

Comparison of Cryotherapy and Thermotherapy on Pain and Functional Mobility in Unilateral Knee Osteoarthritis A Randomize Controlled Trial

Salman Zafar^{1*}, Arif Ali Rana¹, Qasim Idrees¹, Syed Zeeshan Zafar² and Aqsa Imran³

¹University Institute of Physical Therapy, Faculty of Allied Health Sciences, The University of Lahore, Lahore, Pakistan

²National College of Business Administration & Economics, Lahore, Pakistan

³Services Institute of Medical Sciences, Lahore, Pakistan

Abstract:

Among all the pharmacological therapies, the thermotherapy is believed to be a quite advantageous and mostly employed therapy. Typically, Ice is used for acute injuries and warmth is used for sprains and strains. It seems appropriate to use hot and cold packs in osteoarthritis according to targeted problem to be addressed.

Objective:

To compare the thermotherapy and cryotherapy in treatment of unilateral knee osteoarthritis.

Methods:

The study design was a randomized controlled trail. Study was conducted through pre-tested questionnaire at Department of Physiotherapy, Nawaz Sharif Social Security Hospital, Lahore. Total 100 patients were taken in study and randomly divided into 2 groups. In Group-A patients were treated with Thermotherapy and in Group-B patients were treated with Cryotherapy. The grades of pain were assessed on VAS and severity of disease was assessed through WOMAC index.

Results:

In both treatments group 50 patients were enrolled. For pain reduction Group-A patients who were treated with thermotherapy reported less pain during their daily physical activities at the end of 4th week. A significant difference was present for pain in both treatment groups. But for Muscle strength and muscle flexibility both the treatment were not completely effective. For few parameters patients who were treated with thermotherapy shows tremendous results and for other parameters cryotherapy shows effective results.

Conclusions:

Thermotherapy was more effective than Cryotherapy for the management of unilateral knee osteoarthritis. But for few parameters i.e. (Pain, Physical Activity) thermotherapy was effective and for other parameters

cryotherapy is effective.

Keywords:

Cryotherapy, Thermotherapy, Pain, Unilateral Knee Osteoarthritis.

Introduction:

The most common kind among all kinds of osteoarthritis is Knee osteoarthritis. Approximately More than 10 million USA citizens are reported to come with osteoarthritis of knee and it is also reported that it is the most common reason of disability in the America. If early diagnosis is made then that can help to treat its symptoms. The major problem associated with Knee osteoarthritis is deterioration of articular cartilage which is responsible for musculoskeletal as well as physical damage. Reasons like previous history of knee injury, recurrent knee strain, fractures of bone and ligament tear are most frequent causes of Knee osteoarthritis.¹

Different diagnostic procedures like history, physical examination, and radiographs are common methods to diagnose knee osteoarthritis. Among all these methods, X-rays are considered to be extremely helpful as the doctor can clearly judge to see evident signs of narrowing of joint space and exclude other possible reasons of knee pain.² Usually Knee Osteoarthritis develops over a period of years. Symptoms like pain (that may range from mild to moderate, or severe), stiffness, limited range of motion in the knee, localized swelling are primary indications of knee osteoarthritis. Pain specifically, is quite severe when it is associated with Knee osteoarthritis during activity in general, and while overusing the affected knee, in particular³ Stiffness, on other hand, can get worse after sitting for prolonged periods of time. It is suggested that an early stage diagnosis and treatment of knee osteoarthritis is more beneficial and easily managed compared to when it has worsen. Medications such as acetaminophen, can manage and reduce pain. Aside from medications, other non-medical treatments include exercise /

physical therapy, weight loss if overweight, joint protection techniques, heat and cold.⁴ Thermotherapy consist of the heat application, whilst cryotherapy involves the cold application for the purpose of relieving osteoarthritis symptoms in joints affected by osteoarthritis.⁵ In a review article, 3 randomized controlled trials, consisting of 179 patients varied with regard of study design, outcomes measured, cold or heat treatments and overall methodological quality. In one trial, application of 20 minutes of ice massage, 5 days/ week, for 3 weeks, was done and compared with controls groups showed a clinically important improvement for knee OA which results in improving quadriceps strength (29% relative difference). There was also improvement which was statistically significant, but no clinical improvement was seen in knee flexion range of motion (8% relative difference) as well as functional mobility (11% relative difference) was seen. Massaging with ice improved muscle strength in the leg, the range of motion in the knee and decreased time to walk 50 feet compared to no treatment. Second trial showed that cold packs decreased knee edema. Ice packs therapy for 3 days/ week for the period of three weeks reduces pain just as was seen in control group. Third study reported that ice packs for about 20 minutes for 10 sessions reduces inflammation more as compared to control group/without any treatment. Hot packs also require the same time duration showed the similar effect on inflammation as was seen in no treatment/control group.⁶ Briefly it can be stated that, ice massage shown to be beneficial in terms of knee strength, ROM and daily function. Ice packs reported no significant effect to reduce knee pain. Application of cold packs showed beneficial results in reduction of swelling. Hot packs did not significantly reduce inflammation.⁷

Symptomatic knee OA has been documented to exist in approximately 10% of men and 13% of women that were 60 years or older. During the period of one year, 25% of were over 55 years reported sustained episodes of knee pain, among those about 1:6 have to get appointment with their general physician about it in the same time. Literature shows that prevalence of OA of knee in men is lower compared with women.⁸ The results of this study demonstrated sex differences in incidence of knee OA particularly after menopausal age. Females, especially those ≥ 55 years, have relatively severe knee OA than in other sites. The highest prevalence of moderate-to-severe knee osteoarthritis was observed in middle-aged women and this prevalence rates of knee OA may show a

discrepancy with specification of different study populations as well as the methods used for its diagnosis.⁹ The prevalence of knee osteoarthritis was examined and investigated in 2282 people aged ≥ 60 years (1,465 women and 817 men) living in developed areas of Japan. The prevalence rate was significantly higher among women than in men and increased significantly with age. In the study 38% men were reported to have Knee symptoms, radiographical knee OA, symptomatic OA of knee. 28% of symptomatic subjects had radiographic knee osteoarthritis, 16 percent had only symptoms of knee OA, and eight percent had severe radiological knee OA. Afro-Americans had relatively more prevalence of knee OA symptoms, radiographical knee OA and symptomatic OA of knee, but significantly higher cases of severe knee OA that is radiographic as compared with Caucasians. Osteoarthritis is the most common widespread joint disorder in the America as well as throughout world. Osteoarthritis is one of the most common causes of disability and pain in older. Almost 1/3 of people of age 65 years have knee OA which can be seen easily on x-ray. 70 percent of subjects over seventy years have radiographic finding of osteoarthritis. Below 50 years of age, osteoarthritis is said to be more common among males as compared to females but after 50 years, women seen to be more affected by osteoarthritis than men. OA risk factors are as follows: Overweight women are 4-5 times more vulnerable to develop knee OA when compared with normal weight people. Acute injuries are seen to be main reason of knee osteoarthritis. Mill workers and farmers and other operators have high incidences of osteoarthritis. Deformities of the hip and knee can cause early osteoarthritis. Women taking estrogen hormone are at lower risk as compared with that are not taking this hormone. It is reported that OA is more common in Afro-Americans. Pseudogout, Gout, Rheumatoid arthritis and hemochromatosis can increase OA risk. Diet or any other reason of vitamin deficiency is also elevate the knee OA risk.¹⁰ All synovial joints have some fluid in them that is called synovial fluid. This fluid comes from plasma after filtration and moves into knee with hyaluronic acid. This fluid transports nutrition reduces friction and protects the joints.¹¹⁻¹³

Rationale of this study was to compare thermotherapy with cryotherapy in patients of unilateral knee osteoarthritis presented with pain and decreased range of motion. Both procedures can be done easily at home and are cost effective but cryotherapy is more time effective as compared to thermotherapy as it improves

the condition of the patient in lesser period. So that the implementation of the cryotherapy might be suggested as first line treatment for patients of unilateral knee osteoarthritis presenting with swelling.

Methods:

A randomized controlled trial was conducted at Department of Physiotherapy, Nawaz Sharif Social Security Hospital Lahore with objective to compare thermotherapy with cold therapy on unilateral knee osteoarthritis. Duration of study was 6 months in which two groups were made. In group A patients were treated with thermotherapy and in group B patients were treated with cryotherapy. Sample size was 100, non-probability, purposive sampling was used, 50 cases in each group was calculated with 95% confidence level, 4.5% margin of error and taking expected percentage of knee osteoarthritis i.e. 5% among general population. Patients of 35 or more years of age both genders diagnosed with osteoarthritis of unilateral knee joint assessed through clinical examination. The grades of pain were assessed on VAS (Visual Analogue Scale) and severity of disease was assessed through WOMAC (Western Ontario & McMaster Universities Osteoarthritis) index for muscle flexibility, muscle strengthening and tolerance scale and range of motion (ROM) was measured. All the above information was noted on pre-tested questionnaire.

Data was analyzed using SPSS version 11.5. Categorical variables were expressed as frequency and percentages whereas continuous variables were expressed as Mean $\pm$ SD. Chi-square test was applied to compare the categorical variables. Mann-Whitney U-test was used to compare the continuous variables. Repeated measurement ANOVA was applied. p-value ≤ 0.05 was considered significant.

Results:

In both treatments group 50 patients were enrolled.

	Treatment Group	
	Group-A	Group-B
N	50	50
Mean	56.86	57.42
Std. Deviation	6.373	8.612
Range	25	40
Minimum	47	35
Maximum	72	75

Table 1: Descriptive Statistics for Age (Years) with respect to Treatment Groups

Group-A= Thermo Therapy

Group-B = Cryotherapy

In Group-A mean age of patients was 56.86 ± 6.37 and in Group-B mean patients was of age 57.42 ± 8.612 .

		Treatment Group		Total
		Group-A	Group-B	
Stage of Osteoarthritis	Stage 1	0	7	7
	Stage 2	31	18	49
	Stage 3	17	15	32
	Stage 4	2	10	12
Total		50	50	100

Table 2: Stage of Osteoarthritis with respect to Treatment Group

Group-A= Thermo Therapy

Group-B = Cryotherapy

In Group-A 31 patients were presented with Stage-2, 17 patients presented with Stage-3 and 2 patients presented with Stage-4 osteoarthritis. In Group-B 7 patients presented with Stage-1, 18 patients presented with Stage-2, 15 patients presented with Stage-3 and 10 patients presented with Stage-4 osteoarthritis.

		Working hours	Standing hours
Group-A	Mean	10.62	4.86
	Std. Deviation	3.14	1.82
	Range	13.00	8.00
	Minimum	5.00	2.00
	Maximum	18.00	10.00
Group-B	Mean	8.48	4.74
	Std. Deviation	1.58	2.01
	Range	8.00	10.00
	Minimum	6.00	2.00
	Maximum	14.00	12.00

Table 3: Working and Standing Hours with respect to Treatment Group

Group-A= Thermo Therapy

Group-B = Cryotherapy

Above table describes the working and standing hours of patients in both treatment groups

Tables 4 and 5 describe the physical function score measured at different intervals in both treatment groups. These physical function scores were measured for different daily life activities. Overall treatment-A is best in terms of pain reduction during different daily life activities.

Sr. #	Pain Score (0-10)	Group	N	Follow Up			p-value	
				Base Line	1 st	2 nd	Overall	Group
1	Walking on Flat Surface	Group-A	50	4.20±0.15	3.34±0.16	0.84±0.17	0.000	0.000
		Group-B	50	7.30±0.18	6.56±0.172	4.92±0.17		
2	Going up & Down Stairs	Group-A	50	6.26±0.14	5.38±0.15	2.58±0.23	0.000	0.000
		Group-B	50	7.82±0.17	7.22±0.18	5.34±0.17		
3	Sitting or lying	Group-A	50	2.42±0.11	1.24±0.16	0.18±0.08	0.000	0.173
		Group-B	50	5.80±0.14	5.44±0.14	4.72±0.80		
4	Standing Up Right	Group-A	50	3.42±0.14	2.48±0.15	0.50±0.19	0.000	0.000
		Group-B	50	7.20±0.17	6.44±0.16	4.90±0.17		

Table 4: Pain Scores Measured at Different Intervals for Daily Life Activities

Group-A (Treatment) = Thermo Therapy

Group-B (Treatment) = Cryotherapy

Above table describes the pain score measured at different intervals in both treatment groups. These pain scores were measured for different daily life activities. Overall treatment-A is best in terms of pain reduction during different daily life activities.

Sr. #	Physical Function (0-10)	Group	N	Follow Up			p-value	
				Base Line	1 st	2 nd	Overall	Group
1	Descending Stairs	Group-A	50	6.34±0.18	5.36±0.21	2.98±0.27	0.000	0.000
		Group-B	50	6.80±0.14	6.16±0.15	5.28±0.23		
2	Ascending Stairs	Group-A	50	6.02±0.20	4.96±0.20	2.22±0.28	0.000	0.000
		Group-B	50	7.66±0.16	6.88±0.14	5.42±0.23		
3	Rising from sitting	Group-A	50	3.84±0.23	2.76±0.22	0.84±0.25	0.000	0.173
		Group-B	50	6.76±0.16	6.16±0.17	4.92±0.22		
4	Standing	Group-A	50	3.34±0.23	2.10±0.25	0.70±0.24	0.000	0.004
		Group-B	50	7.32±0.16	6.60±0.15	5.44±0.24		

Table.5: Physical Function Scores Measured at Different Intervals for Daily Life Activities

Group-A (Treatment) = Thermo Therapy ; **Group-B (Treatment)** =Cryotherapy

Discussion:

Being the leading cause of pain and disability in older people and also, most common joint disease, the knee OA has grabbed the attention of researchers. Being the leading cause of pain and disability in older people and also, most common joint disease, the knee OA has grabbed the attention of researchers. Though a number of risk factors involve in development as well as progress of this disease, yet Age is a documented risk factor for both radiographic and symptomatic OA at all sites.⁽¹⁴⁾ The prevalence of OA increases significantly after the age of 40 years in women and 50 years in men: about 50% of people aged ≥ 65 years, and 85% in the group aged ≥ 75 years are affected by it.¹⁵ Felson and coworkers found in their Framingham OA Study that 27% of the people aged 63 to 70 years had knee OA diagnosed radiographically whilst ≥ 80 years old people had the prevalence as much as 44%. The effect of Gender in varying the prevalence and incidence of OA, as well as in types of OA is inevitable. Isolated hand and knee OA are common in women, whereas the prevalence of hip OA is higher in men.^{16, 17}

In this current study the average age of male and female patients was observed to be 56.86 ± 6.37 and 57.42 ± 8.61 years respectively. Minimum age of male and female patients was 47 and 35 years and maximum age of male and female patients was 72 and 75 years respectively. Age distribution of patients who presented with Knee Osteoarthritis in current study is highly compatible to the age trend reported in different studies. Gender distribution in current study shows that females presenting with Knee Osteoarthritis were greater in number as compared to males. The gender distribution in our study was also very much similar to other international studies that have found the female gender association with an increased risk of OA. Women aged 50 years have been documented to have higher rates of incident knee OA compared to men and a higher prevalence of radiographic and symptomatic OA as well. The Framingham OA study showed that women had 1.7

times higher risk of disease than in men. Recent epidemiologic studies suggest the possible role of postmenopausal estrogen deficiency in the development of knee OA in older women.¹⁷⁻²³

Keeping in view the fact that currently no cure exists for OA at present, the prime objectives of management of OA of the knee remain confined primarily to lessen pain and stiffness, maintain or improve mobility, and minimize disability. Various treatment options are opted for according to the targeted objectives which include pharmacologic intervention, exercise therapy, surgical procedure and hot/cold treatment, have been shown to help considerable improvement in clinical symptoms and function of knee OA with fewer adverse effects have been documented by different physiotherapy treatments that are better than medical treatment.

Thermotherapy is one such noninvasive therapy that is recommended due to implicit beneficial effects in pain relief.

Cryotherapy, on the other hand, is used in rehabilitation for reducing inflammation, pain and edema that further improves significantly the mobility of the patient. Cold helps relieving the pain by timely by numbing the pain area. This is done by narrowing (vasoconstriction) the blood vessels and blocking pain signals in the joint.^{6, 24}

A number of techniques are employed for cold therapy (cryotherapy) that involves the administration of ice/cold packs and ice massage at affected areas or painful regions. Thermotherapy, contrarily, is also for reducing pain and stiffness, and increasing the movement. The muscles are relaxed increasing the blood supply to the affected/painful area that further reduces pain and joint stiffness. Nevertheless the prime concern about the heat therapy to worsen inflammation and edema cannot be ignored too. Among many economically reasonable and helpful techniques for heat therapy, some commonly used are the application of heat via heat Rolls/packs, diathermy (electromagnetic energy). The most common implication for using heat therapy and cold therapy are the physical improvement/rehabilitation of osteoarthritis (OA) patients mainly by relieving their pain. Both therapies can be easily self-applied, even at home (like the use of hot/cold packs), and can also be collectively used with different rehabilitation treatment techniques for advanced treatment plans.^{6, 25, 26}

In current study 100 patients, who fulfill the selection criteria, were enrolled in the study from Department

of Physiotherapy, Nawaz Sharif Social Security Hospital, Lahore. The patients were easily divided (randomly) into 2 groups by applying lottery method. In first group that is A, the patients were provided with thermotherapy whilst in group B, the patients were given cryotherapy. All the patients were treated by the investigator herself. The grades of pain were assessed on VAS and severity of disease was assessed through WOMAC index for muscle flexibility, muscle strengthening and tolerance scale and range of motion (ROM) was measured. Patients were treated for four weeks to evaluate the progress to be recorded as per objectives.

Pain score in current study was measured at different intervals i.e. on base line at 1st, 2nd, 3rd and at 4th week. Pain was significantly decreased in Group-A during various daily life physical activities like; walking on flat surface, going up & down, at night while in bed, standing up right etc. Similarly Physical function score while performing various daily life activities was statistically different in both treatment groups. In group-A, the physical function score was quite less as compared to group-B patients that suggest the thermotherapy to be more effective for physical functioning compared to Cryotherapy.

The potential advantageous effects of heat therapy in the management of pain and stiffness in OA patients are due to metabolic impact, hemodynamic and neuromuscular. First and foremost influence of therapeutic mechanisms particularly regarding Heat therapy, is in tissue healing and acute nociceptive pain generation, yet its effectiveness in relieving chronic pain is also approved. Assumed mechanism of heat therapy involves mild increase in temperature of tissue that dissociates the oxyhemoglobin curve line shifting it to the right side, and consequently ensuring more oxygen available for tissue repair that relieves pain.

A number of trials have been conducted to assess the utility of heat that is superficial, hot packs and hydrotherapy in the management of advance rheumatoid arthritis. Even though 6 controlled studies showed as beneficial adjunct therapy 27-29 2 report it ineffective 30, 31, with the chances of heat deteriorating the condition through enhance collagenase(enzyme) action which damage weak articular cartilage.

Hence, it is important to take precautionary measures when heat is going to apply at areas with edema, decreased circulation, open wounds or superficial metal devices that are implants, patients of low

thermal regulation, insufficient cardiac functioning, or acute inflammatory conditions³¹; or low blood pressure patients or syncope patients when applying heat at large surface area.³⁰

Discussing the rehabilitation context of cryotherapy, the mechanism involves withdrawing heat from the affected area of body by the applying of mild cooling agents superficially. Cryotherapy is commonly used to reduce pain, swelling and edema, to augment movement and to reduce spasticity.³¹

The current literature supports the importance of cryotherapy more to control acute trauma, yet its role in treating chronic pain conditions should not be avoided. Two uncontrolled comparative studies and case studies have proved cryotherapy as a fruitful adjunct in treating spastic muscle and myofascial pain. Comparative grade II studies have also reported that cryotherapy is beneficial add on therapy to control low back pain. It is contraindicated in cases such hypersensitivity, urticaria, Raynaud disease (cold intolerance), cold hemoglobinuria and open wounds that are deep, regenerating/improving nerves, areas of less blood flow and dermal areas of poor somatosensory distinguishing ability.³¹

Literature favors cryotherapy over hot packs in some studies. On such publication has shown significant outcomes that support ice packs when compared with control group and over hot/Heat therapy knee OA patients after 10 sessions for edema (change in knee circumference). No significant effects were reported for any beneficial effects of hot packs in reducing edema when compared with control/alternate therapy.³²

The comparison of thermotherapy with cryotherapy by using WOMAX scale has not yet been done. However, few studies have evaluated the usefulness of both non pharmacological physical treatments in terms of pain reduction and physical function on individual levels. Despite sparse and conflicting findings, thermotherapy is widely and commonly recommended for a number of musculoskeletal problems because it can be easily apply, safe, effective supportive therapy based on anecdotal reports, patient preferences, expert opinion and it require simple, inexpensive equipment.

Conclusions:

Overall, Thermotherapy was more effective than Cryotherapy for the management of unilateral knee osteoarthritis. However, for few parameters i.e. (Pain, Physical Activity, Muscle Flexibility and Muscle strength) thermotherapy was effective and for other parameters cryotherapy was effective. Hence, it can neither be said that thermotherapy was completely effective for all parameters i.e. (Pain, Physical Activity, Muscle Flexibility and Muscle strength) and nor did the Cryotherapy.

References:

- 1- Felson DT. Osteoarthritis of the knee. *New England Journal of Medicine*. 2006 Feb 23;354(8):841-8.
- 2- Roddy E, Doherty M. Changing life-styles and osteoarthritis: what is the evidence?. *Best Practice & Research Clinical Rheumatology*. 2006 Feb 28;20(1):81-97.
- 3- Jan MH, Lin CH, Lin YF, Lin JJ, Lin DH. Effects of weight-bearing versus nonweight-bearing exercise on function, walking speed, and position sense in participants with knee osteoarthritis: a randomized controlled trial. *Archives of physical medicine and rehabilitation*. 2009 Jun 30;90(6):897-904.
- 4- Stitik TP, Blacksins MF, Stiskal DM, Kim JH, Foye PM, Schoenherr L, Choi ES, Chen B, Saunders HJ, Nadler SF. Efficacy and safety of hyaluronan treatment in combination therapy with home exercise for knee osteoarthritis pain. *Archives of physical medicine and rehabilitation*. 2007 Feb 28;88(2):135-41.
- 5- Jones AC, Doherty MI. The treatment of osteoarthritis. *British journal of clinical pharmacology*. 1992 Apr 1;33(4):357-63.
- 6- Brosseau L, Yonge KA, Welch V, Marchand S, Judd M, Wells GA, Tugwell P. Thermotherapy for treatment of osteoarthritis. *The Cochrane Library*. 2003 Jan 1.
- 7- Brandt KD. The importance of nonpharmacologic approaches in management of osteoarthritis. *The American journal of medicine*. 1998 Jul 27;105(1):39S-44S.
- 8- Peat G, McCarney R, Croft P. Knee pain and osteoarthritis in older adults: a review of community burden and current use of primary health care. *Annals of the rheumatic diseases*. 2001 Feb 1;60(2):91-7.
- 9- Srikanth VK, Fryer JL, Zhai G, Winzenberg TM, Hosmer D, Jones G. A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. *Osteoarthritis and cartilage*. 2005 Sep 30;13(9):769-81.
- 10- Heidari B. Knee osteoarthritis prevalence, risk factors, pathogenesis and features: Part I. *Caspian journal of internal medicine*. 2011;2(2):205.
- 11- Gray H, Standring S. *Gray's anatomy: the anatomical basis of clinical practice*, 40th edn. Churchill-Livingstone.
- 12- Moore KL DA. *Clinically Oriented Anatomy*. 5th, editor. Baltimore: Lippincott Williams & Wilkins; 2006. 684-95 p.
- 13- Courtney P, Doherty M. Joint aspiration and injection and synovial fluid analysis. *Best practice & research Clinical rheumatology*. 2009;23(2):161.
- 14- Dougados M, Gueguen A, Nguyen M, Thiesse A, Lestrat V, Jacob L, et al. Longitudinal radiologic evaluation of osteoarthritis of the knee. *The Journal of rheumatology*. 1992;19(3):378.
- 15- Jordan J, Renner J, Luta G, Dragomir A, Fryer J, Helmick C. Hip osteoarthritis is not rare in African-Americans and is different than in Caucasians. *Arthritis Rheum*. 1997;40:S236.
- 16- Felson DT, Naimark A, Anderson J, Kazis L, Castelli W, Meenan RF. The prevalence of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. *Arthritis & Rheumatism*. 1987;30(8):914-8.
- 17- Jordan JM, Luta G, Renner JB, Dragomir A, Hochberg MC, Fryer JG. Ethnic differences in self-reported functional status in the rural south: The Johnston county osteoarthritis project. *Arthritis & Rheumatism*. 1996;9(6):483-91.
- 18- DAVIS MA, ETTINGER WH, NEUHAUS JM, HAUCK WW. Sex differences in osteoarthritis of the knee. *American Journal of Epidemiology*. 1988;127(5):1019-30.
- 19- Oliveria SA, Felson DT, Reed JI, Cirillo PA, Walker AM. Incidence of symptomatic hand, hip, and knee osteoarthritis among patients in a health maintenance organization. *Arthritis & Rheumatism*. 1995;38(8):1134-41.
- 20- Felson DT, Zhang Y, Hannan MT, Naimark A, Weissman BN, Aliabadi P, et al. The incidence and natural history of knee osteoarthritis in the elderly, the framingham osteoarthritis study. *Arthritis & Rheumatism*. 1995;38(10):1500-5.
- 21- Felson DT, Zhang Y. An update on the epidemiology of knee and hip osteoarthritis with a view to prevention. *Arthritis & Rheumatism*.

- 1998;41(8):1343-55.
- 22-** Nevitt MC, Felson DT. Sex hormones and the risk of osteoarthritis in women: epidemiological evidence. *Annals of the Rheumatic Diseases*. 1996;55(9):673-6.
 - 23-** Spector T, Nandra D, Hart D, Doyle D. Is hormone replacement therapy protective for hand and knee osteoarthritis in women?: The Chingford study. *Annals of the Rheumatic Diseases*. 1997;56(7):432-4.
 - 24-** Fife R. Osteoarthritis: Epidemiology, pathology and pathogenesis. *Primer on the rheumatic diseases*. 1997:216-7.
 - 25-** Cameron MH. Physical agents in rehabilitation: from research to practice. Philadelphia. 1999;7:131-73.
 - 26-** Association APT. Guide to physical therapist practice: American Physical Therapy Association; 1999.
 - 27-** Ayling J, Marks R. Efficacy of paraffin wax baths for rheumatoid arthritic hands. *Physiotherapy*. 2000;86(4):190-201.
 - 28-** Mainardi C, Walter J, Spiegel P, Goldkamp O, Harris Jr E. Rheumatoid arthritis: failure of daily heat therapy to affect its progression. *Archives of physical medicine and rehabilitation*. 1979;60(9):390.
 - 29-** Sukenik S, Neumann L, Flusser D, Kleiner-Baumgarten A, Buskila D. Balneotherapy for rheumatoid arthritis at the Dead Sea. *Israel journal of medical sciences*. 1995;31(4):210.
 - 30-** Dellhag B, Wollersjö I, Bjelle A. Effect of active hand exercise and wax bath treatment in rheumatoid arthritis patients. *Arthritis & Rheumatism*. 1992;5(2):87-92.
 - 31-** Harris Jr ED, McCroskery PA. The influence of temperature and fibril stability on degradation of cartilage collagen by rheumatoid synovial collagenase. *New England Journal of Medicine*. 1974;290(1):1-6.