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The Correlation Between serum Uric Acid and Serum Lipids in the Patients with Colorectal Polyps]

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Abstract: *The Incidence of colorectal polyps reported to be associated with serum lipids abnormalities and with high levels of serum uric acid. Thus, we aimed to examine the correlation between serum lipids and serum uric acid in the patients with colorectal polyps. A total of 279 patients with colorectal polyps and 194 free-colorectal polyps'participantsas normal controls were recruited into current study. Blood samples were obtained after fasting of 8-12 hours, and then analyzedbiochemically. Present study revealed that the ratio of individuals with elevated Uric Acid (UA), Triglyceride (TG), Total Cholesterol (TC), and Low-Density Lipoprotein (LDL) levels, and with decreased High-Densitylipoprotein (HDL) levels were significantly higher in the patients with colorectal polyps compared to healthy controls($p<0.05$). Serum UA levels were positively correlated with TG, TC, LDL ($r=0.31, 0.18, 0.2$) respectively, while UA levels were negatively correlated with HDL in the patients with colorectal polyps ($r= -0.21$). In conclusion,abnormalitiesof serum UA and serum lipids may increase the occurrence of the colorectal polyps. Thus, the investigation of serum lipids and UA may represent a promising blood biomarker in evaluation and preventing of colorectal polyps.*
Keywords:*Colorectal Polyps,Mechanism, Risk factors, Serum lipids, Uric Acid*

I. Introduction

Colorectal polyps (CRP) are an abnormal growth of mucosal tissue protruding into the colorectal cavity. Colorectal polyps can be classified into two major types according to the histological characteristics:Neoplastic(adenomatous) and non-neoplastic (hyperplastic, hamartomatous,andinflammatory polyps).

The precise mechanism of the formation of colorectal polyps is not totallyclear. However, the hypothesis of adenoma to carcinoma pathways promotes researchers to focus on the genetic and epigenetic alteration. These alterations were either asoverexpression or inhibition of genetic expression. Using the reverse transcription PCR array method to assess the histone modification gene expression showed a significant overexpression of PAK1, NEK6, AURKA, AURKB, and HDAC1in colorectal polyps tissue, and no significant differences of PAK1, NEK6, AURKA, or AURKB gene expression between colorectal polyps tissue and colorectal cancer tissue[1].A cohort study comprised of 432 participant, 221 patient were diagnosed as colorectal polyps or colorectal cancer and 211 healthy individuals showed a positive correlation between HFE gene mutations and increase the incidence of colorectal polyps and colorectal cancer[2]. Bae et el demonstrated that increased expression of KITENIN and ErbB4 CYT-2 promotes the progression of colorectal adenomas to colorectal cancer after adenomatous polyposis coli (APC) loss[3]. In the other hand , Hibino et al reported that Inhibit expression of miR-148a was more predominant in high-grade adenoma and colorectal cell and tissue than in low-grade adenoma, and it might contribute to adenoma to cancer progression [4].Another study showed thatexpression of keratins 8, 18 and19 which detected in the lesions tissue or in mucosa contiguous to the lesion were depressed in patient with colorectal polyps[5].

Few previousstudies explored the association between serum biomarkers and the occurrence of colorectal polyps.Cristy et alreported that triglyceride levels were significantly related to the prevalence of colorectal polyps and the serum cholesterol levels were higher in colorectal polyp patients than in normal participants[6]. The case-control study based on Chinese population revealed that TC, TG, LDL-C, and Apo-B levels were significantly increased, whereas HDL-C and Apo-A1 levels were decreased in patients with colorectal adenomas comparing to normal individuals[7]. As was reported by Tomizawa et al, UA levels were significantly higher in the old patients with colorectal polyps than those without colorectal polyps[8]. However, the association between serum uric acid and serum lipids in the patients with colorectal polyps remains unclear. Therefore, this study aimedto evaluatethe correlation between serum uric acid levels and serum lipidslevels in the patients with colorectal polyps.

II. Subjects And Methods

2.1. Subjects

The present study was conducted in Northern Jiangsu People's Hospital during the period 2014-03-10-2014-11-20.Total of four hundred and seventy three participants (age range 26 – 85 years) were recruitedinto this study, two hundred and seventy-nine patients with colorectal polyps, of them, 191Patients were men (68.46%) and 81 patients were women (29.03%), and one hundred and ninety four healthy individuals, among them, 92 participants were men (47.42%) and 102 participant were women (52.58%). The participants who previously received lipids or uric acid-lowering treatment, had history of malignanciesor history of inflammatory bowel disease were excluded from this study.All participants were fluent in Chinese, and residents of Yangzhou city –China.

2.2. Blood Biomarkers Measuring And Polyps Detection

Fasting blood samples were collected from each participant, and then sent to the laboratory department for biochemical analysis. Roche/Hitachi 912/Modular analyzer was used to analyze serum TG, TC, HDL, and LDL using enzymatic colorimetric assay, and Roche/Hitachi P/D Modular analyzer was used to analyze serum UA using enzymatic colorimetric assay. According to the diagnostic criteria, Triglyceride (TG) > 1.70mmol/L, Total Cholesterol (TC) > 5.18mmol/L, High Density Lipoprotein (HDL)<1.04mmol/L,Low Density Lipoprotein (LDL) >3.37mmol/L, Uric Acid (UA) >463μmol/L were considered abnormal results. Colorectal polyps were detected during the colonoscopiesprocedures.For histological assessments, the biopsies were fixed and stained with haematoxylin and eosin (H&E). They were then viewed under light microscopy by an experienced pathologist. Reports were obtained, and then the data were statistically analyzed.

2.3. Statistical Analysis

Chi-square analysis was used to compare the categorical variables. Pearson correlation coefficient employed to assess the correlation between UA levels and serum lipids levels inthe patients with colorectalpolyps. Data analysis was performed by using SPSS19.0, *P* value <0.05 considered statistically significant.

III. Results

279 Patients with colorectal polyps and 194 healthy participants as controls were enrolled into this study. Data were expressed as percentages or as mean ± S.D. As shown in (Table1, and 2).Study results demonstrated a significant differences between the ratio of theindividualswith highUA, TG, TC, and LDL levels, and low HDL levels in the patients with colorectal polypsgroup comparing to healthy participants group(*P*<0.05). These results illustrated that the incidence of colorectal polyps may increase with increased serum UA, TG, TC, and LDL levelsand with decreased serum HDL levels.The results also showed that increased serum UA levels were significantly higher in male patients compared to females (*P*= 0.008). The differences of increased TG, TC, and LDL levels or decreased HDL levels in male patients compared to females were insignificant. Additional statistical details demonstrated in (Table 1 and 2).

Pearson correlation coefficientwas used to assess the correlation between UA levels and TG, TC, HDL, and LDL levelsin the patients with colorectal polyps. Our results showed a positive association between TG, TC, and LDL levels and UA levels in the patients with colorectal polyp(*r*= 0.31, 0.18 and 0.2, respectively). In contrast, HDL levels were inversely correlated with the levels of serum UA in the same patients group, *(r*= -0.21), (Table 3). The association between serum UA and TG, and HDLrepresented in (Fig 1 and 2)

IV. Figuresand Tables

Table 1: Serum Lipids and Serum Uric Acid and the Occurrence of Colorectal Polyps

Variables	Cases (n=279)	Controls (n= 194)	χ^2	*P* - value
UA > 463μmol/L	34 (12.19 %)	6 (3.9%)	12.22	<0.05
TG > 1.70mmol/L	108 (38.71 %)	43 (22.16%)	14.41	<0.05
TC > 5.18mmol/L	42 (15.05 %)	9 (4.64%)	12.90	<0.05
HDL < 1.04mmol/L	42 (15.05 %)	13 (6.70%)	7.77	<0.05
LDL > 3.37mmol/L	66 (23.66 %)	19 (9.79%)	14.92	<0.05

UA, Uric Acid ;TG, Triglyceride, TC, Total Cholesterol; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein ; *P*< 0.05 considered significant

Table 2: Association between Patients' Gender and Serum Lipids and Serum Uric Acid

groups	n=2	TG>1.70m	TC>5.18m	HDL<1.04	LDL>3.37m	UA>463

		79	mol/L	mol/L	mmol/L	mol/L	μmol/L
Sex	Male	191	79(41.4)	27(14.1)	29(15.2)	43 (22.5)	30(15.7)
	Female	88	29(33.0)	15(17.0)	13(14.8)	23 (26.1)	4 (4.5)
	χ^2		1.79	0.40	0.01	0.44	7.01
	P		0.18	0.53	0.93	0.51	0.008

UA, Uric Acid ;TG, Triglyceride, TC, Total Cholesterol; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein ; $P< 0.05$ considered significant.

Table 3: Correlation between Uric Acid and Serum Lipids in the Patients with Colorectal Polyps

Variables	$(\bar{X} \pm S.D)$	UA (μmol/L)	n	*r*	*P*
TG (mmol/L)	1.7±.94	334.92 ± 96.02	279	0.31	<0.05
TC (mmol/L)	4.83±1.15	334.92 ± 96.02	279	0.18	<0.05
HDL (mmol/L)	1.26±0.38	334.92 ± 96.02	279	-0.21	<0.05
LDL (mmol/L)	2.78±0.92	334.92 ± 96.02	279	0.2	<0.05

UA, Uric Acid ;TG, Triglyceride, TC, Total Cholesterol; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; *r*, Pearson correlation coefficient ; $P< 0.05$ considered significant.

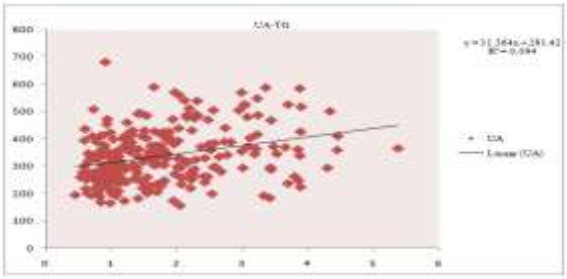

figure 1: scatter diagram of serum UA and serumTG concentration in patients with CRP

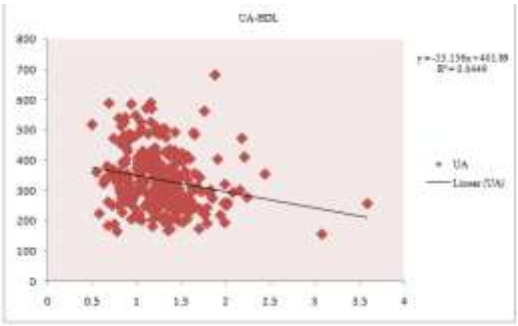

figure 2: scatter diagram of serum UA and serumHDL concentration in patients with CRP

V. Discussion

Whether serum lipids or serum UA cause colorectal polyps still an area of intensive investigations; however, what is well proven is that serum lipids abnormalities were associated with the incidence of colorectal polyps and serum UA levels also reported to be elevated in colorectal polyps patients [6, 8, 9]. Therefore, it is important to investigate the association between UA concentration and serum lipids levels in the patients with colorectal polyps.

Our results revealed that the percentages of the participants with elevated serum TG, TC, and LDL and with decreased serum HDL levels were significantly higher in patientsgroup compared to healthy participants group. These results are in agreement with the most results of the previous studies. The case- control study comprised 320 patients with colorectal polyps and 335 healthy controls reported that serum TG,TC, and LDL- C levels were significantly higher and serum levels of HDL-C were significantly lower in colorectal polyps patients group than those in control group[10]. High levels of TC, TG, and low levels of HDL- C were also reported to be associated with the incidence of colorectal polyps in Korean population [11]. Liuet al reported that high levels of TG and low levels of HDL- C were independent risk factors for colorectal polyps in the patients with metabolic syndrome [12].Another two studies showed positive correlation between triglyceride

levels and an inverse association between serum HDL-C levels and the incidence of colorectal adenoma [13, 14]. On the other hand, some studies did not report a significant association between the prevalence of colorectal polyps and LDL-C levels [13, 15, 16], and another previous studies reported a positive association between the prevalence of colorectal polyps and serum HDL-C levels [6, 14]. The inconsistency between those findings may be related to study design or study population. The possible mechanisms for contribution of serum lipids abnormalities in the occurrence of colorectal polyps is that dyslipidemia could promote colorectal carcinogenesis through several mechanisms[17]. High fat diet, especially over ingestion of animal fat, or saturated fatty acids stimulate the secretion of bile , and then increase the concentration of neutral sterols and bile acid in the colon, under the action of gut bacteria, producing variant of carcinogens. Additionally, low-fibers dietary intake contribute to stagnant of carcinogen and secondary bile Acid in the colon leading to intestinal flora disorders, resulting in carcinogens concentration further increased, the secondary bile acid may activate the α-protein kinas C, which in turn induce the abnormal proliferation of epithelial cells and the adenoma cells of the colorectum. These processes may induce the progression of CRP and CRP [18-20]. The metabolic pattern of increased TG levels and decreased HDL-C levels is also correlated with insulin resistance, and increased circulating insulin/insulin-like growth factor-1 is correlated with the risk of colorectal cancer. Furthermore, increased LDL–C could be associated with increases an oxidative stress, which in turn induce the formation of neoplastic[21, 22].

The prevalence of colorectal polyps is trend to be higher in male patients than female patients [23-25]. This study illustrated that the ratio of individuals with elevated serum TG levels and decreased serum HDL levels were higher in male patients than females, but the differences didn't reach significant. Coppola et al reported that the differences of the incidence of colorectal adenoma between male and female patients for LDL and TC levels were not significant. But HDL levels were significantly lower and TG levels were significantly higher in male patients[13]. Another study demonstrated that low HDL-C and high triglyceride was significantly correlated with colon adenoma in men, but not to women[12]. The differences between the incidence of colorectal polyp in males with dyslipidemia comparing to females may be associated with bad dietary habits and lifestyle of males[26]. Present studyshowed that the percentages of the participants withelevated serum UA levels were significantly higher in patients with colorectal polyps relative to healthy controls. The same findings were observed in the cross sectional study of Korean Population and Retrospective study of elderly Japanesepopulation [8, 27].The possible mechanism for the relation between increased UA levels and the prevalence of colorectal polyps is that serum UA may be induce inflammation, oxidative stress, and insulin resistance, and these factors were reported to be key precursors for the development of colorectal polyps and colorectal cancer [28-30]. The ratio of male patients with high levels of UA was significantly higher than females(P<0.05), the differences may be due to the bad dietary habits or life style in males or may be due to estrogen inducing uric acid excretion in females, therefore, it is more important for male patients to avoid hyperuricemia[31].This study revealed a positive association between UA levels and TG, TC, and LDL levels in the patient with colorectal polyps, whereas, UA levels were negatively associated with HDL levels in the same patients group. This new findings might contribute to further understanding for the pathogenesis of colorectal polyps. The possible mechanism involved in this relation is that synthesis of fatty acids in the liver is linked with increased synthesis of purines, causing the increaseof the production rate of UA. Furthermore, increase the demand for reduced coenzyme Ⅱ during synthetic process of free fatty acid, resulting in increased the synthesizing of uric acid, and elevated uric acid resulting in reducing the activity of lipoprotein lipase, leading to reduce the breakdown of TG, which in turn cause increased serum TG levels[32, 33]. The negative correlation between serum uric acid levelsandserum HDL levels seems to be mediated by insulin resistance[34].

VI. Conclusion

Our study demonstrated that abnormalitiesof serum lipids and serum uric acid are linked withthe incidence of colorectal polyps. In addition, serum TG, TC, and LDL levels were positively associated with UA levels, but HDL levels were negatively associated with UA levels in the patients with colorectal polyps.Therefore, the evolution of thesebiomarkers may provide additional diagnostic values in predicting colorectal polyps. Further studies should investigatewhether anti-hyperlipidemia or serum uric acid lowering medications can decrease the incidence rate of colorectal polyps.

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