International Journal of Medicine Research
ISSN: 2455-7404; Impact Factor: RJIF 5.42
Received: 22-11-2019; Accepted: 23-12-2019; Published: 22-01-2020
www.medicinesjournal.com
Volume 5; Issue 1; 2020; Page No. 90-97

Knees osteoarthritis: the effect on general health score SF-12 and its association with aging disorder especially cardiovascular diseases

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Abstract
The study was conducted on 75 patients who fulfilled the diagnostic criteria of knee osteoarthritis (OA) established by the ACR and radiological finding, another group consists of 50 subjects who had no history of knee pain or clinical signs of asymptomatic OA. The aim of this study was to see whether OA of the knees is only a knee aging process or is part of systemic aging. Furthermore the impact of knees OA on general health score Short Form- 12 (SF-12) & its association with aging disorders especially cardiovascular diseases (CVD). The parameters studied including; body mass index (BMI), hand grip strength, electrocardiography (ECG), erythrocyte sedimentation rate (ESR), C- reactive protein (CRP) and malondialdehyde (MDA)and data about co-morbidities including; hypertension (HT), Hyperlipidemia, coronary heart disease (CHD), heart failure (HF), cerebrovascular accident (CVA) and diabetes mellitus (DM) were obtained by questioning subjects or from clinica and laboratory evaluation of cardiac chest pain, HF, Blood pressure, random blood sugar (RBS) and non-fasting serum cholesterol of all patients and control individuals. In addition health related quality of life (HRQoL) and general health was assessed by means of Short form- 12 (SF-12) questionnaire and the data were licensed and scored by the Quality Metric Incorporated/ Health outcomes Scoring Software. The results obtained from the study revealed that knee OA is age related diseases and it is more common in women (90.6% than men. Obesity was present in 80% of patients while was present in 32% of control ($P<0.01$) and this results confirmed the strong association between obesity and OA knee but not with overweight. Patients were significantly more likely to have high levels of comorbidity than controls (85.3% of osteoarthritic patients have co-morbid conditions, while it was in 46% in control ($P<0.01$) and the study had been demonstrated that CVD (HT, HF, CHD, Hyprlipidemia) being most common co-morbidities (82.6% patients had CVD while it is found in 42% of the control, so highly significant difference is fond between patients and control, $P<0.01$). The results of this study revealed that OA and co-morbidities associated with elevated inflammatory markers (ESR and CRP) compared to control ($P<0.01$, $P<0.05$ respectively). Furthermore OA and co-morbidities associated with elevation of oxidative stress (MDA) so a highly significant difference in comparison to control had been found ($P<0.01$). The grip strength of dominant hand found to be much lower than control with highly significant difference ($P<0.01$). OA and co-morbidities such as, HT, CHD and DM considered to have great influence on patients' outcome in this study. The results of general health score (SF-12) showed that health status of patients was worse than control with a significant statistical difference ($P<0.5$, $P<0.01$respectivel). This revealed that comorbidity in patients with OA of the knee is negatively affect the general health status and HRQoL of individuals.

Keywords: osteoarthrosis, aging process, dynamic

Introduction
The aging process is dynamic and involves various changes both in the biological/ physiological level and in the ability to perform daily activities (Avlund, 2004) [7]. The regeneration capacity of cells and other processes due to growth and maturation is lost over time (Canbaz *et al*., 2003) [12]. A wide variety of chronic human disorders are age related; as the population ages, the incidence, prevalence and impact of these disorders increases (Martin and Buckwalter, 2002) [39]. Example for these disorders are: Alzheimer's disease, Parkinson's disease, Atherosclerosis, Myocardial infarction, Hypertension (HT), Diabetes (DM), varicose vein, and Rheumatoid arthritis (RA) (Patrick and Edith 2004). In addition to these, the prevalence of many musculoskeletal disorders also increases markedly with increasing age such as Osteoarthritis (OA) and Osteoporosis (Woolf and Pfleger, 2003) [60]. OA is the most common cause of musculoskeletal disability and it is one of the most common joint disorders in the elderly (Flatharta *et al*., 2006: Zhang *et al*., 2002). OA is a complex, slowly-evolving multifactorial disorder that affects many different joints, particularly those of knee, hand, hip, and spine (Andrianakos *et al*., 2006) [6]. A variety of etiologic risk factors and pathophysiologic processes contribute to the progressive nature of the disease and serve as targets of behavioral and pharmacologic interventions. Risk factors such as age, sex, trauma, overuse, genetics, and obesity can each make contributions to the process of injury in different compartments of the joint. Such risk factors can serve as initiators that promote abnormal biochemical processes involving the cartilage, bone, and synovium (Abramson and Attur, 2009) [1]. The knee is the most frequently involved joint site associated with disability in OA (Andriacchi *et al*., 2000) It is associated with significant morbidity, disability, and medical cost particularly in its advanced stage when total knee replacement may be needed (Wolfe and Lane, 2002) [59]. Since OA knee is characterized by an age- related cartilage degeneration, other age- related disabling conditions are likely to coexist with it (Chan *et al*., 2009) [14]. Numerous studies have described changes in articular cartilage that are relatively consistent and inevitable consequences of aging. These include mild fibrillation (fraying) and softening of the articular surface, a decrease in

the average size of the proteoglycan monomers along with a decrease in the aggregation capacity of these molecules, and overall loss of matrix tensile strength and stiffness. These molecules, and overall loss of matrix tensile strength and stiffness. These types of changes may be related to the proposed age-related shift in the chondrocyte phenotype rendering the remaining resident cells less capable of maintaining cartilage homeostasis and setting the stage for overt degenerative cartilage disease (Horton *et al*., 2006) [29]. Importantly, increasing age is a risk factor for many diseases that greatly affect our health status. For example cardiovascular diseases (CVD) such as atherosclerosis, coronary heart diseases, HT, stroke, heart failure and peripheral arterial occlusive diseases (Yang, 2007) [29]. There is credible evidence that people with OA and RA are significantly associated with increasing risk for CVD (Singh *et al*., 2009) [51], Furthermore, a recent study showed that disability in older people was an important risk factor for increased mortality independent of age and co-morbid conditions (Nuesche *et al*., 2011). These co-existing health problems can interact with each other and produce high level of disability and management problems that complicate health care use and costs, therefore general practitioners should be alert to the presence of co-morbidities when managing patients with OA of the knee (Chan *et al*., 2009) [15]. Disability in knee OA influenced by many factors including pain, increasing age, decreasing educational status, obesity, female gender, comorbidity, and quadriceps muscle weakness; the role of psychosocial factors, notably depression and anxiety, is less clear (Creamer *et al*., 2000). Measurement of disability has been achieved by many instruments; some of these are designed for use in specific diseases, whereas others are applicable to various conditions (Hasrrison and Mandi 2006). At present the most popular generic (disease nonspecific) measure of clinical outcome is probably the 36-item short form health survey (SF-36), subsequently, a 12-item subset of original 36 item was developed (SF-12) this short form includes a physical component summary scale scores (PCS) and mental component summary scale scores (MCS) (Jenkinson *et al*., 1997). These generic instruments measure "quality of life" and more specifically "health related quality of life" (HRQoL) refer to the physical, psychological, and social domains of health, seen as distinct areas that are influenced by person's experiences, beliefs, expectations, and perceptions (Cote *et al*., 2004). The impact of non-traumatic hip or knee disorders oon HRQOL is substantial, especially on the physical aspects of HRQOL, because of their strong effect on functional disability, health care costs and work disability (Vander Waal *et al*., 2005) [56].

Aim and Specific objectives

1. To see Whether OA of the knees is only a knee aging processor it is a part of systemic aging.
2. The effect of knees OA on general health score SF-12& its association with aging disorder especially cardiovascular diseases.

Subjects and Methods

This clinical study was conducted in the rheumatology outpatient clinic of Ibn-Sena teaching hospital. Patient collection started in December 2010 with co- operation of medical staff.

Study design

It is controlled case- series study.

Subjects

Patients

Seventy five patients aged 50 years and older of both sexes, who fulfilled the diagnostic criteria of knee osteoarthritis (OA) established by the ACR and confirmed by radiographic film, were included in this study (Hiadari, 2011) [28].

Table 1: Criteria of knee osteoarthritis

Knee pain+ 30 of 6	Rt.	Lt.
Age > 50		
Stiffness <30 minutes		
Crepitus on active motion		
Bony tenderness		
Bony enlargement		
No palpable warmth of synovium		

Controls

Fifty individuals matched for age and sex with the patients. They had no history of knee pain or clinical signs of asymptomatic OA.

Inclusion criteria

1. Fifty years and older of both sexes.
2. Knee(s) pain.

Exclusion criteria

1. Secondary osteoarthritis (History of traumatic injury of the knee, local and systemic inflammatory conditions).
2. Crystal joints diseases History of (Gout, Calcium deposition diseases.
3. Neoplastic conditions.

Data collection

The main source of data was obtained directly from all the studied subjects during interviews with them. The study was designed as controlled case- series study. Basic demographic and clinical data were collected during the study using a questionnaire concerning: age, gender, history of hypertension (HT), hyperlipidemia, coronary heart disease (CHD), heart failure (HF), cerebrovascular accident (CVA), diabetes mellitus (DM) in addition health related quality of life questionnaire. Body weight in (kg), height in (m), results of clinical and laboratory evaluation had been recorded.

Methods

Doubts have been expressed about the validity of ACR criteria (Peat. 2006) [4] therefore the specificity of the criteria was strengthen by excluded criteria and radiographic film. Radiological interpretation was done for all patients on standing anterior- posterior radiograph of the two legs with both knees fully extended. the radiologist evaluate the severity and distribution of joint space narrowing (JSN) and osteophytes in the osteoarthritic knee using semi quantitative grading system (score, 0 to 3). The severity of JSN was graded as 0= normal, 1= mild or 1-33% narrowing of joint space, 2= moderate or 34-66% narrowing of joint space, 3= severe or 67- 100% narrowing of joint space. Osteophytes were graded as 0= absent, 1= small beak like, 2= intermediate size, 3= proliferating or mushroom- like osteophytes. (Chan *et al*., 2008) [14].

For both the patients and control the following clinical assessment had been done.

- Weight, Height and body mass index (BMI) calculation was done according to the following equation: BMI= weight (Kg)/ height (m2). (Hanlon *et al*., 2010).
- Questionnaire concerning the history and duration of chronic systemic diseases [CHD, HT, HF, CVA, hyperlipidemia, DM].
- The subjects who had no history of CHD were furthermore interviewed about previous or recent symptoms of chest pain, the initial clinical evaluation will help to determine whether chest pain is due to CHD or other causes depending on the clinical classification of chest pain (Snow *et al*., 2004) [52].
- The subjects who had no history of CHF, clinical evaluation had been done according to Framingham criteria for HF diagnosis. (Yturralde and Gaasch, 2005) [62].
- Measurement of blood pressure for subjects without history of HT, in the sitting position with the arm supported and repeated after 5 mints rest if the first recording is high. A reading of systolic blood pressure (BP) ≥ 140 mm Hg and diastolic BP ≥ 90 mmHg considered to be HT. while reading of systolic blood pressure ≥ 140 mmHg and diastolic BP < 90 mmHg considered to be systolic HT (Newby *et al*., 2010).
- Resting ECG for all subjects had been done and the cardiologist recorded the results.
- For all subjects grip strength measurement for both hands had been done. The sphygmomanometer cuff was evenly rolled and inflated to 30 mmHg, which is the starting measurement of each subject, for the arm to be tested, the elbow flexed to 90, the forearm and wrist were in neutral positions, and the fingers were flexed as needed for maximal contraction. Each subject instructed to breathe through the nose and blow out through pursed lips in order to demonstrate maximum hand grip (Hamilton *et al*., 1992) [25].
- Physical composite summary scale (PCS) & Mental composite summary scale (MCS) are computed using the scores of twelve questions, and range from 0 to 100, where a zero score indicates the lowest level of health measured by the scales and 100 indicates the highest level of health (Wee *et al*., 2008) [57]. The data of Short from- 12 (SF-12) questionnaires were licensed and scored by the Quality Metric Incorporated/ Health outcomes Scoring Software. This SF- 12 questionnaires has been extensively used in the literatures and it is validity has been used previously (Kontodimpopoulos *et al*., 2007).
- Erythrocyte sedimentation rate (ESR) by Westrengreen method, C-reactive protein (CRP) using Capillary Tub Method.
- The amount of lipid peroxidation products present in the serum samples was estimated by thiobarbituric acid (TBA) method for random sample of patients and all control, which measures malondialdahyde (MDA) reactive products using High Pressure Liquid Chromatography (HPLC).
- For those not known case of hyperlipidemia a non-fasting sample of total serum cholesterol has been done (Huang *et al*., 2011) [15].
- Individuals free of CHD with total cholesterol level from 200- 239 mg/di (5.18-6.22 mmol/L) are classified as borderline high blood cholesterol (Craig *et al*., 2000) [19] further evaluation had been suggested.
- For those not known case of DM, a non-fasting sample of random blood sugar (RBS) has been done. Using Glucose- Oxidase- Peroxidase Colorimetric Method. If RBS≥ 200 mg/di (11 mmol/L) plus symptoms (Thirst, Dry mouth, polyuria, nocturia, wt. change (obesity), malaise, fatigue, blurring of vision, genital Candida, nausea, headache) (Chau and Edelman 2001) [16], they were marked as having hyperglycemia and further evaluation had been suggested.

Results

Table 1: The number and percentage of males and females in all studied groups.

Groups	Male		Female	
	No.	%	No.	%
Control	6	12	44	88
Patients	7	9.3	68	90.7

Table 2: The age of control and patients groups, data expressed as Mean ± SD

Group	Control	Patients
Age (in years)	59.5±5.97	60.6±7.36

Table 3: Body Mass Index (BMI) of control and patient groups.

BMI (Kg/m^2)	Control	Patients	P. value
Normal Weight (18.5- 24.9)	17(34%)	7(9.3%)	0.001
Over Weight (25- 29.9)	17(34%)	8(10.7%)	0.002
Obese (≥30)	16(32%)	60(80%)	0.001

Table 4 shows a comparison of number and percentage of chronic disease between control and patients, a statistically significant difference is present in the number and percentage of hypertension and hyperlipidemia between control and patients.

Table 4: Comparison of number and percentage of chronic disease between control and patients.

Diseases	Control	Patients	P. value
HT	17(34%)	47 (62.7%)	0.001
Hyperlip.	6(12%)	29(38.7%)	0.001
CHD	5(10%)	16(21.3%)	0.074
HF	2(4%)	8(10.7%)	0.148
DM	8(16%)	16(21.3%)	0.447
CVA	2(4%)	1(1.3%)	0.385

HT=hypertension, Hyperlip= Hyperlipidemia, CHD= Coronary heart diseases, HF= Heart failure, DM= diabetes mellitus, CVA= Cerebrovascular accident.

Table (5) shows a comparison of number and percentage of chronic disease between control and patients (without previous history of any chronic conditions) were obtained by clinical and laboratory evaluation. A statistically significant difference is found in the number and percentage of hyperlipidemia and high BP only between control and patients (P-value= 0.034, 0.021 respectively.).

Table 5: Comparison of number and percentage of chronic disease between control and patients (without previous history of any chronic conditions).

Diseases	Control	Patients	P. value
Cardiac chest pain	4(5.3%)	5 (6.6%)	0.78
HF	0	3(4%)	0.07
Hypergl.	3(6%)	3(4%)	0.62
Hyperlip.	7(14%)	23(30.6%)	0.021
High BP.	1(2%)	8 (10.7%)	0.034

Hypergl= hyperglycemia, BP=blood pressure, HF= Heart failure, Hyperlip= Hyperlipidemia.

Table 6: Number and percentage of control and patients with CVD and ischemic changes in the ECG.

Parameter	Control	Patients	P. value
CVD	21(42%)	62(82.7%)	0.001
ECG	15(30%)	46(61%)	0.001

CVD= Cardiovascular diseases, ECG=Electrocardiography.

Table 7 shows a comparison of the ESR, CRP, MDA and hand grip between control and patients, there is a significant difference in the mean of ESR between control (15.44mm/hr) and patients (22.28mm/hr), p-value- 0.002. A statistically significant difference was also found in the mean of CRP between control (1.32) and patients (5.45), p-value 0.04. A significant difference in the mean of MDA between control (1.32) and patients (1.48), p-value= 0.001. A statistically significant difference was also found in the strength of hand grip between control (56.9) and patients (34.9), p-value= 0.001.

Table 7: Comparison of the ESR, CRP, MDA and hand grip between patients and control. Data expressed as Mean±SD.

Parameter	Control	Patients	P. value
ESR (mm/hr)	15.4±9.55	22.2±12.28	0.002
CRP (mg/L)	1.3±4.20	5.4±1401	0.048
MDA (µmol/l)	1.4±0.33	3.4±1.139	0.001
HG (mm/Hg)	56.9±27.51	34.9±26.54	0.001

ESR= Erythrocyte sedimentation rate, CRP=C-reactive protein, MDA= malondialdahyde, HG= Hand grip strength of dominant hand.

Table 8 shows a comparison of SF-12 between control and patients, the mean of PCS in the control is 48.18. While in patients is 31.9, so a statistically significant difference is found between patients and control, p-value= 0.01. Again, the mean of MCS in the control is 52.9 while in patients is 40.6, so a statistically significant difference is found between patients and control, p- value= 0.001.

Table 8: comparison of SF-12 between patients and control. Data expressed as Mean ± SD.

SF-12/ mean	Control	Patients	P. value
PCS	48.1±5.98	31.9±9.12	0.017
MCS	52.9±7.12	40.6±11.66	0.001

SF-12=Short form-12, PCS=physical composite summary scale, MCS=Mental composite summary scale.

Table 9 shows the correlation between PCS, MCS with age, JSN and hand grip. PCS and MCS were negatively correlated with the age (r = -0.236, r = -0.171 respectively), significant correlation present between the PCS and the age p-value= 0.04. PCS and MCS were negatively correlated with the JSN (rho= -0.348, rho= -0.16 respectively), and significant correlation present between the PCS and the JSN p-value=0.002. There was positive correlation between the PCS, MCS and hand grip (r = 0.291, r = 0.490 respectively) and significant correlation present between PCS, MCS and hand grip (p-value=0.01, 0.001 respectively).

Table 9: association of SF-12 of the patients with age, JSN and HG.

Parameter	PCS	MCS
Age	-0.236*	-0.171
JSN	-0.348**	-0.160
HG	0.291*	0.490**

***** Correlation significant at 0.05 level.
****** Correlation significant at 0.01 level.
JSN= joint space narrowing, **HG**=hand grip.

Discussion

The co-existence of multiple chronic diseases is common especially in the older population and it is associated with decline in many health outcomes, such as quality of life, mobility, functional ability, and increase psychological distress (Caughey *et al*., 2008) [13]. The present study was performed to further explore the concept of systemic aging which may involve more than one organ through related mechanisms. And to assess the effect of knees OA on general health score Short Form012 (SF-12) & its association with aging disorder especially cardiovascular diseases (CVD). Since OA knee is age related condition, other co-existing chronic and disabling conditions can be expected (kadam *et al*., 2004) [32]. The present study showed that, the mean age of patients was 60.6 years, and 90.7% were female. These result are in concordance with previous large studies in which OA of knee is the most common musculoskeletal problem in individuals older than 50 years (Beary and Luggen, 2006) [9]. Another study had been done by Iqbal *et al*., 2011 revealed that females of age greater than 55 years mostly noted to visit a tertiary care hospital due to knee OA. The role of estrogen and other sex hormones in osteoarthritis had a long standing theme in osteoarthritis research and the symptomatic osteoarthritis is clearly more common in women than in men, and its dramatic rise in incidence around the time of menopause (Rosenthal, 2007: Mahajan *et al*., 2005) [47, 37]. The present result confirmed the strong association between obesity (BMI≥ of 30) and OA knee, we found that 80% of patients were obese while obesity was present in only 32% of control with significant statistical difference ($p<0.01$) however overweight was not associated with knee OA in this study. Obesity, is a known risk factor for OA knee, may explain this association (Grotle *et al*., 2008) [23]. This agree with study had been done in morocco confirmed that obesity represents independent risk factor for Knee OA (Mounach *et al*., 2007) [41]. Marks, 2007 [38] said that that even being overweight is associated with increases in the amount of forces across a weight-bearing joint, and development of OA at all joints studies and at knee in the particular. Teichtahl *et al*., 2007 demonstrated that elevated weight or BMI, is unequivocal risk factor for the onset, progression, and symptoms of the knee OA. ALObaidi, 2007 [3] found that idiopathic osteoarthritis of the knee occur more in women in addition age and overweight has a direct effect on the development of primary osteoarthritis of the knee joint. In this study we find that alongside OA there are other co-morbid conditions, including HT (62.66%), Hyperlipidemia

(38.66%), CHD (21.33%), Heart failure (HF) (10.66%), DM (21.33%), CVA (1.33%). The significant difference between control and patients is found in both HT and hyperlipidemia ($p<0.01$). Previous studies revealed that age group commonly affected by HT is 50 years and above. OA and HT are thus two common conditions which may co-exist (Mackenzie and MacDonald, 2009). Furthermore, Canbaz *et al*., 2003 [12] note that the major health problems of the elderly are chronic and degenerative diseases whose frequencies increase with age. In 85.3% of osteoarthritic patients have co-morbid conditions, while it is 46% in control with significant difference ($p<0.01$), Since OA knee is a possible explications for the relation between OA and those co-morbidities include shared etiology and pathophysiology or the result of aging biological process, in which different events occur more frequently (cartilage degeneration, increased insulin resistance, weight gain, dyslipidemia), and, thus, can appear simultaneously, even if not interrelated (Leite *et al*., 2011) [35]. This study agree with other studies of kadam *et al*., 2005 [32]; Leite *et al*., 2011 [35] which revealed that comorbidity in OA patients was very high such as metabolic syndromes, HT, dyslipidemia, obesity, DM and depression. The results of clinical and laboratory evaluation of subjects without previous history of any chronic conditions showed that; 6.6% of patients fulfilled the clinical classification criteria of cardiac chest pain, four percent of patients fulfilled the Framingham criteria of congestive heart failure diagnosis, hyperglycemia (Random blood sugar ≥ 200 mg/dl plus symptoms) is found in 4% of patients. In this study the results of laboratory evaluation of subjects without previous history of hyperlipidemia, high cholesterol level reported in 30.6% of patients while 14% in control with significant difference ($p<0.05$), Al-Arfaj, 2003 [32] reported an association between high cholesterol levels in both knee and generalized OA. In addition the results of blood pressure (BP) measurement also revealed increased BP in 10.6% of patients and 2% of control. There is significant difference ($p<0.05$). Breedveld, 2004 [11] note that comorbidities such as HT, CHD, peripheral vascular disease, HF, renal function impairment, DM and respiratory disease are common in OA patients. In this study, the results demonstrated the percentage of patients with history of cardiovascular diseases (CVD) including (HT, HF, CHD and Hyperlipidemia) which is higher than control with statistically significant difference ($p<0.05$). Furthermore, the ischemic changes in the ECG is present in 61% of patients group which is much more higher than control 30% with statistically significant difference ($p<0.05$), this is consistent with previous study which had been demonstrated that CVD being most common non- musculoskeletal co-morbidities (Chan *et al*., 2009) [14]. In this study there is significant association between patients and control regarding inflammatory markers [Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)] ($p<0.01$, $p<0.05$ respectively). Although OA inherently lack significant inflammatory response, a low- grade inflammatory response has been suggested by earlier studies, and the systemic markers of inflammation are associated with severity of clinical course of OA (Bassiouni *et al*., 2010) [8]. The results correlated with study revealed that modest elevation of ESR are seen in OA and more persistently in patients with generalized polyarticular osteoarthritis (Saraf *et al*., 2002) [48]. Other study demonstrated that CRP but not ESR rate is associated with clinical severity in patients with osteoarthritis of the knee or hip (Wolfe, 1997) [58]. In the present study there was a highly significant difference between patients with knee OA and control regarding oxidative stress ($p<0.01$). Shah *et al*., 2005 [50] demonstrate that in age-related degenerative diseases, such as those of the brain and cardiovascular systems, lipid peroxidation has been implicated as the key source of oxidative stress. Another study had been done by Tetik *et al*., 2010 [54] confirmed the role of free radical reactions in the pathogenesis of primary OA and Rheumatoid arthritis. It is known that mechanical and chemical stresses may change the cellular adaptation to hypoxia, and leading to oxidative damage, resulting in down regulation of chondrocyte synthesis in osteoarthritis, furthermore, oxidative stress which is often arises as a result of an imbalance in the human oxidative/ ant oxidative status, has been implicated in aging and a number of diseases such as cancer, atherosclerosis, rheumatoid arthritis, osteoarthritis, fibromyalgia and osteoporosis (Altindag *et al*., 2007) [4]. Grip strength has been used as indicator of overall muscle strength which is declined in patients with arthritis, CHD, CVA, and DM (Rantanen *et al*., 1998) [46]. The results of dominant hand grip measurement for both patients and control demonstrated the much lower strength of hand grip in patients, with a highly significant difference ($P<0.01$). Beside OA commonly affecting the cervical and lumbar spine, most epidemiological studies report a disease predilection for lower extremity weight bearing joints and certain hand joints (Gunther *et al*., 1998). Among individuals with radiographic hand OA, increasing radiographic severity is associated with reduced grip and pinch strength (Dominick *et al*., 2005) [21]. Hand-grip strength is a useful marker to assess patient's physiologic status furthermore co-morbidities such as DM, HT, CHD, or other disease considered to have great influence on patients' outcome (Chen *et al*., 2011) [15]. Clinical outcomes for people with OA typically involve pain, limitation of daily living activities, and over all diminution of health related quality of life (HRQoL). One of the most commonly used instruments to measure HRQoL is Medical Outcome Study 36-item Short Form (SF) health survey (Moskowitz, 2009) [40]. However, the SF- 36 contain 36 items and thus places considerable burden on both patients and investigator. Ware and colleagues, therefore, decided to develop a substantially shorter questionnaire the SF-12- reducing the number of items from 36 to 12 (Nordhorn *et al*., 2004) [43]. The data of SF-12 questionnaires were licensed and scored on line by the Quality Metric Incorporated/ Health outcomes Scoring Software. The results of general health score both physical composite summary scale (PCS) and Mental composite summary scale (MCS) showed that health status of patients was worse than control with a significant difference ($P<0.05$, $P<0.01$ respectively). The causal relation is not due to OA only but the high percent have coexisting disease (86.6%). The impact of OA is substantially increased by the common occurrence of comorbid conditions such as HT (Breedveld, 2004) [11] in addition comorbidity was significantly associated with reduced HRQoL (Tuominen *et al*., 2007) [55]. A study in England has concluded that the presence of co-morbidities increases the frequency of physical disability in OA patients, and the influence of the combination is higher than that expected for OA alone or for each disease in isolation (Leite *et al*., 2011) [35]. Other study showed that rapidly increasing burden of chronic diseases such as; CVD, DM and OA, is a key determinant of global public health and it is negatively affect the general health status and HRQoL of individuals (Boume *et al*., 2009) [10]. The validity of the Arabic

conversational SF-12 had been tested and the results demonstrated that the PCS & MCS of SF-12 in patients is negatively correlated with age (r= -0.236, r=- 0171 respectively) and the significant correlation present in PCS (P<0.05). A possible explanation of this finding is presence of co-morbidities which is associated with decline in many health outcomes such as functional ability and increase psychological distress (Caughey *et al*., 2008) [13]. This result agree with the study had been done by kontodimopoulos *et al*., 2007. Negative association present between PCS, MCS and radiological feature in concern to joint space narrowing (JSN) (rho= -0.348, rho= -0.16 respectively) with significant correlation is present between JSN and PCS (P<0.01). This agree with studies In Korean community residents aged 50 years and older, the presence of radiographic tibiofemoral OA significantly impaired the HRQoL and function (Kim *et al*., 2010) [33]. The positive association is present between PCS, MCS and grip strength of dominant hand (r=0.291, r=0.490 respectively) with a significant correlation is present for both PCS and MCS. (P<0.05, P<0.01 respectively). Co-morbidity is a possible explanation for the associations. Previous study suggest that lower grip strength is associated with reduced HRQoL in older men and women (Sayer *et al*., 2006) [49].

Conclusions & Suggestions

On the basis of the result obtained in the present study, the following conclusions can be concluded:

1. Knee Osteoarthritis is age related diseases and it's more common in women than men. Obesity is one of the most important risk factors for OA in knee (s), while over weight is not a risk factor in this study.
2. The co-existence of multiple chronic diseases is common especially in the older population and OA associated with high levels of co-morbidities. Furthermore the study had been demonstrated that Cardiovascular disease CVD (Hypertension, Heart failure, Coronary heart diseases, Hyperlipidemia) being most common comorbidities.
3. Elevated inflammatory markers Erythrocyte sedimentation rate and C- reactive protein in addition to Malondialdahyde may reflect underlying chronic inflammation in patients group.
4. Comorbidity in patients with osteoarthritis of the knee is negatively affected the general health status and Health related quality of life of the individuals.
5. Clearly there is a need for more studies on multimorbidity in old age group to provide a strong evidence base on which to develop appropriate guidelines for the care and management of the patients. Furthermore the specific combinations of chronic diseases need further exploration, in order to gain more insight into patterns of disease clustering and hypothetically common etiology.
6. Physicians should be alert to the presence of co-morbidities a long side with OA because these problems can interact with each other to produce high level of disability. Moreover, comorbidity also lead to management problems.
7. For osteoarthritic patients who had no history of chronic disease, further evaluation should be suggested for any hidden problems such as: Ischemic heart disease, Hypertension, Heart failure, Hyperlipidemia, Diabetes mellitus and Electrocardiographic abnormalities.
8. General health assessment most be performed regularly in order to define the impact of diseases and to direct the patients for proper management.

Abbreviations

Abbreviations	The original form
ACR	American College of Rheumatology
BMI	Body Mass Index
CHD	Coronary heart disease
CRP	C-Reactive Protein
CVA	Cerebrovascular Accedent
CVD	Cardiovascular Disease
DM	Diabetes Mellitus
ECG	Electrocardiography
ESR	Erythrocyte Sedimentation Rate
HF	Heart Failure
HRQol	Health related quality of life
HT	Hypertension
JSN	Joint Space Narrowing
MCS	Mental composite Scores
MDA	Malondialdahyde
OA	Osteoarthritis
OP	Osteoporosis
PCS	Physical Composite Scores
PG	Proteoglycan
ROS	Reactive oxygen species
SF-12	Short form- 12

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