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An intervention study on the effectiveness of isometric quadriceps hamstrings exercise in the treatment of osteoarthritis, knee joint

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Abstract

Objective: The purpose of this research was to verify the effectiveness of 6 months isometric quadriceps hamstring strengthening exercises on pain, function and joint stiffness of patients with knee osteoarthritis
Materials and method: It was intervention study (pre/post-test study) among 30 patients with Osteoarthritis knee done for a period of 6 months. Outcome measure was improvement in WOMAC Score (pain, physical function and knee joint stiffness). WOMAC Score before and after intervention were compared.

Results: WOMAC Score showed a significant difference between before and after the intervention showing effectiveness of exercises.

Conclusion: The 6 months isometric quadriceps exercise showed beneficial effects on Quadriceps muscle strengthening, pain and functional disability.

Keywords: Isometric quadriceps hamstrings exercise, treatment, osteoarthritis, knee joint

Introduction

It is estimated that approximately 3.8% of the world's population ^[1], that is approximately '277 million people' worldwide can't run or can't walk with ease. This is because of a progressive, painful and inflammatory condition due to the involvement of the articular cartilage, soft tissues and bone, which is Osteoarthritis knee joint. The prevalence of OA is similar across the globe and it is expected to increase dramatically as the population ages, especially in low and-middle income nations Osteoarthritis of knee is a condition that can seriously affect the quality of one's life ^[2, 3]. But mostly is found to affect people in early middle age and thereafter. Middle aged women also constitute a majority among the affected. The reasons for osteoarthritis that can be attributed the changing lifestyle of people and increase in their sedentary behavior. Osteoarthritis can be acute or chronic in nature. It can be progressive in nature and can serve as an impediment to once routine activities.

Research shows that exercise is one of the best treatments for osteoarthritis. Exercise can improve mood and outlook, decrease pain, increase flexibility, strengthen the heart and improve blood flow, maintain weight, and promote general physical fitness. Exercise is also inexpensive and, if done correctly, has few negative side effects. Implementing regular home based exercises can help to alleviate the symptoms and prevent progression of osteoarthritis ^[4]. In this study I am trying to evaluate the effectiveness of a home based exercise programme in alleviating pain of osteoarthritis patients attending Orthopedics outpatient department of Medical College Thiruvananthapuram, Kerala, India.

Osteoarthritis (OA) is the most common musculoskeletal condition affecting the quality of life of older adults Osteoarthritis ^[5, 6] (OA) is the most common type of arthritis found worldwide especially in the elderly. With the population ageing, the prevalence of OA is increasing, and its consequences have a significant impact on the society.⁷It is a disease characterized by pain and inflammation due to the involvement of the articular cartilage, soft tissues and bone ^[8] Osteoarthritis is the single most common cause of disability in older adults ^[9] The 2010 Global Burden of Disease Study reports that the burden of musculoskeletal disorders is much larger than estimated in previous assessments and accounts for 6.8% of DALYs % to 15% of all

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adults aged over 60 have some degree of OA, with prevalence higher among women than men.^{4 [11]}. The prevalence of OA is increasing due to population ageing and an increase in related factors such as obesity. According to the United Nations, by 2050 people aged over 60 will account for more than 20% of the world's population [12] of that 20%, a conservative estimate of 15% will have symptomatic OA, and one-third of these people will be severely disabled. This means that by 2050, 130 million people will suffer from OA worldwide, of whom 40 million will be severely disabled by the disease [12] Costs associated with OA include costs for adaptive aids and devices, medicines, surgery, and time off at work [13]. Osteoarthritis is currently diagnosed by physical examination and, where necessary, with x-ray, MRI scan and arthroscopy. However, these diagnostic tools have low sensitivity and specificity. There are no biomarkers for OA that can be used in clinical practice at this time. The treatment of OA involves: treating associated pain; viscosupplementation with intra-articular hyaluronate injections; intra-articular corticosteroid injections; joint replacement surgery; and, in rare circumstances, autologous chondrocyte implantation into the damaged areas [14-16].

While protective factors such as exercise, healthy diet, and occupational injuries can all be addressed, many risk factors such as gender, age, and genetics are not modifiable. The physical disability arising from pain and loss of functional capacity reduces quality of life and increases the risk of further morbidity. Although there is a wide range of devices and palliative medicines available that can relieve pain and improve quality of life, there is no pharmaceutical product that can halt or reverse the onset of OA.

Objective

To evaluate the Effectiveness Of isometric Quadriceps Hamstring Exercise in the treatment of the Patient with Osteoarthritis of Knee Joint.

Methodology

This study was an Intervention Study (Pre/Post Test). Study was conducted in the previously diagnosed patients with osteoarthritis knee joint attending the Outpatient Department of Orthopedics, Medical College, Thiruvananthapuram Patients with Coronary heart disease /stroke or any other chronic debilitating diseases were excluded. Patients who had severe knee pain and were unable to do this exercise were also excluded. duration of the study was six months (May to November 2017) Sample size was calculated using n Master software using mean and SD of VAS/WOMAC Scoring using pretest and post-test, mean and SD of 9.63(1.28) [34] and 11.93(1.86) [34] with α error 0.1% and β error 99%, to get a sample size of 30. Consecutive patients, previously diagnosed with osteoarthritis knee were selected for the study. The baseline status of symptoms of people suffering from osteoarthritis were recorded using semi-structured questionnaire The WOMAC Score is used for assessing functional ability for osteoarthritis knee patients before and after 6 months of home based exercise. Collected data were entered in an excel sheet. Quantitative variables were expressed in terms of mean and SD and qualitative variables were expressed as proportions. Statistical significance was assessed by doing Wilcoxon Sign Rank Test. SPSS trial version 16 was used for analysis Institutional ethics committee clearance was obtained from the Ethics Committee Medical College Thiruvananthapuram. Written Informed consent was obtained from each study participants.

Confidentiality is ensured to participants throughout the study.

Results

The analysis includes 30 patients with osteoarthritis The mean age of the population was 51.13, with a Standard Deviation of 8.114. Minimum age was 34 years and maximum age was 68 years. Out of 30 study participants with OA Knee joint, 16 (53.3%) were male patients and 14 (46.7%) were females Out of total patients 53.3 percent had underwent only primary education that is upto fourth standard, while 16.7 percent of them had studied upto the middle class that is up to eighth standard, remaining 13.3% had been educated up to the high school, rest 16.7% were graduate. Out of the total 30 patients with OA Knee participated in the study, 70 percent were unskilled Workers including house wives while 26.7% were skilled workers like carpenters, mechanics, technicians etc. Remaining 3.3% were clerical/government job workers. Out of total patients 7(23%) were diabetic and rest 23(76.7%) were non diabetic. Out of total patients participating in the study 17 (56.7%) were hypertensive while 13 (43.3%) were non hypertensives.

Among the total patients with Osteoarthritis knee joint, 15 (50%) presented with osteoarthritis of right knee, while 7(23.3%) presented with Osteoarthritis of left knee and 8 (26.7%) presented with bilateral involvement.

23 (76%) of the total patients participated in this study were suffering with the pain of Osteoarthritis knee joint for more than one year, and the remaining 7(23%) of them were having pain of osteoarthritis knee joint for less than one year.

Among the study participants 25(83.3%) of the study participant had other joint involvement along with knee joint. but 5(16.7%) had only knee involvement.

21(70%) of the study participants had polyarticular involvement, that is affecting many joints [37] like spine, elbow, ankle while 3(10%) of the study participants had only elbow involvement and 1(3.3%) have involvement of the spine other than knee joint. 5(16.7%) had only knee joint involvement.

26(86.7%) of the study participants were able to perform daily routine activities like, walking, taking bathe, or using rest room by themselves. But 4(13.3%) of them couldn't perform daily routine activities without the help of others.

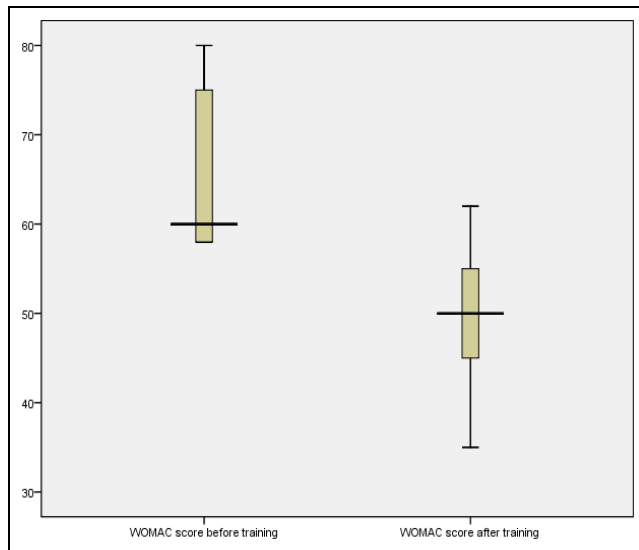
Obesity is an important risk factor for developing Osteoarthritis knee joint [12]. In my study 20 subjects were overweight and obese, linking Osteoarthritis knee with increasing BMI in WOMAC Score the patients with higher scores would have maximum pain and lower the score the pain will be lesser. In this study mean WOMAC score before the home based exercise programme was 66.3 (8.676),. Minimum value was 58 and the maximum score was 80 in this study WOMAC Score of patients came down after 6 months exercise programme. The mean WOMAC score after the exercise programme was 50.67 (4), minimum value was 45 and the maximum score was 60.

Wilcoxon Sign Rank Test was used to compare the WOMAC Score before and after the 6 month home based exercise intervention programme,

Wilcoxon Signed Rank Test indicated that WOMAC score was statistically significantly after the 6 month home based intervention $Z= 4.643 p<0.000$

Table 1: Wilcoxon Signed Ranks Test result of WOMAC Score Before after the training

	WOMAC score (before intervention)	WOMAC score (after intervention)	P value
Mean (SD)	66.33(8.6)	50.67(4)	<0.001
Median (IQR)	60(58,75)	50(50,50)	

**Fig 1:** Whisker Box Plot showing WOMAC Score before and after the Intervention

Discussion

In this study 30 patients were recruited from the Physical Medicine and Rehabilitation OPD of urban health center Pangappara and they were given training to the home based isometric exercise for six months. At the end of the six month it was found that there was remarkable symptomatic improvement in the sufferings of the patients. According to the World Health Organization report on burden of disease ²⁵Knee OA is one of the most important cause of disability in men and women. The Osteoarthritis Research Society International (OARSI) recommended non pharmacological interventions like patient education programmes, weight reduction, coping strategies, and exercise programs for treatment of knee OA ^[30]. “isometric exercises” are simple and inexpensive to perform and that they rapidly improve strength ^[32,33].

In the present study the mean age of the patients with osteoarthritis knee joint was 51 years with a maximum of 68 years and a minimum of 34 years. Indian Society of Hip and Knee Surgeons (ISHKS) has established a joints registry and has been collecting data for last 6 years. In joint registry’s report the average age of Osteoarthritis was 64.4 years with a range of 45 to 88 years ^[38]. In a cross sectional study carried out in patients attending the orthopedics outpatient department of Medical College Hospital in Thiruvananthapuram, Kerala, India in 2010 by Anu Anna George *et al.*, the median age of the patients was found to be 55.5 years and 65% were above 50 years ^[39]. mean age of 52.21 years (57.32 in males and 51.33 in females) among osteoarthritis patients was noted in a study carried out in the Outpatient Department and Lifestyle Disease Management Clinic, Department of Physical Medicine and Rehabilitation, Government Medical College, Kozhikode, Kerala, India by Anit Antony *et al.* ^[40] In the above mentioned studies conducted in Kerala. The mean age of patients with osteoarthritis was found to be lesser than national mean age,

which is conclusive with present study.

Out of 30 study participants with OA Knee joint 16 (53.3%) were male patients and 14 (46.7%) were females. women are more affected and burdened by osteoarthritis of the knee than men ^[14, 26] The results of a meta-analysis of sex differences in OA prevalence, incidence and severity by Sreekanth V K *et al.*, demonstrated the presence of sex differences in OA prevalence and incidence, with females generally at a higher risk. Females also tend to have more severe knee OA, particularly after menopausal age ^[41]. In the present study, proportion of females were less because of the smaller sample size to estimate the proportion.

Kerala is the diabetes capital of India with a prevalence of diabetes as high as 20% – double the national average of 8% ^[42]. Progression to pre-diabetes and diabetes occurred at a very fast rate in Kerala population by K. R. Thankappan *et al.* ^[43]. The proportion of diabetes in patients in this study is 23.3% which was comparable to general population, There exists evidence of an association between OA and diabetes or increased blood glucose ^[44, 45]. In a prospective study, Nüesch *et al.* showed that OA subjects are at increased risk for mortality due to diabetes, cardiovascular disease, and cancer ^[46].

Yi-min Zhang *et al.* in a meta-analysis with eight studies including 2 cohort studies and 6 cross-sectional studies with 9762 participants were finally showed that hypertension was significantly associated with higher radiographic knee OA and symptomatic knee OA risks ^[47]. In the present study 56% were hypertensive.

In this study 24% of the patients had experienced pain of osteoarthritis with in a year, which restricted their routine activities. Peat *et al.* in their narrative review published in 2001 stated that during one year period, 25% of people over 55 years may demonstrate persistent episode of knee pain ^[48]. This is consistent with the finding of the present study.

83% of the patients enrolled in the study were on irregular treatment before participating. They had been seeking medical care for osteoarthritis knee joint at frequency less than one visit per months any health facility. In patients with osteoarthritis knee joint only one in six have to consult their general practitioner in a period of one year ^[48].

Majority of the study participants that is 86.7% of them could be able to perform daily routine activities without the help of others. But 13.3% of them couldn’t perform their daily routine activities themselves because of the severity of the disease, according to Peat *et al.*, about 10% of people aged over 55 years have painful disabling knee OA of whom one quarter are severely disabled ^[48].

Osteoarthritis commonly affects large weight-bearing joints, such as the hips and knees and the joints of hands, feet, spine ^[49]. In the current study 10% of the participants had hand involvement and 3.3% have involvement of the spine 16.7% had only knee joint involvement in this study 70% of the participants had polyarticular involvement, that is more than four joint involvement ^[50]. In across sectional study conducted by Amanda E. Nelson *et al.* it was noticed that 13% had hand involvement, 25% knee, 11% hip, and 28% had Lower spine involvement ^[50]. WOMAC score showed a significant difference in score before and after training showing effectiveness of home based isometric quadriceps exercises. Males had a more significant difference in score compared to females with more improvement. Osteoarthritis impairs strength of knee muscles, increases pain and stiffness around knee joint and all of hence need to be treated to reduce sufferings from osteoarthritis knee. Study showed a

significant decrease in WOMAC Score over 6 months after training showing a improvement in pain, stiffness and muscle strength of knee joint 16.0% reduction in WOMAC score was observed in a study conducted by Ihsane Hmamouchi *et al.*, [56]. The results of the present study showed that home based isometric quadriceps exercise programme brought about a significant reduction in knee pain and improvement in function in 6months. The significant reduction in pain and improvement in function in the study participants may be attributed to improved quadriceps power and hence improved stability of the knee joint.in a randomized control trial conducted by Shyam D. Ganvir *et al.* in Maharashtra, in between groups the experimental group had significant reduction in pain and improvement of knee function after the 5 week isometric exercise programme than the control group, which hadn't performed any exercise [34]. Brandit, *et al.* found that an exercise program may effective to increased muscle strength of quadriceps and knee joint become stronger and reduced the symptoms of the patients [5]. Further study done by Boon Whatt LIM, *et al.* concluded that quadriceps strengthening exercise has beneficial effect on function of knee joint [51]. The study done by Shreyasee Amin *et al.* reported that subjects having stronger quadriceps strength had less knee pain and better physical function as compared with those with the least strength. Strong muscles stabilize the joints in a proper alignment, attenuate shocks that are transmitted to the joints and minimize the effect of impact by spreading the forces out over a greater area so it may be hypothesized that improvement in muscle strength is one of the main causes of reduced pain and disability [32]. The Fitness Arthritis and Seniors Trial reported a modest 8% to 10% improvement in pain and functioning scores as a result of 18 months of aerobic or resistance exercise among their sample of knee OA patients [52]. Further Deyle *et al.* [53], Falconer *et al.* [54] and Fisher *et al.* [28] found the same positive effects of exercise programs on pain and function. It is well documented in the literature that impaired quadriceps strength has been found to be the greatest single predictor of lower limb functional limitation [55].

In this study it is proved that by doing home based Isometric quadriceps hamstring exercise in daily and systematic way under the supervision of their caregiver for a period of six months, can bring down sufferings of the patients with osteoarthritis to an extent in a cost effective way.

Conclusion

Osteoarthritis (OA) is the most common type of arthritis found worldwide especially in the elderly [7] It is a disease characterized by pain and inflammation due to the involvement of the articular cartilage, soft tissues and bone [8]. Osteoarthritis is the single most common cause of disability in older adults [9] Three major physical impairments, such as knee pain, stiffness, and decreased quadriceps strength, are highly associated with a knee OA and are believed to contribute to physical disability and progression of the disease [26-28] As the quadriceps muscle plays the role of shock absorber, a weakness of this muscle decreases the joint protection resulting in greater stress and overload on the knee [25]. Quadriceps strengthening exercises proved effective in function improvement of knee joint.

The mean age of the population was 51.13(8.114.) Obesity is an important risk factor for developing Osteoarthritis knee joint [12]. In this study 46% of the Osteoarthritis knee patients were pre-obese and obese warranting a need to reduce the BMI to improve the pain.

70% of the Osteoarthritis knee patient had polyarticular involvement. 13.3% of the patient with osteoarthritis couldn't perform their daily routine activities themselves because of the severity of the disease, which shows the progressing and debilitating nature of the disease and need for active intervention.

In this study it was proved that by performing home based Isometric quadriceps hamstring exercise in daily and systematic way under the supervision of their caregiver for a period of six months, could improve the function and strength of the knee joint of the patients with osteoarthritis to in a cost effective way.

References

1. Sancheti P, Shetty VD, Dhillon MS, Sprague SA, Bhandari M. India-Based Knee Osteoarthritis Evaluation (iKare): A Multi-Centre Cross-Sectional Study on the Management of Knee Pain and Early Osteoarthritis in India. *Clin Orthop Surg.* 2017; 9(3):286-94.
2. Population Foundation of India; Population Reference Bureau. The future population of India: a long-range demographic view.
3. Das SK, Farooqi A. Osteoarthritis. *Best Pract Res Clin Rheumatol.* 2008; 22(4):657-75.
4. Snapshot [Internet]. [cited 2018 Mar 25]. Available from: <https://www.medicinenet.com/script/main/art.asp?articlekey=90187#treatment>
5. Brandit KD. Non-surgical management of osteoarthritis with an emphasis on non-pharmacological measures. *Arch Fam Med.* 1995.
6. Hurley MV, Scott DL, Rees J, Sensorimotor changes and functional performance in patients with knee osteoarthritis. *Ann Rheu.*
7. Brooks PM. Impact of osteoarthritis on individuals and society: How much disability? Social consequences and health econo.
8. De Filippis L, Gulli S, Caliri A, Romano C, Munaò F, Trimarchi G *et al.* Epidemiology and risk factors in osteoarthritis:
9. Laupattarakasem W. Arthroscopic debridement for knee osteoarthritis. *Cochrane Database of Syst Rev.* 2008, 1.
10. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the.
11. WHO Department of Chronic Diseases and Health Promotion. Available at: <http://www.who.int/chp/topics/rheumatic/en/>.
12. United Nations. World Population to 2300. Available at: <http://www.un.org/esa/population/publications/.../WorldPop2300fi>.
13. Maetzel A. The economic burden associated with osteoarthritis, rheumatoid arthritis, and hypertension: a comparat.
14. Blagojevic M, Jinks C, Jeffery A, Jordan KP. Risk factors for onset of osteoarthritis of the knee in older adults: a sys.
15. Hunter DJ, Felson DT. Osteoarthritis: clinical review. *BMJ.* 2006, 332:639-42.
16. Bellamy N. Intra-articular corticosteroid for treatment of osteoarthritis of the knee. *Cochrane Database of Syst R.*
17. Haq I, Murphy E, Dacre J. Osteoarthritis. *Postgrad Med J.* 2003; 79(933):377-83.
18. Jan MH, Lai JS. The effects of physiotherapy on osteoarthritic Knees of females. *J Formosan Med Assoc.,* 1991; 90:1008-13.

19. Veerapan K. Osteoarthritis-Asian perspective. In: Howe HS, Feng PH, editors. Textbook of Clinical Rheumatology. Singapore.
20. Jadhav MP, Jadhav PM, Mutke AP, Sonawane SD, Patil BD, Naik NB *et al.* A prospective observational study to assess quality.
21. de Bock GH, Kaptein AA, Touw-Otten F, Mulder JD. Health-related quality of life in patients with osteoarthritis in a fami.
22. Zakaria ZF, Bakar AA, Hasmoni HM, Rani FA, Kadir SA. Health-related quality of life in patients with knee osteoarthritis.
23. Lam CL, Lauder IJ. The impact of chronic diseases on the health-related quality of life (HRQOL) of Chinese patients in pr.
24. Harsha Kumar HN, Nagaraj K, Luthra K, Gupta P, Sagar P, Gupta S *et al.* Health-related quality of life among osteoarthritis.
25. Slemenda C, Brandt KD, Heilman DK. Quadriceps weakness and osteoarthritis of the knee. *Ann Intern Med*, 1997, 127.
26. Felson DT, Naimark A, Anderson JJ, KazisL, Castelli W. Prevalence of knee osteoarthritis in the elderly: The Framing.
27. Tornvall G. Assessment of physical capabilities with special reference to the evaluation of maximum voluntary isometric.
28. Fisher NM, Gresham G, Pendergast DR. Effects of a quantitative progressive rehabilitation program applied unilaterally to t.
29. Lim BW, Hinman RS, Wrigley TV. Does knee mal alignment mediate the effects of quadriceps strengthening onknee adduc.
30. Rosa UH, Velásquez Tlapanco J, Lara Maya C. Comparison of the effectiveness of isokinetic vs isometric the rapeutice.
31. Sharma MK, Swami HM, Bhatia V. An epidemiological study of correlates osteoarthritis in geriatric population of UT C.
32. Amin S, Baker K, Niu J. Quadriceps strength and the risk of cartilage loss and symptom progression in kneeosteoarth.
33. Hurley MV, Scott DL. Improvements in quadriceps sensorimotor function and Source of disability of patients with kneeosteo.
34. Shyam D, Ganvir BR, Zambare DB, Naikwade. Effects of open chain exercises on muscle strength and function in elderly.
35. Community Medicine | Medical College - Trivandrum [Internet]. [cited 2018 Apr 3]. Available from: <https://tmc.kerala.gov.in/?q=departments/community-medicine>
36. WOMAC Osteoarthritis Index - WOMAC 3.1 - Knee and Hip Osteoarthritis [Internet]. [cited 2018 Apr 2]. Available from: <http://www.womac.org/womac/index.htm>
37. Polyarticular Medical Definition | Merriam-Webster Medical Dictionary [Internet]. [cited 2018 Apr 5]. Available from: <https://www.merriam-webster.com/medical/polyarticular>
38. Pachore JA, Vaidya SV, Thakkar CJ, Bhalodia HKP, Wakankar HM. ISHKS joint registry: A preliminary report. *Indian J Orthop*. 2013; 47(5):505-9.
39. George AA, Anoop S, Jayan A, Nujum ZT. Obesity and Severity of Osteoarthritis. *Academic Medical Journal of India*. 2014; 2(2):52-5.
40. Antony A, Chandran RR, Shahulhameed AG, Sudha SMM, Viswanath S. Metabolic Syndrome; Osteoarthritis of knee. The Prevalence of Metabolic Syndrome in Patients with Osteoarthritis of Knee Attending Physical Medicine and Rehabilitation Department of a Tertiary Care Centre [Internet]. 2017 May 18 [cited 2018 Apr 6];(13505). Available from: https://www.jemds.com/latest-articles.php?at_id=13505
41. Srikanth VK, Fryer JL, Zhai G, Winzenberg TM, Hosmer D, Jones G. A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. *Osteoarthr Cartil*. 2005; 13(9):769-81.
42. Mohan V, Sandeep S, Deepa R, Shah B, Varghese C. Epidemiology of type 2 diabetes: Indian scenario. *Indian J Med Res*. 2007, 14.
43. Thankappan KR, Mini GK, Sarma PS, Varma RP. Incidence of type-2 diabetes among industrial Workers in Kerala, India. *Int J Diabetes Dev Ctries*. 2017; 37(3):280-5.
44. Rahman MM, Cibere J, Anis AH, Goldsmith CH, Kopec JA. Risk of Type 2 Diabetes among Osteoarthritis Patients in a Prospective Longitudinal Study [Internet]. *International Journal of Rheumatology*. 2014 [cited 2018 Apr 6]. Available from: <https://www.hindawi.com/journals/ijr/2014/620920/>
45. Hart DJ, Doyle DV, Spector TD. "Association between metabolic factors and knee osteoarthritis in women: the.
46. Nüesch E, Dieppe P, Reichenbach S, Williams S, Iff S, Jüni P. All cause and disease specific mortality in pat.
47. Zhang W, Ouyang H, Dass CR, Xu J. Current research on pharmacologic and regenerative therapies for osteoarthritis. *Bone Res*. 2016; 4:15040.
48. Peat G, McCarney R, Croft P. Knee pain and osteoarthritis in older adults: a review of community burden and current use o.
49. Dicesare PE, Abramson SB. Pathogenesis of osteoarthritis.
50. Nelson AE, Golightly YM, Renner JB, Schwartz TA, Kraus VB, Helmick CG *et al.* Differences in Multi-joint Symptomatic Osteoarthritis Phenotypes by Race and Gender: The Johnston County Osteoarthritis Project. *Arthritis Rheum*. 2013; 65(2):373-7.
51. Lim BW, Hinman RS, Wrigley TV. Does knee malalignment mediate the effects of quadriceps strengthening on knee a.
52. Ettinger WH, Jr, Burns R, Messier SP. A randomized trial comparing aerobic exercise and resistance exercise wit.
53. Deyle GD, Henderson NE, Matekel RL. Effectiveness of manual physical therapy and exercise in osteoarthritis of.
54. Falconer J, Hayes KW, Chang RW. Effect of ultrasound on mobility in osteoarthritis of the knee. A randomized clinical tr.
55. McAlindon TE, Cooper C, Kirwan JR. Determinants of disability in osteoarthritis of the knee. *Ann Rheum Dis*, 199.
56. Hmamouchi I, Allali F, Tahiri L, Khazzani H, Mansouri LE, Ali Ou Alla S *et al.* Clinically important improvement in the WOMAC and predictor factors for response to non-specific non-steroidal anti-inflammatory drugs in osteoarthritic patients: a prospective study. *BMC Res Notes*. 2012; 5:58.