Role Some Risk Factors : Age ,Sex And Lipid Profile In Colorectal Cancer In Iraqi Patient

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ABSTRACT

Dyspraxia raises the risk of cancer of the colon and rectum, and plays a significant role in raising the risk of severity. Cholesterol, triglycerides, HDL- Cholestrol, LDL-Cholestrol and VLDL are the five kinds of fats throughout the blood.In addition to knowing whether there was a link between the risk of developing the disease with age and sex, 50 patients were included in this research, as well as 20 healthy people who did not suffer from any diseases of the colon and rectum. The current study determined that the risk factor for this form of cancer is increased by both cholesterol and triglycerides with an increase in blood in CRC, as for what is linked to harmful fats when they grow, the risk of infection decreases, and good fats offer a good indication of CRC cancer. The research also determined what is related to age and gender and their relationship to the risk of infection, because in terms of gender, the majority of cases were over the age of 50 for both sexes, although there is very little difference in the rate of registered patients, but there is no substantial difference between the sexes and in terms of gender and risk of injury, it is not related. These findings showed that elevated levels of blood lipids were considered a significant biological risk factor for the development of CRC. Aims of the study: the research aimed to examine the degree to which fats in the blood influenced the risk of developing CRC cancer.Based on their exposure to

Keywords: Colorectal Cancer, Cholesterol, HDL, LDL, VLDL

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INTRODUCTION

Cancer: Cancer is a disease characterized by the unchecked division and survival of abnormal cells. When this type of abnormal growth occurs in the colon or rectum, it is called colorectal cancer (CRC) 1. CRC usually begins as a noncancerous growth called a polyp that develops on the inner lining of the colon or rectum and grows slowly, over a period of 10 to 20 years 1.An adenomatous polyp, or adenoma, is the most common type. Adenomas arise from glandular cells, which produce mucus to lubricate the colorectum. About one-third to one-half of all individuals will eventually develop one or more adenomas¹. Although all adenomas have the potential to become cancerous, fewer than 10% are estimated to progress to invasive cancer ². The likelihood that an adenoma will become cancerous increases as it becomes larger 3. Cancer arising from the inner lining of the colorectum is called adenocarcinoma and accounts for approximately 96% of all CRCs 4.

Epidemiology: The fourth most widely diagnosed cancer by adults in the United States is colorectal cancer (CRC). It is estimated that 140,000 Americans will be diagnosed with CRC in 2018 5. It is the second largest cause of death from cancer, contributing to over 50,000 deaths worldwide. CRC disease load varies across cultural groups, with blacks, American Indians, and Alaska Natives reporting the highest incidence and mortality rates. 6,5. There were 1391 CRC cases in both sexes, representing 5.5 percent of all newly diagnosed cancer cases, according to the Iraqi Cancer Registry 2018. Among them, there were 763 male cases and 628 female cases. In both sexes, it ranks seventh in 2018; 6.8 percent of the total is fourth among men, and 4.5 percent is third among women. Most cases occur at the age of over 60 in both sexes 7.

Risk factors

Age: The risk of CRC cancer rises with age in middle-aged patients, as has been recorded in men with a mean age of 68 years and in women with a mean age of 72 years. Adults have sustained more injuries than the elderly, and the age of 40 years has risen 8 .

Lipid profile

In developing and increasing the risk of developing CRC, lipids are a risk factor that plays an important role. In different studies, their are in contrast to the risk of CRC cancer ^{9,10}. A negative relationship between them was shown by some studies. A negative correlation between lipids and cancer risk had shown by some of them ¹¹. A diet rich in animal fats, which had provided to be a risk factor for CRC cancer, raises blood cholesterol and supplies it in large amounts ¹².

Sex

Studies have estimated that colorectal cancer incidence varies with gender.

The risk of developing this form of cancer among females and males is very similar, according to a study conducted by Lee et al.,2015¹³, but it varies according to the site of injury in parts of the colon.

METHODS

Collection of samples

In this study, a total of 70 serum samples included 20 normal control samples and 50 colon and rectum cancer samples. During March 2019-March 2020, the Medial City Hospital in Baghdad Province attended the Gastrointestinal Hospital. In order to coagulate the blood, 4 ml of the veins of sick and healthy patients were collected and inserted in special tubes called vacuum tube gel, and left at room temperature for 20 minutes. A centrifuge was used to extract the samples, 3000 cycles

per minute, for which the serum was taken and put in tubes for lipid analysis.

Data Analysis

IBM SPSS version 26.0 [1] was used to measure the mean and SE of the mean. By using the student T-test and ANOVA table, the likelihood was also investigated.

RESULTS

Age -Standardized related to CRC

Patient age ranged from (21-74) years, with an average of (50.70 ± 1.97) years in colorectal cancer groups, while the average age in the ulcerative colitis group was (52.80 ± 2.91) years, but the mean age in the polyp group was (56.90 ± 4.25) years, with respect to age, the findings were of a significant difference between the groups, as the highest lesions were documented at the age of more than tumors. Table (1):

Table (1): Distribution of sample study according to

Age in difference groups

Group Least 40-50 More than 40 No. (%) than 50 No. (%) Cancer 12 13 25 8.64 (No. = (24.00% (26.00 (50.00%) *** Control 7 4 9 8.61	Age in unier	ence group	3		
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Age group (year)			Chi-
No. (%) No. (%)	Group	Least	40-50	More	Squar
Cancer 12 13 25 8.64 (No. = (24.00% (26.00 (50.00%) ** 50)) %) Control 7 4 9 8.61		than 40	No. (%)	than 50	e (χ²)
(No. = (24.00% (26.00 (50.00%) ** 50)) %) ** Control 7 4 9 8.61		No. (%)		No. (%)	
(NO (24.00% (26.00 (30.00%) 50)) %) Control 7 4 9 8.61	Cancer	12	13	25	8.64
Control 7 4 9 8.61	(No. =	(24.00%	(26.00	(50.00%)	**
	50))	%)		
	Control	7	4	9	8.61
(No. (35.00% (20.00 (45.00%) **	(No.	(35.00%	(20.00	(45.00%)	**
=20)) %)	=20))	%)		
* (P≤0.05), ** (P≤0.01).					

Sex.

The total number of males was (35) but females were 35, 48 percent males (24 cases) in colorectal cancer cases, while 52 percent females (9 cases), in control groups males was 55% while female was 45%, in CRC cases no significant between them but in control group found significant ($P \le 0.05$). As shown in the Table (2).

Table (2): Distribution of sample study according to sex

in difference groups

m amerence gi	oups		
			Chi-
Group	Male	Female	Squar
	No. (%)	No. (%)	e (χ²)
Cancer	24 (48.00%)	26 (52.00%)	0.762
(No. = 50)			NS
Control	11 (55.00%)	9 (45.00%)	4.38 *
(No. =20)			
* (P≤0.05), ** (P≤0.01).			

Lipid profile Related to CRC

lipids are one of the complex molecules that are important in human health and play an important role in a group of diseases, including cholesterol, triglycerides, high-density Lipid, low-density Lipid, and very-low-density Lipid, they were measured for the four groups

Cholestrol estimation in patients

The results showed that the mean of patients with CRC cancer was (187.13 \pm 8.51) compared with other groups, there was significant difference between them (P < 0.05) Table (3-5).

Table (3) The mean and SE of cholesterol level between

Studied groups	Cholesterol level means ± SE	Probability	
	Total		
Cancer	187.13 ± 8.51 ^A	0.252	
Control	136.20 ± 6.74 ^A	0.839	
The different letters referred to a significant difference ($P < 0.05$)			

Triglyceride related to CRC

The findings showed that there was no statistical difference between the mean number of patients with CRC cancer (136.69 ± 129.51) relative to the other classes, but the P-value was 0.074. Table (4)

Table (4): The mean and SE of triglyceride level between the studied groups

the studied groups			
Studied	Triglyceride level means ± SE	Pro	
groups		bab	
		ility	
	Total		
Cancer	136.69 ± 129.51 ^A	0.0	
74			
Control	133.20 ± 146.26 ^A	0.2	
		05	
The different letters referred to a significant difference			
(P < 0.05)			

Amino acids form triglycerides and are concentrated in adipose tissue. They are the main energy storage and circulation ¹⁴, play an important role in the transport of proteins and serve as sources of energy obtained from dietary fats (National Cholesterol Education Program, 2002).

HDL-Cholestrol

Compared with the control groups, the mean percentage of HDL cholesterol was 48.90 ± 5.65 in CRC patients. No statistically relevant difference existed. Table (5)

Table (5): The mean and SE of HDL level between the

studied group:	S	
Studied	HDL level means ± SE	Prob
groups		abilit
		у
	Total	
Cancer	48.90 ± 5.65 ^A _a	0.67
		8
Control	29.27 ± 1.17 ^A _a	0.99
		8
The different letters referred to a significant difference		

The different letters referred to a significant difference (P < 0.05)

LDL-Cholestrol

In patients with colon and rectal cancer, the average amount of harmful cholesterol in the blood is 109.6 ± 9.70 , since there is no significant difference between this group and control groups. Table (6)

Table (6): The mean and SE of LDL level between the studied group

studied group		
Studied	LDL level means ± SE	Prob
groups		abili
		ty
	Total	
Cancer	109.64 ± 9.70 ^A	0.78
		6
Control	82.40 ± 5.59 ^A	0.83

		5	
The different letters referred to a significant difference			
(P < 0.05)			

Discussion

In a study at the General Teaching Hospital in Karbala Governorate, data were reported during the period 2009-2017, where injuries and tumor incidence were estimated to increase in rates in age groups over 45 years of age and that is lower than it Ias it was of great value 41.7% much higher than the age groups Less than 45 vears of age and that is referred to 14,15. The rate of infection rises between the ages of 70 and 80. As with Western countries, ¹⁶. The median age of the injured was (51.68), according to other reports, and this is similar to what we observed during the study ¹⁷. As far as Turkish studies are concerned, the average patient age was (58.9) relative to other studies in more developed countries 18. In the United States of America, studies show that people over the age of 65 years are more likely to develop colorectal cancer than people between the ages of 50-64 years, as well as 30 times more than those between the ages of 25-49 years19. In 2016 in Karbala, an increase in the incidence of colorectal cancer was observed, as Iraqi studies also recorded high rates of infection for patients who were under the age of 40 years 20. This is also what has been proven recently in Najaf, with a large number of injuries in the age of fewer than 50 years ²¹. The reason for the increase in the incidence of advanced ages has been due to the change in lifestyle and the nature of food, This has been agreed upon, As for the reason that explains in some studies the higher rate of infection in adults than the elderly, especially in some Iraqi studies, it has been due to the short life span of the elderly in Iraq and the fact that they represent a small percentage of the population. The results of the study showed that the rate of incidence of tumors for males and females is very near, as there is no statistically significant difference between them. This is related to tumors Table (3-3), found among the results a significant difference between the percentage of males with colorectal cancer with the control groups, and this includes females as well Table (2), Support for this study came from several other studies according to Alhilf et al.,2019 where it was proved that there is no significant difference between males and females. This is what was obtained by another study accompanied in Iraq. Also, statistically, there is no significant difference .From the studies that disturbed our results, where White et al., 2019, the incidence of tumors in males is higher than in females. These results are explained by the fact that they are due to the percentage of patients who come to hospitals for the purpose of diagnosing colon and rectal cancer early. This opinion is agree in terms of patients reviewing the endoscopy unit for diagnosis. As for the research that recorded a higher percentage of males than females, it has been due to the reason that women undergo gFOBT at a higher rate than males, but to no benefit, it has not given results that cause women to have been examined by endoscopy 22. They scored more than females, as for the other reason depends on the quantification of hemoglobin in the stool in women, which appears in less than men ²³. This opinion has been agreed in terms of studies that recorded different results from our results. Some study showed that high blood cholesterol was associated with a lower risk of CRC, as cholesterol levels in the blood were inversely correlated. The higher the cholesterol level, the lower the

risk. One study showed a surveillance analysis of more than 10,000 people indicating that it was cholesterol levels that influenced risk, not drug use ²⁴. This opinion is in agreement with the results that appeared from the study. The reason for this has been attributed to the occurrence of an improvement in the immunity to antitumors in people with hyperlipidemia relative to its deficiency. This has explained by the fact that patients with low cholesterol have a low percentage of T-lymphocytes compared to other types and this is what he establish ²⁵.

Other studies have examined the relationship between dietary cholesterol and colon cancer risk, where two studies showed that the rate of increase in colorectal cancer is associated with increased dietary cholesterol reduction ²⁶. It was recorded in this study that eating food that contains cholesterol such as eggs and red meat increases the risk of injury, as the results showed that the rate of infection increases by eating fried eggs more than eating boiled eggs, and these results have no significant statistical significance in terms of statistical analysis. Due to the difference in lifestyle, as well as the study showed on animals, it has shown that dietary cholesterol acts as a carcinogen and precursor to cancer 27,28. Patients with obesity also suffer from elevated triglyceride levels. In cases of metabolic syndrome, it also improves, and that is what was shown by ²⁹ the occurrence of colorectal cancer.Previous studies have revealed that high triglyceride levels raise the risk of colon and rectal cancer by 20% 30. In another study, the findings found a relationship between the risk of colorectal cancer and high TG levels. It showed that high TG levels increased the risk of infection by 6 percent, but these studies were not statistically significant, and this is what we agree in our study that acceptance of the opinion related to these studies was carried out because they gave an indication of an incident 30. There was an increased risk of developing CRC in one of the studies conducted on the role of TG, as it was closely related to them, and it was recorded double as much in men as in women³¹. The TG ratio rate was estimated (170.90±173.5) while the ratio rate was observed in females (104.20± 52.38). The reason for all of this is the increased chronic inflammatory response in patients with elevated TG, and this stimulates an increase in CRC with the growth of cancer cells 32. The other explanation has been that TG levels are positively associated with cell-toxic fecal bile acids that trigger DNA damage and facilitate the development and increase of CRC infection ³³. Another possibility is that an enzyme utilizes fatty acids, which then in turn affects the forming of tumors ^{34, 35}.

Some studies have shown that the risk of colon and rectal cancer decreases with a rise in its level in the blood 36. This research was similar to what we found, such as the levels of good blood cholesterol in colon and rectal cancer patients, which is a higher-than-normal blood level predictor. In terms of its role in controlling levels of inflammatory stimulant cytokines and modifying oxidative stress, this type of fat is important, but what scientists have proven is a major function for this type of fat that deserves more study. The role and effect of LDHcholesterol in raising the risk of developing CRC cancer has been shown by studies conducted on the intestine of rats, as it has been shown that harmful cholesterol has played a significant role in increasing the risk of infection in people with CRC and those with liver cancer metastasis more than others ^{37,38}. There is a convergence of outcomes when comparing the above studies with ours, as well as the purpose for that is that harmful cholesterol enhances ROS in cancerous cells in the colon and rectum ³⁹. In the process of cell proliferation, survival and apoptosis, ROS is one of the free radicals that are important signals. These roots are created inside the cells, especially in the mitochondria, which increases the accumulation and oxidation of proteins, DNA and fats, contributing in an imbalance of oxidative stress, reduction and oxidative stress, which in turn increases inflammation, causing damage to cells and tissues ⁴⁰

CONCLUSION

Taken together These findings indicate that the rise in blood lipids in CRC cancer patients can be considered a risk factor for the disease and an indication of the elevated risk of the disease, including cholesterol, triglycerides and the remaining organisms. In addition to that sex, diet and its representation and fat content play an important role in raising the risk of injury Despite the disparity in the incidence of its percentage between men and women and the reported findings related to this form of cancer, there was no strong differentiation between the sexes, as for age, we created an increase in the risk of the disease and there were more cases of cancer.

REFERENCES

- American Cancer society ,2019
- 2. Risio M. The natural history of adenomas. Best Pract Res Clin Gastroenterol. 2010:24: 271-280.
- 3. Pickhardt PJ, Kim DH, Pooler BD, et al. Assessment of volumetric growth rates of small colorectal polyps with CT colonography: a longitudinal study of natural history. Lancet Oncol. 2013;14: 711-720.
- 4. Stewart SL, Wike JM, Kato I, Lewis DR, Michaud F. A populationbased study of colorectal cancer histology in the United States, 1998-2001. Cancer. 2006;107: 1128-1141.
- 5. 1.Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin. 2018;68:730.
- Siegel RL, Miller KD, Fedewa SA, et al. Colorectal cancer statistics, 2017. CA Cancer J Clin. 2017;67:177-193
- 7. Iraqi cancer Register ,2018
- 8. Noone AM, Cronin KA, Altekruse SF, Howlader N, Lewis DR, Petkov VI, Penberthy L. Cancer Incidence and Survival Trends by Subtype Using Data from the Surveillance Epidemiology and End Results Program, 1992-2013. Cancer Epidemiol Biomarkers Prev. 2017 Apr;26(4):632-641. doi: 10.1158/1055-9965.EPI-16-0520. Epub 2016 Dec 12. PMID: 27956436; PMCID: PMC5380602.
- 9. Järvinen R, Knekt P, Hakulinen T, Rissanen H, Heliövaara M: Dietary fat, cholesterol and colorectal cancer in a prospective study. Br J Cancer 2001; 85:357-361
- 10. Chung YW, Han DS, Park YK, et al.: Association of obesity, serum glucose and lipids with the risk of advancedcolorectal adenoma and cancer: A case-control study in Korea. Dig Liver Dis 2006; 38:668-672.
- 11. Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Speizer F: Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. N Engl J Med 1990; 323:1664-

- 1672.
- 12. Norat T, Lukanova A, Ferrari P, Riboli E: Meat consumption and colorectalcancer risk: doseresponse meta-analysis of epidemiological studies. Int J Cancer 2002; 98:241-256.
- Lee GH, Malietzis G, Askari A, Bernardo D, Al-Hassi HO, Clark SK. Is right-sided colon cancer different to left-sided colorectal cancer?
 A systematic review. Eur J Surg Oncol. 2015;41:300-308.
- 14. Eriksson M, Carlson LA, Miettinen TA, Angelin B. Stimulation of fecal steroid excretion after infusion of recombinant proapolipoprotein A-I. Potential reverse cholesterol transport in humans. Circulation. 1999 Aug 10;100(6):594-8.
- Mosli MH, Al-Ahwal MS. Colorectal cancer in the Kingdom of Saudi Arabia: need for screening. Asian Pacific Journal of Cancer Prevention. 2012;13:3809-13
- Rafiemanesh H, Pakzad R, Abedi M, Kor Y, Moludi J, Towhidi F, Makhsosi BR, Salehiniya H. Colorectal cancer in Iran: Epidemiology and morphology trends. EXCLI journal. 2016;15:738.
- 17. Chou JF, Row D, Gonen M, Liu YH, Schrag D, Weiser MR. Clinical and pathologic factors that predict lymph node yield from surgical specimens in colorectal cancer. Cancer. 2010 Jun 1;116:2560-70.
- Talib A.Majid, Wasem Muhamed Shakir, Aqeel Shakir Mahmmod. Colorectal Carcinoma Presentation and Management, THE IRAQI POSTGRADUATE MEDICAL JOURNAL. VOL.8, NO.3, 2009.
- 19. Edwards BK, Ward E, Kohler BA, et al. Annual report to the nation on the status of cancer, 1975-2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. Cancer 2010; 116: 544-73.
- 20. Rahman Ma ad M.,Al-Janabyi Khuder A. pattern of colorectal and anal tumor and its surgical treatment .May 1999,J.Fac,Med. Baghdad,2000,38-44.16.
- 21. . 21.Noor WK. Histopathological study of colorectal cancer in AL-Najaf province. AlKufa Journal for Biology. 2016 Nov 11;8.
- 22. Quyn AJ, Fraser CG, Stanners G, Carey FA, Carden C, Shaukat A, et al. Uptake trends in the Scottish bowel screening Programme and the influences of age, sex, and deprivation. J Med Screen. 2018;25:24–31. 63.
- 23. 23.Steele RJC, McClements P, Watling C, Libby G, Weller D, Brewster DH, et al. Interval cancers in a FOBT-based colorectal cancer population screening programme: implications for stage, gender and tumour site. Gut. 2012;61: 576–81
- 24. 24. Skopec R (2015) Intelligent Evolution, Complexity and Self-Organization. Neuro Ouantology 13.
- 25. Skopec R (2016) Fighting cancer with growing complexity. J Transl Sci 2.
- 26. Skopec R (2017) Coding by Quantum Entanglement Entropy. Neuro Quantology 15.
- 27. 25. Muldoon MF, Marsland A, Flory JD, Rabin BS, Whiteside TL, et al. (1997) Immune system differences in men with hypo- or hypercholesterolemia. Clin Immunol

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- Immunopathol 84: 145-149
- 28. 26.R Järvinen, P Knekt, T Hakulinen, H Rissanen, M Heliövaara. Dietary fat, cholesterol and colorectal cancer in a prospective study
- 29. Br J Cancer. 2001 Aug; 85(3): 357-361.
- 30. 27.Cruse JP, Lewin MR, Feruland GP and Clark CG (1978) Co-carcinogenic effects of dietary cholesterol in experimental colon cancer. Nature 276: 822–825
- 31. 28.Hiramatsu Y, Takada H, Yamamura M, Hioki K, Saito K and Yamamoto M (1992) Effect of dietary cholesterol on azoxymethane- induced colon carcinogenesis in rats. Carcinogenesis 4: 553–558
- 32. 29.Fasshauer M and Paschke R: Regulation of adipocytokines and insulin resistance. Diabetologia 46: 1594 1603, 2003.
- 33. 30. Melvin JC, Holmberg L, Rohrmann S, Loda M and Van Hemelrijck M: Serum lipid profiles and cancer risk in the context of obesity: Four meta analyses. J Cancer Epidemiol 2013: 823849, 2013.
- 34. 31.Borena W, Stocks T, Jonsson H, Strohmaier S, Nagel G, Bjørge T, Manjer J, Hallmans G, Selmer R, Almquist M, et al: Serum triglycerides and cancer risk in the metabolic syndrome and cancer (Me-Can) collaborative study. Cancer Causes Control 22: 291 299, 2011
- 35. 32. Kim MH, Kim HN and Choi WS: The association between subclinical inflammation and abnormal glucose and lipid metabolisms in normal-weight Korean individuals. Nutr Metab Cardiovasc Dis 28: 1106-1113, 2018.
- 36. 33. McKeown-Eyssen G: Epidemiology of colorectal cancer revisited: Are serum triglycerides and/or plasma glucose associated with risk? Cancer Epidemiol Biomarkers Prev 3: 687 695, 1994.
- 37. 34. Migita T, Ruiz S, Fornari A, Fiorentino M, Priolo C, Zadra G, Inazuka F, Grisanzio C, Palescandolo E, Shin E, et al: Fatty acid synthase: A metabolic enzyme and candidate oncogene in prostate cancer. J Natl Cancer Inst 101: 519 532, 2009.
- 38. 35.Flavin R, Zadra G and Loda M: Metabolic alterations and targeted therapies in prostate cancer. J Pathol 223: 283 294, 2011.
- 39. 36. Chen X, Wu P, Liu D, Yan S, Shen X and Yang L: Prognostic significance of high triglyceride and apolipoprotein B levels in patients with stage III and high-risk stage II colorectal cancer undergoing curative surgery. Oncol Lett 20: 705-714, 2020.
- 37. DeClercq V, McMurray DN, Chapkin RS: Obesity promotes colonic stem cell expansion during cancer initiation. Cancer Lett 2015; 369: 336-343.
- 41. 38.Beyaz S, Mana MD, Roper J, Kedrin D, Saadatpour A, Hong SJ, Bauer-Rowe KE, Xifaras ME, Akkad A, Arias E, Pinello L, Katz Y, Shinagare S, Abu-Remaileh M, Mihaylova MM, Lamming DW, Dogum R, Guo G, Bell GW, Selig M, Nielsen GP, Gupta N, Ferrone CR, Deshpande V, Yuan GC, Orkin SH, Sabatini DM, Yilmaz OH: High-fat diet enhances stemness and tumorigenicity of intestinal progenitors. Nature 2016; 531: 53-58.

- 42. 39.Gough DR, Cotter TG: Hydrogen peroxide: a Jekyll and Hyde signalling molecule. Cell Death Dis 2011; 2:e213.
- 43. 40.Rimessi A, Previati M, Nigro F, Wieckowski MR, Pinton P: Mitochondrial reactive oxygen species and inflammation: Molecular mechanisms, diseases and promising therapies. Int J Biochem Cell Biol