Study the Relationship between Omega-3 Dietary Intake and Rheumatoid Arthritis

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Abstract		Original Research Article

Problem and background: with low prevalence of RA as its affect only 1% of adult population worldwide most physicians and patients do not have adequate knowledge and experience about nutritious role in managing the disease activity, the aim is to study the relationship between omega-3 fatty acid intake and rheumatoid arthritis. ***Method:*** In this cross sectional study conducted in 2020 included a sample of 100 RA patients we trying to prove the role of omega-3 anti-inflammatory properties in RA disease activity also to study patient's knowledge of omega3 and their dietary attitude. ***Result:*** Chi square test was used to indicate the relationship of omega-3 intake and symptoms of RA. There was significant statistic difference in these symptoms: {morning stiffness P = 0.000, standing and sitting pain P = 0.000, getting heavy things P = 0.000, up stair pain P = 0.02, bending down hardness P = 0.000, household hardness P = 0.000}. Also indicate significant statistical difference between educated level and omega-3 knowledge P = 0.000. however, there was no statistical difference between family income and omega-3 intake P = 0.1, "Chi-square test" also indicate significant statistic difference between the kind of treatment used and these symptoms (morning stiffness, standing and sitting pain, getting heavy things, house hold hardness, praying on a chair). ***Conclusion:*** Our study found that omega3 rich diet is associated with decrease RA disease activity.
Keywords: Omega-3 polyunsaturated fatty acids, EPA, DHA, Fish oil, Rheumatoid arthritis.

INTRODUCTION

Rheumatoid arthritis is long term progressive and disabling autoimmune disease, caused by interaction of genetic and environmental factors result in cascade of immune reactions. Rheumatoid arthritis characterized by synovial inflammation and hyperplasia (swelling), auto antibodies production, cartilage and bone destruction (deformity), systemic complications include cardiovascular, pulmonary, psychological, skeletal disorder, early death and socioeconomic costs and the mortality rate is higher among patients with RA than healthy people [1]. Another definition to rheumatoid arthritis (RA) is a chronic autoimmune disease which causes chronic inflammation and pain in the joints, leading to destruction of the cartilage over time [2]. Pain is one of the most significant problems for patients with RA, and is caused by infiltration of inflammatory cells into the synovial of the joints. Activation of these cells results in secretion of pro-inflammatory cytokines, eicosanoids and other mediators resulting in inflammation, pain and swelling of the joint [3].

Rheumatoid arthritis results in more than 9 million physicians visits and more than 250.000 hospitalizations per year, and its affect 1% of the adult population worldwide, this low prevalence, means that the average physician often develops little experience with its diagnosis or management [4, 5, 6]. Omega-3 polyunsaturated fatty acids (PUFAs) are long chain PUFAs found in plants and marine source such as fish, mussel, oyster ,shrimp, but primarily cold water fish ,also exist in a wide range of plant products such as nuts, seeds, flax seeds and vegetable oils such as soybean and canola besides olive [7]. n-3 omega fatty acid, unlike saturated fatty acid, have been associated with various health benefits relating to treatment of Rheumatoid arthritis and coronary artery diseases [7]. The first elements of the omega-3 fatty acid is the essential fatty acid alpha-linolenic acid, other members of this family are derivatives of ALA with longer more unsaturated hydrocarbon chain, the main ones are eciosapentaenoic acid EPA, docosahexaenoic acid DHA [8]. Cod liver oil supplement are also rich source of the two most important omega-3 fatty acid (EPA, DHA) as they typically contain 30-50% of the omega-3 fatty

acid, the main different between the cod liver oil and omega-3 fatty acid is that cod liver oil also contain vitamin A and D [9]. Diet contains a complex mixture of fats and oils whose basic structural components are fatty acids, as Marc E Surette suggested that western societies generally consume at least 20 different fatty acids, not all dietary fatty acids are created equally, because human don't have the enzymatic machinery required to synthesize Omega-3 fatty acids, they must be obtained from diet(termed essential fatty acid). Omega-3 fatty acids from fish and fish oil are not to be confused with those from plant source, such as flax and canola oil , these plant oil are enriched in an omega 3 fatty acids called alpha linolenic acid , which is a metabolic precursor of the omega 3 fatty acids found in fish and fish oil [9]. In the last decade there has been an increased interest in the role of omega-3 fatty acids in the reduction of articular inflammation as well as in the improvement of clinical symptoms in subjects affected rheumatic diseases, in particular rheumatoid arthritis [10]. The effect of omega-3 fatty acids in the treatment of inflammation disease, including rheumatoid arthritis, has been shown in several studies as significant reducing for morning stiffens, the number of swollen joints, inflammatory markers that play large role in joint destruction, pain and daily use of analgesic, as increased omega-3 fatty acids intake lead to reduction in arachidonic acid binding to cell membrane, causing a markers such as tumor necrosis factor notably reduce [11].

The important of our study is to expending our observation on the extent to which omega-3 fatty acids contribute to decrease disease activity (symptoms) and lower the use of anti-inflammatory drugs and to highlighting the importance of these fatty acids along with therapeutic treatment; this study trying to prove the significant roles of omega-3 anti-inflammatory properties in rheumatoid arthritis disease activity ,also study the patient's knowledge about omega-3 fatty acids and their dietary attitude , in order to encourage the patients to consume omega-3 rich foods and the doctors to prescribe omega-3 fatty acid supplement beside the therapy. The importance of this study comes primarily to know the awareness of rheumatoid arthritis patients about the importance of eating foods rich in omega-3 and do they have sufficient knowledge of its importance in relieving pain caused by arthritis, and are they aware of the foods rich in them, in fact the main goal is not knowledge in itself, but Studying the relationship between omega-3 and rheumatoid arthritis disease initially as a hypothesis, we think awareness will be great about the importance of eating it, but knowing its role in relieving pain is not enough. The results of this study will be important in raising the nutritional awareness of rheumatoid arthritis patients with regard to foods rich in omega-3 source and its relationship to relieving pain caused by the disease, as it is supposed to issue awareness plans in coordination with the Nutrition Department after completing this study and circulating

its results to the community to benefit from them, and to clarify the relationships that appeared in the study and the concern for the quality of the food provided to patients with rheumatoid arthritis and the conduct of educational courses clearly and smoothly.

In view of the importance of omega-3, we need to clarify and know the relationship between eating foods rich in omega-3 and the extent of its effect on decreased activity of rheumatoid arthritis, also to study the level of cultural awareness of rheumatoid arthritis patients in Benghazi, and their knowledge of foods rich in Omega-3 and whether it has a positive or negative impact on their health. The specific Objectives of the current paper are to assess the rheumatoid arthritis patient's knowledge about omega3, to determine whether more frequent consumption of diet rich with omega3 is associated with lowering rheumatoid arthritis disease activity. To study the relationship between rheumatoid arthritis symptoms to omega3 and analgesic.

The role of Omega3 PUFA in shaping and regulating of inflammatory process, suggest that the level of these exposure of these fatty acid might be important in determining the development and severity of disease. Inflammation is involved in the pathophysiology of many chronic diseases including RA; several studies have evidenced the important anti-inflammatory and immuno-modulatory properties of omega-3 long chain fatty acid (EPA-DHA). Its well established that n-3 LC are substrates for synthesis of novel series of lipid mediators (eg . resolvins , protectins , and maresins),With potent anti-inflammatory and pro-resolving properties which have been proposed to partly mediate the protective and beneficial action of n-3 PUFA [12,13]. The role of Omega-3 as an anti-inflammatory can prescribes as:

1-Decrease production of eicosanoid mediators from arachidonic acid (omega-6) many of which have pro-inflammatory role. 2- Eicosanoid originated from omega-3 (EPA, DHA) act as anti-inflammatory agents. 3- Decrease production of pro-inflammatory proteins and cytokines and reduce chemotactic response of leukocytes.

Series of PG and LT originate from (EPA, DHA) inhibit inflammation ,so altering content of EFA in diet or by supplement can modifying the type formed, therefore as result of the ant-inflammatory action of omega-3 several studies determine their therapeutic efficacy in rheumatoid arthritis [14]. A double blind placebo-controlled randomized study carried out between August 1997 and December 2002, patients randomized to take either 10g of cod liver oil or air filled identical placebo capsule ,the study shown that out of 49 patients 19 (39%) in cod liver oil group and out of 48 patients 5 (10%) in the placebo group were able to reduce their daily use of non-steroidal anti-

inflammatory drugs requirements by >30%,this study suggest that cod liver oil supplements containing n-3 fatty acids can be used as NSAID- sparing agents in rheumatoid arthritis patients [15]. On the other hand, a meta-analysis study have been done in 2012 on consumption pure Omega-3 PUFAs suggests that the use of omega-3 PUFAs at dosages >2.7 g/day for >3 months reduces NSAID consumption by RA patients. Further studies are needed to explore the clinical and NSAID-sparing effects of omega-3 PUFAs and cod liver oil in RA [16] Another meta-analysis study in Canada, reported that the consumption Omega 3 PUFA supplementation in patients with rheumatoid arthritis or joint pain secondary to another diseases, it can reduces joint pain intensity, morning stiffness, number of painful and/or tender joints, and NSAID consumption. Omega3 PUFA supplementation is an attractive adjunctive treatment for joint pain. Further studies in human's arerequired to optimize the analgesic effects of EPA/DHA in patients with arthritis [17]. Ingestion of dietary supplements of n-3fatty acid has been consistently shown to reduce both number of tender joints on physical examination and amount of morning stiffness in patients with RA, a study review recommended that patients consume dietary supplements containing 3-6g n-3 fatty acid daily for >12 wk. the dietary supplements should not replace the standard therapeutic medical regimen but be added to it [18]. A cross sectional analysis study carried out between October 2004 and may 2006, was aimed to assess whether more frequent fish consumption is associated with lower rheumatoid arthritis disease activity, the frequency of fish consumption was assessed by a baseline food frequency questionnaire assessing usual diet in past year, the study shown that among 176 participants, there is significantly lower DAS28-CRP among subjects consuming fish > 2 times/week compared to those eating fish never to <1 time/month , and for each additional serving of fish per week, DAS28-CRP was significantly reduced by 0.18 [19]. Another case control study have been done in Sweden during (1996-2005), to investigate the possible influence of consumption of oily fish and fish oil supplement on the risk of developing RA, the study found that intake of oily fish was associated with modest decrease risk of developing RA [20]. In another hand A double blind randomized study was conducted on 1994, comparing daily supplementation with either 2.6gm of omega-3 or 1.3gm of omega-3 + 3gm of olive oil, the study found that daily supplementation with 2.6gm of omega-3 result in significant clinical benefit and may reduce the need for concomitant artitheumatic medication [21]. In contrast a dose response meta-analysis study the association between fish consumption and risk of developing rheumatoid arthritis was conducted on 2013, the result shown a non-statistically significant inverse association between fish consumption and rheumatoid arthritis [22]. A randomized double blind clinical trial which conducting in Iran, patients were randomized placed into of two

(omega-3 and placebo) groups, the dose of omega-3 and placebo was constant throughout the treatment, 76% of patients receiving omega - 3 expressed satisfaction from participation in this project which was considerably higher than the placebo group (37.5%), the study shown that early use of omega-3 supplements along with DMARDS treatment in patients with newly diagnosed RA can be effective in reducing symptoms such as pain, the need for analgesics, the number of swollen joints, and inflammatory markers that play a large role in joint destruction, and lead to an increase in physical strength Significant improvement in the patient's global evaluation and in the physician's assessment of disease was observed in those taking omega-3 [11]. Study was conducted in January 2003 on patients with definitive rheumatoid arthritis, were matched into two groups, one group was observed for 8 month on a normal western diet, (In which western diet exclusively are high in arachidonic acidderives from nutrient of animals origin), and other group on an anti-inflammatory diet providing an arachidonic acid intake of less than 90 mg\day. Patients in both groups were allocated to receive placebo or fish oil capsule "30 mg\kg" for three months in a double-blind crossover study. the result of this study was in anti-inflammatory diet patients, as compared to western diet patients, fish oils led to significant reduction in the number of tender (28% vs 11%) and swollen (34% vs 22%) joints, the study found that the diet low in arachidonic acid ameliorates clinical sign of inflammation in patients with rheumatoid arthritis and augments the beneficial effect of fish oil supplementation. This implies that taking more anti-inflammatory fish oil will not reduce systemic inflammation if one dose not reduces pro-inflammatory omega-6 "arachidonic acid" in diet [20] other study indicate that omega-6 _omega-3 ratio should be lower than that presently found in the general population with a view to improving general health and reducing risk of diseases. This means that evolutionary aspects of diet indicate changes in our diet particularly in the type and amount of essential fatty acids, with increase in omega-6 fatty acid _ and decrease in omega-3 fatty acid resulting in omega-6 fatty acid/ omega-3 fatty acid ratio in the range of 20-30:1 which is very different from the original 1:1 of the human in the past [24-27].

METHODS AND MATERIALS

A cross-sectional study was conducted from October 2019 to February 2020 on rheumatoid arthritis patients in Benghazi. The second largest city in Libya, all patients was attending the Benghazi Medical Center. A sample randomly selected of 100 people (male and female) and range of their ages from (20 - 85) was asked in the study to fill out a questionnaire by interview, which lasted about a quarter of an hour for each patient. We encountered objections from patients participating in the study for their own reasons. In this study, we include any patient who wishes to participate without exception, and we do not define specific characteristics for participation other than the disease

condition on which the study is based. Weight and height were measured after completion of the questionnaire, height was measured to nearest 0.1 cm using standard calibrated scale attached to the balance against a wall, and weight is measured using weighing machine. All those measurements were collected with the participants in either thin sock or barefoot and with heavy clothing items taken away. In this study the questionnaire has been used based on 30 items divided into 6 basic sections. All questionnaires were carried out by direct interview with the subjects. Information such as; personal information, demographic and socioeconomic characteristics, medical history food habit and patterns, anthropometric (weight and height) and others items to assess the knowledge and study correlations of food habit and life style patterns to their health statues were collected, questions about dietary intake by using modified food frequency questionnaire FFQ, we assess the intake of omega-3 among the patients based on the consumption of at least 3 sources of the diet rich with omega-3 daily (fish, nuts, flax seeds, olive oil), and omega-3 supplement This study was granted approval by the local Ethics Committee of the Benghazi province. Informed written consent was obtained through a consent form that was given to the participants along with the questionnaire. The data collected from questionnaire was loaded on Excel. Data set was exported to (SPSS Inc. Chicago, USA v. 20) and analysed to describe general information, food intake, health characteristics, anthropometric, and life style patterns and others. The BMI was calculated and classified according to World Health Organization. Chi-square test (t test) was done the ssignificance level: $P \leq 0.05$ was considered to be statistically significant. Data presentation: frequency distribution table; cross tabulation; column charts; and pie chart were used to describe and compare variables. Statistics testing: A significance testing such as Chi-square test was used to examine relationships of variables; and Spearman rho correlation was used to correlate between two variables. Generally, a value of "r" greater than 0.7 is considered a strong correlation. Anything between 0.5 and 0.7 is a moderate correlation, and anything less than 0.4 is considered a weak correlation. Whereas; "+" means direct correlation, "-" means indirect correlation. Data analysis was executed using the Statistics Package Social Science (SPSS) program version 20.

Pilot Study

Before we starting the actual study, in fact we made an experimental study in 2019, the number of participants in it was about 50 people, and the purpose of this step is to ensure the reliability and sequence of questions, as we formulated the questionnaire after reviewing the previous studies and then judged by the research supervisors, as they were modified according to their observations and they reach their final form. In order to ensure the understanding of the questionnaire, its clarity and knowledge of its reliability and validity, we relied on (Cronbach Alpha) because it reflects the level of coherence and coherence between the paragraphs of the questionnaire, according to (George and Mallery 2003), the basic rules of Alpha Cronbach and the percentage was more than 70%, and this according to the classification is considered Very acceptable. The findings of this study have to be seen in light of some limitations that could be addressed in future research. *Firstly* was the relatively small-size sample, only 100 participants were involved in this study which may make the result inaccurate, and also may because the data was not completely collected. *Secondly* in this study we have information on the intake of omega-3 fatty acid through food frequency questionnaire -FFQ only based on the daily consumption of the richest sources. *Thirdly* our study did not examine the impact of the other dietary factors such as omega-6 fatty acid (arachidonic acid) and it is adverse effect as pro-inflammatory agent. As some studies mentioned that restricting arachidonic acid intake is prerequisite for the anti-inflammatory effect and benefits of omega-3 in patients with rheumatoid arthritis [27].

RESULT

One hundred questionnaires were filled and complete by respondent's males and females who had active Rheumatoid Arthritis; the average age in the respondents was 52.7 years (range from 20 years to 85 years). Socio-demographic characteristics details of the respondents were presented in Table (1). The majority of the respondents who had active Rheumatoid Arthritis were the age range of 46-65 years (64%). followed by 20% of the respondents were the age range of 26-45 years. Forty-six percent of the respondents have a primary educational level; while, 33% of them have academic certificates. Most of the respondents were married (70%); whereas, 14% of them were single, and 14% of the respondents were widowed. Regarding occupation, 58% of the respondents were housewives, and 17% of them were teachers. The majority of the respondents (88%) have a good family income; whereas, 8% of them have low family income.

Table-1: Socio-demographic characteristics of the respondents

Socio- demographic char.	No.	%
Age in years		
≤ 25	5	5%
26-45	20	20%
46-65	64	64%
66-85	11	11%
Educational level		
Primary	46	46%
Secondary	21	21%
Academic	33	33%
Social status		
Single	14	14%
Married	70	70%
Widowed	14	14%
Divorced	2	2%
Occupation		
Housewife	58	58%
Student	7	7%
Teacher	17	17%
Other	18	18%
Income		
Low	8	8%
Good	88	88%
High	4	4%
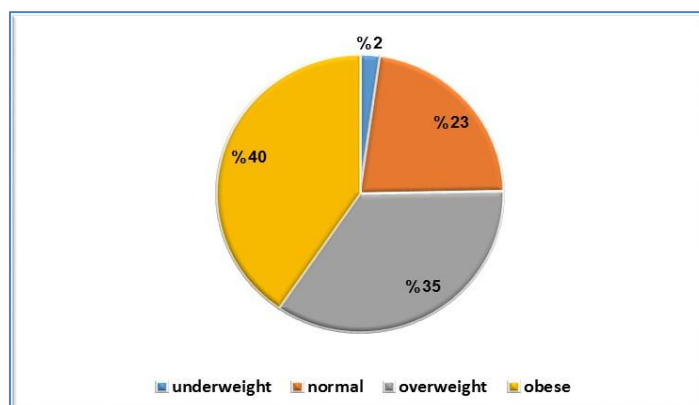
Fig-1: Body Mass Index of the respondents

The majority of the respondents suffered from Rheumatoid Arthritis for more than 2 years; while 6% of them suffered from one year to two years. And 11% of the respondents suffered from Rheumatoid Arthritis for less than one year. Regarding pain intensity, 59% of the respondents estimated their pain as intense; whereas, 35% of them estimated their pain as moderate. Only 6% of the respondents estimated their pain as light. Moreover, 81% of the respondents used analgesics to relieve their pain. As shown in Table (2).

Table-2: Health status of the respondents

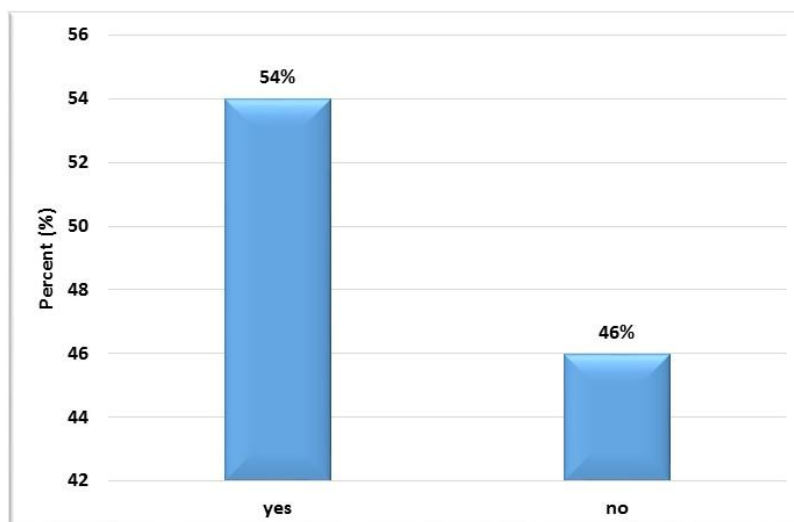|	No.	%
Duration of illness in years		
less than year	11	11%
1 to 2 years	6	6%
more than 2 years	83	83%
pain intensity		
Light	6	6%
Moderate	35	35%
Intense	59	59%
taking analgesic		
Yes	81	81%
No	19	19%

Fig-2: Omga3 knowledge among the respondents

A comparison of educational level and omega3 knowledge is presented in Table (3). There was a significant statistical difference between educational level and omega3 knowledge (P= 0.001); in which the omega3 knowledge is increasing when the educational level increases. 26 out of 33 of the respondents who have academic certificates as educational level, have the omega3 knowledge compare to 7 out of 33 of them not have the omega3 knowledge. Only 18 out of 46 of the respondents who have primary educational level, have the omega3 knowledge compare to 28 out of 46 of them not have the omega3 knowledge.

Table-3: Educational level and omega3 knowledge

Educational Level	Omega3 knowledge		Total
	Yes	No	
	No. (%)	No. (%)	No. (%)
Primary	18 (18%)	28 (28%)	46 (46%)
Secondary	10 (10%)	11 (11%)	21 (21%)
Academic	26 (26%)	7 (7%)	33 (33%)
Total	**54 (54%)**	**46 (46%)**	**100 (100%)**
Chi-square test	**P = 0.001***		

* P<0.05 is statistically significant

A comparison of the respondents' age and omega3 knowledge is presented in Table (4). There was a significant statistical difference between the respondents' age groups and omega3 knowledge (P= 0.003); in which the omega3 knowledge is increasing at young the respondents. 15 out of 20 of the respondents aged between 26-45 years have omega3 knowledge; compared with only 1 out of 11 of the respondents aged between 66 - 85 years has omega3 knowledge.

Table-4: A comparison of the respondents' age and omega3 knowledge

Age in years	Omega 3 knowledge		Total
	Yes	No	
	No. (%)	No. (%)	No. (%)
≤ 25	3 (3%)	2 (2%)	5 (5%)
26-45	15 (15%)	5 (5%)	20 (20%)
46-65	35 (35%)	29 (29%)	64 (64%)
66-85	1 (1%)	10 (10%)	11 (11%)
Total	**54 (54%)**	**46 (46%)**	**100 (100%)**
Chi-square test	**P = 0.003***		

* P<0.05 is statistically significant

Table-5: Relation between omega3 intake and rheumatoid arthritis

Symptoms		Good intake	Poor intake	P value
Morning stiffness	Yes	17(17%)	55(55%)	**P = 0.000***
	No	23(23%)	5(5%)	
Standing and sitting pain	Yes	9(9%)	47(47%)	**P = 0.000***
	No	31(31%)	13(13%)	
Pain after 15 min Standing	Yes	30(30%)	52(52%)	P = 0.1
	No	10(10%)	8(8%)	
Up stair pain	Yes	30(30%)	55(55%)	**P = 0.02***
	No	10(10%)	5(5%)	
Getting heavy things pain	Yes	17(17%)	52(52%)	**P = 0.000***
	No	23(23%)	8(8%)	
Bending down hardness	Yes	6(6%)	56(56%)	**P = 0.000***
	No	34(34%)	4(4%)	
Opening and catching hardness	Yes	26(26%)	48(48%)	P = 0.09
	No	14(14%)	12(12%)	
House work hardness	Yes	5(5%)	56(56%)	**P = 0.000***
	No	35(35%)	4(4%)	
Praying on chair	Yes	6(6%)	31(31%)	**P = 0.000***
	No	34(34%)	29(29%)	
Total		**40 (40%)**	**60 (60%)**	

* P<0.05 is statistically significant

A relationship between omega 3 intake and rheumatoid arthritis symptoms regardless of analgesic is presented in Table (5). There was a significant statistical difference between omega 3 intake and "morning stiffness" (P= 0.000); in which the respondents who had a good intake of omega 3, suffered less from "morning stiffness" than those who had a poor intake of omega 3. Thus, only 17 out of 40 of the respondents who eat enough of omega 3, suffered from "morning stiffness" compared with 55 out of 60 of the respondents who did not eat enough of omega 3 suffered from "morning stiffness". There was a significant statistical difference between omega 3 intake and "standing and sitting pain" (P= 0.000); in which the respondents who had a good intake of omega3, suffered less from "standing and sitting pain" than those who had a poor intake of omega3. Thus, only 9 out of 40 of the respondents who eat enough of omega 3, suffered from "standing and sitting pain" compared with 47 out of 60 of the respondents who did not eat enough of omega3 suffered from "standing and sitting pain". As shown in Table (5). However, there was no significant statistical difference between omega3 intake and "pain after 15 min standing" (P= 0.1); most of the respondents who eat enough of omega3 or did not, suffered from "pain after 15 min standing". As shown in Table (5). While, there was a significant statistical difference between omega 3 intake and "up stair pain" (P= 0.02); in which the respondents who had a good intake of omega 3, suffered less from "up stair pain" than those who had a poor intake of omega 3. Thus, 30 out of 40 of the respondents who eat enough of omega 3, suffered from "up stair pain" compared with 55 out of 60 of the respondents who did not eat enough of omega3 suffered from "up stair pain". As shown in Table (5). Also, there was a significant statistical difference between omega 3

intake and "getting heavy things pain" (P= 0.000); in which the respondents who had a good intake of omega 3, suffered less from "getting heavy things pain" than those who had a poor intake of omega 3. Thus, only 17 out of 40 of the respondents who eat enough of omega 3, suffered from "getting heavy things pain" compared with 52 out of 60 of the respondents who did not eat enough of omega3 suffered from "getting heavy things pain". As shown in Table (5). And, there was a significant statistical difference between omega 3 intake and "bending down hardness" (P= 0.000); in which the respondents who had a good intake of omega 3, suffered less from "bending down hardness" than those who had a poor intake of omega 3. Thus, only 6 out of 40 of the respondents who eat enough of omega 3, suffered from "bending down hardness" compared with 56 out of 60 of the respondents who did not eat enough of omega3 suffered from "bending down hardness". As shown in Table (5). However, there was no significant statistical difference between omega 3 intake and "opening and catching hardness" (P= 0.09); most of the respondents who eat enough of omega3 or did not, suffered from "opening and catching hardness". As shown in Table (5). While, there was a significant statistical difference between omega 3 intake and "housework hardness" (P= 0.000); in which the respondents who had a good intake of omega 3, suffered less from "housework hardness" than those who had a poor intake of omega 3. Thus, only 5 out of 40 of the respondents who eat enough of omega 3, suffered from "housework hardness" compared with 56 out of 60 of the respondents who did not eat enough of omega3 suffered from "housework hardness". As shown in Table (5). Moreover, there was a significant statistical difference between omega 3 intake and "praying on chair" (P= 0.000); in which the respondents

who had a good intake of omega 3, suffered less from "praying on chair" than those who had a poor intake of omega 3. Thus, only 6 out of 40 of the respondents who eat enough of omega 3, suffered from "praying on chair" compared with 31 out of 60 of the respondents who did not eat enough of omega3 suffered from "praying on chair". As shown in Table (5). A comparison of family income and omega3 intake are presented in Table (6). There was no significant statistical difference between family income and omega3 intake (P= 0.1); in which the family income did not affect omega3 intake.

Table-6: Family income and omega3 intake

Family income	Omega3 intake		Total
	Good intake	**Poor intake**	
	No. (%)	**No. (%)**	**No. (%)**
Low	1 (1%)	7 (7%)	8 (8%)
Good	37 (37%)	51 (51%)	88 (88%)
High	2 (2%)	2 (2%)	4 (4%)
Total	**40 (40%)**	**60 (60%)**	**100 (100%)**
Chi-square test	P = 0.1		

* $P<0.05$ is statistically significant

Table-7: Association between rheumatoid arthritis symptoms and Duration of illness in years

Symptoms	Correlation Coefficient	
Morning stiffness	r = - 0.1	Indirect weak correlation
Standing and sitting pain	r = 0.03	Direct weak correlation
Pain after 15 min Standing	r = 0.1	Direct weak correlation
Up stair pain	r = 0.11	Direct weak correlation
Getting heavy things pain	r = - 0.2	Indirect weak correlation
Bending down hardness	r = -0.03	Indirect weak correlation
Opening and catching hardness	r = 0.02	Direct weak correlation
House work hardness	r = -0.1	Indirect weak correlation
Praying on chair	r = -0.1	Indirect weak correlation

Association between rheumatoid arthritis symptoms and duration of illness in years is presented in Table (7). The indirect weak correlation between "Morning stiffness" and the duration of illness. This means "Morning stiffness" more associated with patients who suffered from rheumatoid arthritis for more than 2 years; although, weak correlation. While the direct weak correlation between "Standing and sitting pain" and the duration of illness. This means "Standing and sitting pain" more associated with new patients; although, weak correlation. Whereas, the indirect weak correlation between symptoms "Getting heavy things pain", "Bending down hardness", "Housework hardness" and "Praying on chair" with the duration of illness. This means these symptoms more associated with patients who suffered from rheumatoid arthritis for more than 2 years; although, weak correlation. While the direct weak correlation between symptoms "Pain after 15 min Standing", "Up stair pain", and "Opening and catching hardness" with the duration of illness. This means these symptoms more associated with new patients; although, weak correlation.
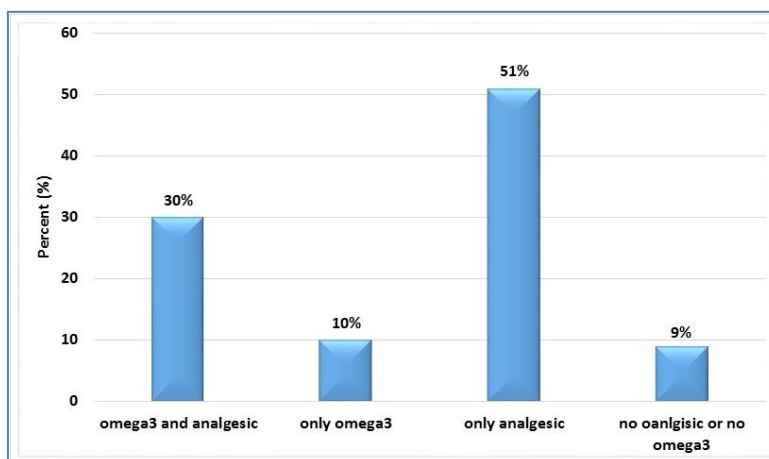

Fig-3: Treatment used to relieve pain of rheumatoid arthritis symptoms among the respondents

The researchers asked the respondents in this study about treatment that use to relieve their pain of rheumatoid arthritis symptoms. 51% of the respondents used analgesics only to relieve their pain; while 30% of them used omega3 and analgesic to relieve their pain.

Also, 10% of the respondents used omega-3 only to relieve their pain, and 9% of them did not use omega3 or analgesic to relieve their pain. As shown in Figure (5).

Table-8: Relationship between rheumatoid arthritis symptoms and kind of treatment

Symptoms		omega3 and analgesic	Only omega3	Only analgesic	no analgesic or omega3
Morning stiffness	Yes (n=72)	15	3	47	7
	No (n=28)	15	7	4	2
P = 0.000*					
Standing and sitting pain	Yes (n=56)	7	2	40	7
	No (n=44)	23	8	11	2
P = 0.000*					
Pain after 15 min Standing	Yes (n=82)	21	8	45	8
	No (n=18)	9	2	6	1
P = 0.2					
Up stair pain	Yes (n=85)	23	7	47	8
	No (n=15)	7	3	4	1
P = 0.1					
Getting heavy things pain	Yes (n=69)	13	5	43	8
	No (n=31)	17	5	8	1
P = 0.000*					
Bending down hardness	Yes (n=62)	7	0	48	7
	No (n=38)	23	10	3	2
P = 0.000*					
Opening and catching hardness	Yes (n=74)	17	9	40	8
	No (n=26)	13	1	11	1
P = 0.06					
Housework hardness	Yes (n=61)	6	0	48	7
	No (n=39)	24	10	3	2
P = 0.000*					
Praying on chair	Yes (n=37)	4	3	27	3
	No (n=63)	26	7	24	6
P = 0.003*					
Total		**30**	**10**	**51**	**9**

* P<0.05 is statistically significant

From Table (8), there was a significant statistical difference between the kind of treatment that used to relieve pain and symptoms "Morning stiffness", "Standing and sitting pain", "Getting heavy things pain", "Bending down hardness", "Housework hardness", and "Praying on chair", in which (P<0.05) in all. Most of the respondents who suffered from these symptoms; used the analgesic only to relieve their pain. While about from 0% to 8% of the respondents used omega3 only to relieve their pain; and about 10% to 20 of the respondents used omega3 and analgesic to relieve their pain from these symptoms. Whereas there was no significant statistical difference between the kind of treatment used to relieve pain and symptoms "Pain after 15 min Standing", "Up stair pain", and "Opening and catching hardness", in which (P>0.05) in all. 54% to 55% of the respondents who suffered from these symptoms; used the analgesic only to relieve their pain; while about 24% to 28% of the respondents used

omega3 and analgesic to relieve their pain from these symptoms. As shown in Table (8).

DISCUSSION

The findings from this cross sectional study demonstrate that, frequent consumption of omega-3 rich foods is associated with modest decrease in rheumatoid arthritis disease activity. According to our analysis of socio-demographic data, we observed the highest percentage of 100 respondents were 46-65 years old, 70% were married, 58% were housewife, 88% had a good income, and 40% were obese. The results shown that 83% of rheumatoid patients was suffering from the disease more than two years ago, 59% of them were had an intense pain, 81% were taking an analgesic. There was a significant statistical difference between educational level and the age of the respondents withtheiromega-3 knowledge which was the p-values (0.001, 0.003) respectively, 26% of 54% whose had the knowledge were on academic educational level, we

found that the knowledge was increasing in young groups 15 out 20 of them aged between 26-45 years, had the knowledge compared with only 1 out 11 whose between 66-85years.we also observed that There was no significant statistical difference between family income and omega-3 intake (p=0.1), in which 51% from 60% of patients whose had a poor intake were had a good income. Our result shown a significant statistical difference between omega-3 intake and symptoms(morning stiffness, standing and sitting pain, getting heavy things pain, bending down hardness, house work hardness, prying on chair hardness, and finally up stair pain) in which (P< 0.05), which is confirm the positive result obtained in the previous studies [18-20, 22]. Few studies have explored the role of the diet in the development of rheumatoid arthritis ; in line with a recent case control study comprised 1889 incident cases of rheumatoid arthritis and 2145 randomly selected controls, data on the consumption of oily fish and fish oil supplements, has been obtained through questionnaires, this study found that regular consumption of oily fish was associated with modest decreased risk of developing rheumatoid arthritis, this result support the hypothesis that omega-3 fatty acids may protect against rheumatoid arthritis [20]. Additionally, Joel M Kremer also recommended that patients consume dietary supplements contain 3-6 g of omega-3 daily for >12 week without replace the standard therapeutic medical regiment but be added to it [18]. An American cross sectional analysis using baseline data from participants of average age 60 years, suggested that higher intake of fish >2 time/week may be associated with lower disease activity and significantly lower C-PR in rheumatoid arthritis patients [19] in contrast in a dose response meta-analysis, a non-statistically significant inverse association between fish consumption and rheumatoid arthritis was recently reported [22]. In our analysis we divided the subjects into 3 groups reflecting differences in kind of treatment that used to relieve pain and to assess how omega-3 fatty acids contribute to relive pain. There was a significant statistical difference between the kind of treatment that used to relive pain and symptoms (morning stiffness, standing and sitting pain, bending down hardness, house work hardness, and praying in chair hardness) in which (P < 0.05) in all. Somewhat surprisingly these symptoms was significantly higher among respondents who used analgesic only to relive their pain compared with those (0% -8%) who used omega-3 only to relive their pain, and (10%-20%) who used omega-3 and analgesic to relive their pain from these symptoms. In other hands there was no significant statistical difference between the kind of treatment used and role of omega-3 fatty acids in the relive of pain and symptoms (pain after 15 min standing, up stair pain opening and catching hardness) in which (P>0.05) in all. We observed the highest percentage (54%-55%) of the respondents who suffered from these symptoms used the analgesic only to relive their pain; while about 24% to 28% of the respondents used omega3 and analgesic to relieve their pain from these symptoms.

CONCLUSION

In conclusion we found that frequent consumption of omega-3 rich foods is associated with modest decrease in rheumatoid arthritis disease activity. Based on the finding, the patients especially older people and housewives, should be educated to increase their knowledge and awareness about omega-3 benefits and it is importance in reducing disease's symptoms beside the therapy, increase daily consumption of omega-3, whether from dietary sources or supplementation also should be encouraged .The social class differences should be considered by providing alternative dietary options which is less expensive. However, further research is hence needed to determine whether more frequent consumption of omega-3 rich foods is associated with lower rheumatoid arthritis disease activity.

REFERENCES

1. McInnes, I. B., & Schett, G. (2011). The pathogenesis of rheumatoid arthritis. *New England Journal of Medicine*, *365*(23), 2205-2219.
2. Calabresi, E., Petrelli, F., Bonifacio, A. F., Puxeddu, I., & Alunno, A. (2018). One year in review 2018: pathogenesis of rheumatoid arthritis. *Clin Exp Rheumatol*, *36*(2), 175-184.
3. Calder, P. C. (2013). Omega- 3 polyunsaturated fatty acids and inflammatory processes: nutrition or pharmacology?. *British journal of clinical pharmacology*, *75*(3), 645-662.
4. Szekanecz, Z., Pakozdi, A., Szentpetery, A., Besenyei, T., & Koch, A. E. (2009). Chemokines and angiogenesis in rheumatoid arthritis. *Frontiers in bioscience (Elite edition)*, *1*, 44.
5. Kwoh, C. K., Anderson, L. G., Greene, J. M., Johnson, D. A., O'Dell, J. R., & Robbins, M. L. (2002). American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 update. *Arthritis Rheum*, *46*, 328-346.
6. Gibofsky, A. (2012). Overview of epidemiology, pathophysiology, and diagnosis of rheumatoid arthritis. *The American journal of managed care*, *18*(13 Suppl), S295-302.
7. Gogus, U., & Smith, C. (2010). n- 3 Omega fatty acids: a review of current knowledge. *International Journal of Food Science & Technology*, *45*(3), 417-436.
8. Bourre, J. M. (2005). Where to find omega-3 fatty acids and how feeding animals with diet enriched in omega-3 fatty acids to increase nutritional value of derived products for human: what is actually useful. *J Nutr Health Aging*, *9*(4), 232-42.
9. Surette, M. E. (2008). The science behind dietary omega-3 fatty acids. *Cmaj*, *178*(2), 177-180.

10. Sales, C., Oliviero, F., & Spinella, P. (2008). Role of omega-3 polyunsaturated fatty acids in diet of patients with rheumatic diseases. *Reumatismo*, 60(2), 95-101.

11. Rajaei, E., Mowla, K., Ghorbani, A., Bahadoram, S., Bahadoram, M., & Dargahi-Malamir, M. (2016). The effect of omega-3 fatty acids in patients with active rheumatoid arthritis receiving DMARDs therapy: double-blind randomized controlled trial. *Global journal of health science*, 8(7), 18.

12. Lorente-Cebrián, S., Costa, A. G., Navas-Carretero, S., Zabala, M., Laiglesia, L. M., Martínez, J. A., & Moreno-Aliaga, M. J. (2015). An update on the role of omega-3 fatty acids on inflammatory and degenerative diseases. *Journal of physiology and biochemistry*, 71(2), 341-349.

13. Fernandes, G., & Venkatraman, J. T. (1993). Role of omega-3 fatty acids in health and disease. *Nutrition research*, 13, S19-S45.

14. Calder, P. C. (2013). Omega- 3 polyunsaturated fatty acids and inflammatory processes: nutrition or pharmacology?. *British journal of clinical pharmacology*, 75(3), 645-662.

15. Galarraga, B., Ho, M., Youssef, H. M., Hill, A., McMahon, H., Hall, C., ... & Belch, J. J. F. (2008). Cod liver oil (n-3 fatty acids) as an non-steroidal anti-inflammatory drug sparing agent in rheumatoid arthritis. *Rheumatology*, 47(5), 665-669.

16. Lee, Y. H., Bae, S. C., & Song, G. G. (2012). Omega-3 polyunsaturated fatty acids and the treatment of rheumatoid arthritis: a meta-analysis. *Archives of medical research*, 43(5), 356-362.

17. Goldberg, R. J., & Katz, J. (2007). A meta-analysis of the analgesic effects of omega-3 polyunsaturated fatty acid supplementation for inflammatory joint pain. *Pain*, 129(1-2), 210-223.

18. Kremer, J. M. (2000). n− 3 Fatty acid supplements in rheumatoid arthritis. *The American journal of clinical nutrition*, 71(1), 349s-351s.

19. Tedeschi, S. K., Bathon, J. M., Giles, J. T., Lin, T. C., Yoshida, K., & Solomon, D. H. (2018). Relationship between fish consumption and disease activity in rheumatoid arthritis. *Arthritis care & research*, 70(3), 327-332.

20. Rosell, M., Wesley, A. M., Rydin, K., Klareskog, L., Alfredsson, L., & EIRA Study Group. (2009). Dietary fish and fish oil and the risk of rheumatoid arthritis. *Epidemiology*, 896-901.

21. Geusens, P., Wouters, C., Nijs, J., Jiang, Y., & Dequeker, J. (1994). Long- term effect of omega-3 fatty acid supplementation in active rheumatoid arthritis. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*, 37(6), 824-829.

22. Di Giuseppe, D., Crippa, A., Orsini, N., & Wolk, A. (2014). Fish consumption and risk of rheumatoid arthritis: a dose-response meta-analysis. *Arthritis research & therapy*, 16(5), 1-7.

23. Adam, O., Beringer, C., Kless, T., Lemmen, C., Adam, A., Wiseman, M., ... & Forth, W. (2003). Anti-inflammatory effects of a low arachidonic acid diet and fish oil in patients with rheumatoid arthritis. *Rheumatology international*, 23(1), 27-36.

24. Patterson, E., Wall, R., Fitzgerald, G. F., Ross, R. P., & Stanton, C. (2012). Health implications of high dietary omega-6 polyunsaturated fatty acids. *Journal of nutrition and metabolism*, 2012.

25. Candela, C. G., López, L. B., & Kohen, V. L. (2011). Importance of a balanced omega 6/omega 3 ratio for the maintenance of health. Nutritional recommendations. *Nutricion hospitalaria*, 26(2), 323-329.

26. Bhardwaj, K., Verma, N., Trivedi, R. K., Bhardwaj, S., & Shukla, N. (2016). Significance of ratio of omega-3 and omega-6 in human health with special reference to flaxseed oil. *Int. J. Biol. Chem*, 10(1).

27. Simopoulos, A. P. (2009). Evolutionary aspects of the dietary omega–6: omega–3 fatty acid ratio: medical implications. *A balanced omega-6/omega-3 fatty acid ratio, cholesterol and coronary heart disease*, 100, 1-21.

28. Ko, G. D., Arseneau, L., Nowacki, N., & Mrkoboda, S. (2008). Omega-3 fatty acids and neuropathic pain. *Pract Pain Manage*, 8(7), 21-31.