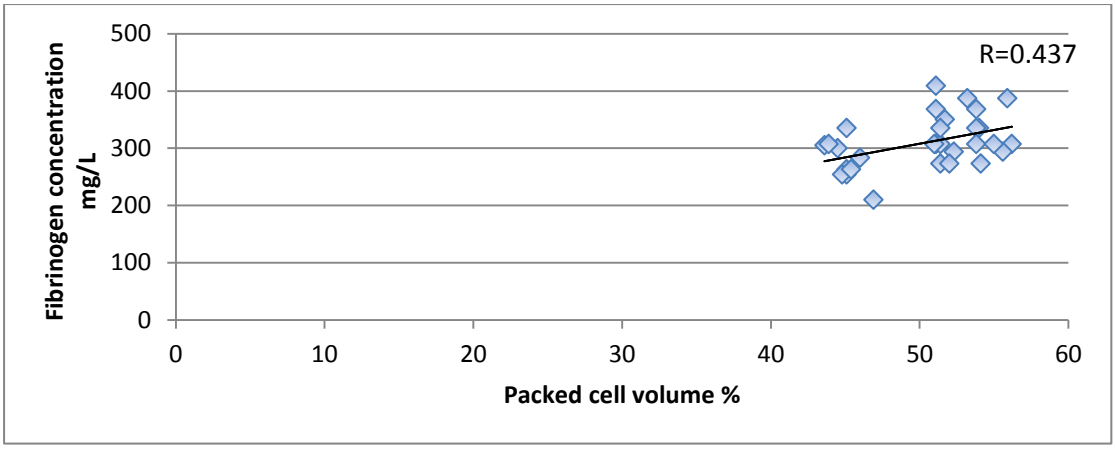

Figure 1: Correlation between fibrinogen concentration (mg/L) and packed cell volume (PCV %) of control group and two groups of polycythemic smokers.

5: Serum prothrombin conversion accelerator (Factor VII) concentration (pg/mL)

The findings of factor VII concentration elucidated in figure (2) indicate a significant increase ($p < 0.05$) in both groups of polycythemic smokers (316.27 ± 155.33, 298.92 ± 112.41 pg/mL, respectively), in compare with control group (197.33 ± 99.89 pg/mL). The results of correlation between PCV values and factor VII indicate a positive correlation ($r = 0.382$) as indicated in figure (3).

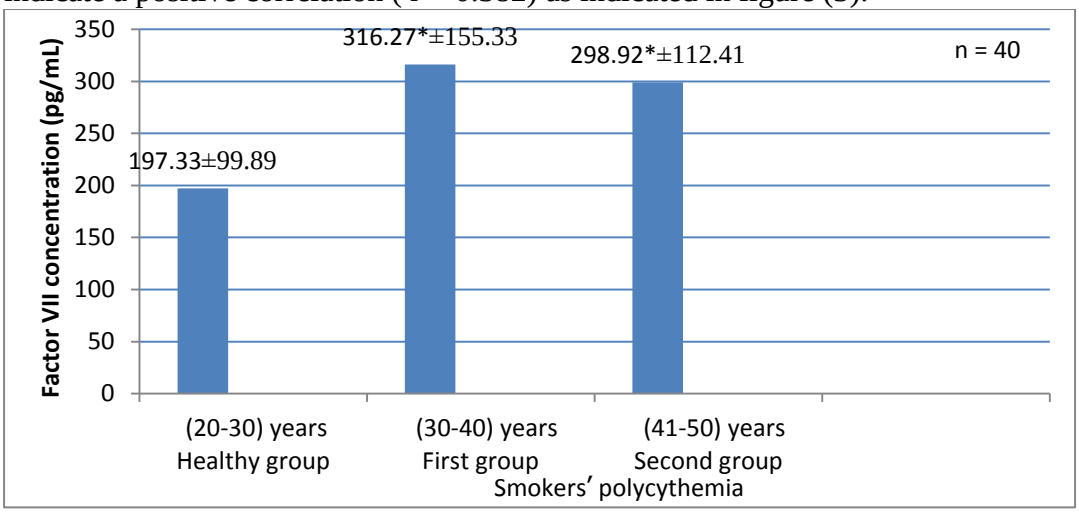

Figure 2: Means of serum prothrombin conversion accelerator factor (Factor VII pg/mL) of healthy group and two groups of smokers males affected with polycythemia.

-Values are mean ± SD

- Means with asterisk * are significantly different at $p < 0.05$
- n= number of males in one group

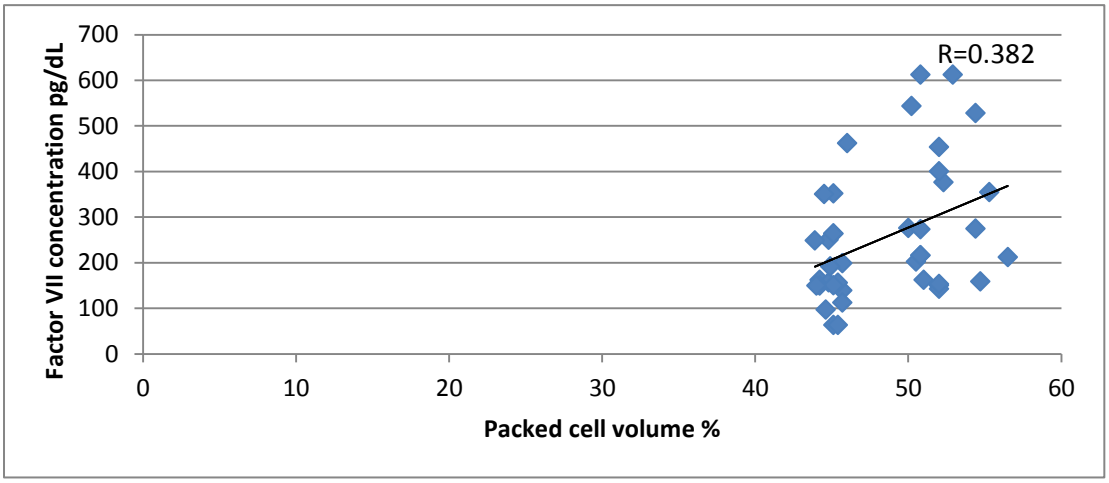

Figure 3: Correlation between serum prothrombin conversion accelerator (Factor VII pg/ml) and packed cell volume (PCV) of control group and two groups of polycythemic smokers.

6: Anti-hemophilic factor (Factor VIII) concentration (pg/ml)

The results of factor VIII concentration in figure (4) have been appeared markedly drop ($p< 0.05$) in two groups of smokers' polycythemia (0.761 ± 1.16, 0.894 ± 2.11 pg/mL, respectively), when compared to that of healthy control group (3.36 ± 4.11 pg/mL). The results of correlation between PCV values and factor VIII concentration show a positive correlation ($r = 0.017$) as described in figure(5).

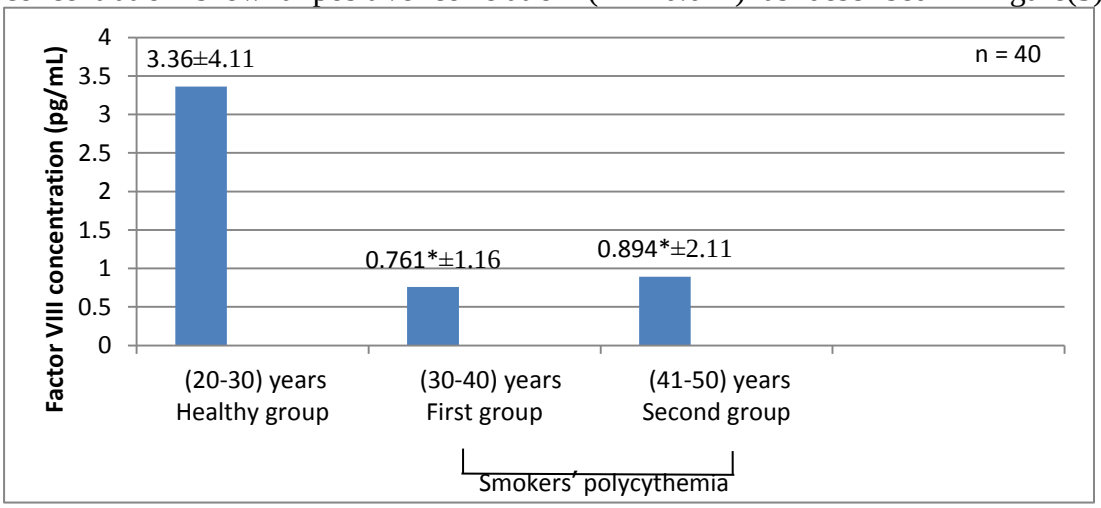

Fig.4: Means of anti-hemohpilic factor (Factor VIII pg/mL) of control group and two groups of polycythemic smokers.

-Values are mean ± SD

-Means with asterisk * are significantly different at $p < 0.05$

- n= number of males in one group

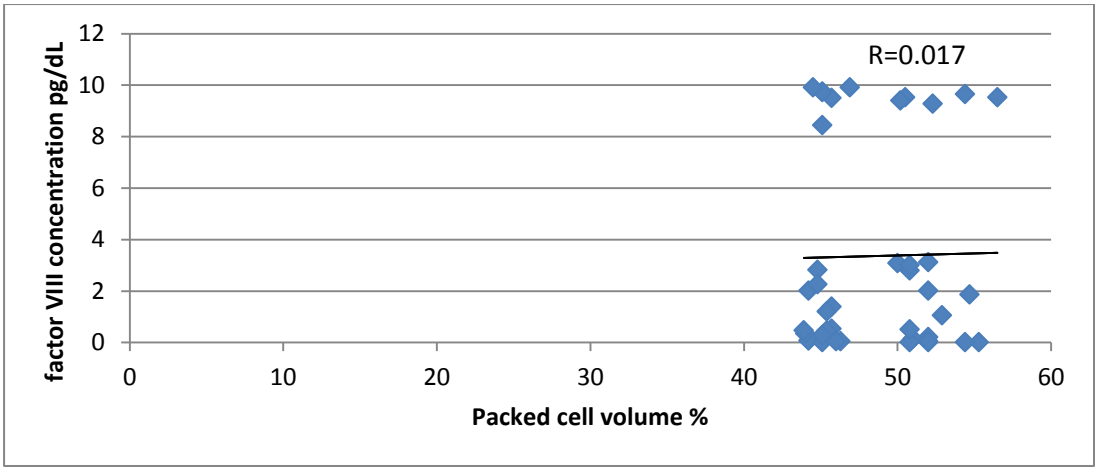

Figure 5: Correlation between anti-hemophilic factor (Factor VIII pg/mL) and packed cell volume (PCV) of control group and two groups of polycythemic smokers.

Discussion

1:Prothrombin time (PT) and activated partial thromboplastin time (APTT) :

The results of present study appear a significantly increase (P< 0.05) for PT and APTT in both groups of polycythemic smokers in compare with those of control group. Previous study showed that hematocrits are more than 55% because of the possibility of longtime of routine coagulation test (PT, aPTT) (Austin *et al*., 2013). Many studies confirmed that samples from subjects with maximum hematocrit (>55%) may result in increasing time of PT and aPTT (Marlar *et al*., 2006 ; Hood and Eby, 2008).

The facts which have been explained previously showed that prolonged smoking triggers hemostatic disorder producing from continuous smoking. Although the persons were generally influenced where those who have smoked for duration about 12 years and above, PT where changed even in those who have smoked for only 2 years. (Ngozi and Ernest, 2014). One can hypothesize that prolonged time of PT and APTT in this study may return to effects of smoking on extrinsic and intrinsic pathways of coagulation, since, it may be either increased concentration and activity of some clotting factors or decreased the activity of other that might implicated in prolongation of PT and APTT. As explained from the data of FVIII, there is a decrease of FVIII that may be implicated in delay of intrinsic pathway.

2: **Fibrinogen factor (FI):**

The results which have been obtained from the present study referred to a significant elevation (P< 0.05) of fibrinogen in two groups of polycythemic smokers when compared with control group. These data agree with the following study, which recognized that fibrinogen concentration are more in smokers than non-smokers, and it had been documented that the progression dangerous of cardiac arrest in heavy smokers might be related with increase fibrinogen concentration through arterial wall deposition and effects on HCT, platelet aggregation and adhesive, blood viscosity and fibrin production, significant marker for increased fibrinogen concentration in the heavy smokers can be observed in the recorded short time seen in the coagulation indicators (Danesh *et al*., 2000 ; Ngozi and Ernest, 2014). In healthy males who were smoking for 5 years or more, further, smoking is related with 22% minimum clot permeability and 35% longer clot lysis compared with never smokers. These observations of smoking-related fibrin changes seem to be estimated largely by

increased fibrinogen and accelerated oxidative stress (OS) (Undas *et al*., 2009). The present results conflict with fact that illustrate fibrinogen protein is especially subjected to oxidation, ≈20% higher than of albumin. So that fibrinogen may also relief a free radicals and impair other proteins from exposure to oxidation. Fibrinogen oxidation subsequently exposure to oxygen, metal, and myeloperoxidase-derived oxidants drop the rate of clot develop (Olinescu and Kummerow, 2001). From the facts mentioned above, one can suggest that smoking induce inflammatory reactions and oxidative stress that acts together to increase production of fibrinogen by hepatocytes.

3:Serum prothrombin conversion accelerators factor (FVII):

The results of present study document a significant increase ($P< 0.05$) of factor VII concentration in both groups of smokers' polycythemia when compared with healthy control group. This study agrees with the previous studies revealed that cigarette smoking is consider one of the main carcinogenic agents because of chemical elements that stimulate the liberation of free radicals (oxidative-stress), drop prostacyclin release causing to clot production, as well as increased production of fibrinogen (FI) and coagulative factor VII (Butkiewicz *et al*., 2006 ; Padmavathi *et al*., 2010). Also, a study of McBride (1992), documented an increased factor VII activity in smokers. It is well known that smoking activates a hypercoagulable state of the blood, but its effect on plaque thrombogenicity is not understood and the researches indicate that tissue factor (TF) plays an essential role in thrombus production after plaque disruption (Toschi *et al*., 1997). Other study indicate that smoking elevates the plasma level of fibrinogen but seems to have lower effect on the level of factor VII (Powell, 1998). The present data were inconsistent with Delgado *et al*. (2015), which confirmed that there was a drop in level of factor VII (included in the activation of extrinsic clotting cascade). The present data may be attributed to the fact that smoking stimulates activity of clotting factor VII and because of tissue damage may increase levels of tissue factor (TF).

4: Anti – hemophilic factor (Factor VIII) :

The results of factor VIII concentration in the present study showed a significant drop ($P< 0.05$) in both polycythemic smoker groups when compared with those of control group. Previous study explained the effect of smoking on the clotting reactions presented that smokers appeared significantly lower levels of factor VIII than never smokers (Wannamethee *et al*., 2005 ; Viel *et al*., 2007). Zabala and Guzzetta, (2015) noticed that secondary erythrocytosis is associated with physiological response purposed to elevation in the whole blood viscosity and decrease in plasma volume leading to a marked deficiencies in numerous coagulation proteins including clotting factors.

Because of FVIII is consider an acute-phase reactant, its plasma levels may be transiently influenced by different status, including inflammation (Reitsma *et al*., 2003). In addition, other researches had explained that the possible effect of inflammation on clotting factors disorder in all smokers and indicated that plasma factor VIII levels did not vary when matched with nonsmokers (Tapson, 2005).

The present data disagree with the previous study that explained the effect of smoking on the coagulation reactions presenting elevated concentration of factor VIII, prothrombin, factor XI, peptide and factor X peptide in smoker people (Miller *et al*., 1998). It is possible to suggest that smoking may influence liver function to synthesize FVIII or because of oxidative stress that initiates deterioration effects on clotting factors indicating a fall in the levels of FVIII.

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