

Study on Epidemiology, Etiology, Pathology, Pathogenesis, Mode of Presentation and Clinical Features of Osteoarthritis of Various Joints from Cases Who are Attending Tertiary Care Hospital

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Abstract: ***Aim:** To study the clinical profile, epidemiology, causes and clinical features of osteoarthritis. To identify the commonest joint involvement in osteoarthritis. To evaluate the incidence of primary OA from secondary osteoarthritis. To extrapolate the clinical features with pathology and pathogenesis of osteoarthritis. To how to avoid pitfalls in the diagnosis of primary osteoarthritis from secondary arthritides. **Objective of the Study:** Across the globe, osteoarthritis is a commonest disability prone disease. As against in the past, quite large number of cases are presenting with this disease are not just in old but from above middle ages. All over the countries, in both sexes, the life expectancy is being appreciably increased and likewise, because of the rise in affluency and easy reach of opulent diets, most of them became obese with plumb and bellies and unfortunately, it's often being seen in young and above middle ages. Thus, ultimately leads to secondary flat foot and increase in intra-articular hypertension, medial and lateral tibiofemoral compartmental stress and repetitive injuries. If any one or all these modifiable, non-modifiable and perpetual causes are not removed, then one has to welcome the early onset of osteoarthritis. As there are numerous cases are coming with features of OA to rheumatology out-patient department, We have aimed to do systematic and prospective study on osteoarthritis from August 2006 to August 2019 and it was conducted in three different centres, namely in rheumatology out-patient department of the Government Mohan Kumaramangalam Medical College and Hospital, Salem where I have been there for more than a decade as Senior Assistant Professor of Rheumatology and K. A. P. Viswanatham Government Medical College, Mahathma Gandhi Memorial Hospital where I have been promoted as Associate Professor of Rheumatology, Tiruchirappalli and another one in Akitha Hospital, Centre of Excellence for Autoimmune Diseases, Seelanaickenpatti, Salem, Tamil Nadu State, India. **Material and Methods:** More than a decade of my experiences on osteoarthritis of various joints from cases who has attended to rheumatology out-patient department of Government Mohan Kumaramangalam Medical College and Hospital where I have been there for more than a decade as Senior Assistant Professor of Rheumatology and K. A. P. Viswanatham Government Medical College, Mahathma Gandhi Memorial Hospital where I have been promoted as Associate Professor of Rheumatology, Tiruchirappalli and from Akitha Hospital, Centre of Excellence for Auto Immune diseases, Salem, Tamil Nadu State of India are have been included for this systematic and prospective on going study on osteoarthritis for the epidemiology, causes, pathology, pathogenesis and clinical features. Quite often, rheumatologist see OA cases at bit late and mostly they are coming either with wrong diagnosis or with or after erroneous treatments with high dose steroid and various DMARDs as rheumatoid arthritis. Thus, in this article, attempts have been taken for the ways to reduce or avoid pitfalls either in the investigations or in the diagnosis of primary OA from secondary osteoarthritis before initiating proper treatment. There are 3208 cases (M-1759 & F-1449) have been enrolled for this study and based on the age of presentation, they were categorized into 3 groups. Ages from 35-50 years are in Group-A, (in 538, M-177 & F-361), 51-70 years of ages in Group-B, (in 1846, M-1181 & F-665) and from 71 years and above are in Group- C (in-824, M-401 & F-423). **Results:** The youngest and oldest ages was seen, 35 and 92 years old, female and male, respectively. In Group-I, female outnumbered the male (female 67.10% (n-361) and male 32.89% (n-177) and in Group- B, male with OA are higher than female (male 63.97% and female 36.02%, whereas, more or less equal in both sexes in Group-C, as 48.66% and 51.33%, in male and female, respectively. Among both sexes, knee is most commonly involved joint. Unilateral OA knee is the usual clinical presentation in age group less than 50 years but after fifty, bilateral knee involvement was noted. Next to knee, OA hand was found and least was found in elbow joint. Another interesting features was observed that obesity has strongest association with OA and it was the predominant cause for the OA in young female. In our study, obesity was found as a significant cause in age group less than 50 years and it was predominantly seen in female (57.06%) than male (30.50%), whereas in other two groups, it was found equally in both sexes. **Conclusion:** Osteoarthritis is a common articular disease and it often limits the activities and earning capacity of above middle aged individuals and it is a crippling disease in ages after 70 years. Strongest associations was noted in larger proportions of obese young individuals as a predominant cause for OA as because of every country in world are increasingly experienced with plumb and belly's population. Osteoarthritis of knee was found as a common presentation to our two centres, next is hand and least was found in elbow joint.*

Keywords: Epidemiology, Etiology, Pathology, Pathogenesis, Osteoarthritis

1. Introduction

Around the world, there are more than 100 million people are suffering from osteoarthritis in one or other joints and it is one of the leading cause of disability, not just in aged but from above middle ages. (Hinman RS et al 2010;

Heiden T et al 2009). In our country, the prevalence of osteoarthritis are in the range of 17- 60.6% (Sharma MK et al 2007) and as per Bhigwan, Pune, epidemiological study by Chopra et al, among more than 740 rheumatic diseases, OA was the second most commonest disease (Chopra A et al 2001). The same scenario was found in American study

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that, OA is a universal disease and found second to ischemic heart disease. In another study by Barbour KE et al, 2013 and Hootman JM et al 2016, OA affects more than 52.5 million people and it is the leading cause of disability after 50 years of age for admission than rheumatoid arthritis and probably this numbers, surely can swell more, as every country in the globe has experienced with remarkable increases in the lifespan of either sex. Likewise, whenever affluency come, most of them follows opulent diet and happily spends sedendary life styles and eventually result in obesity. Thus, on one aspect, there will be absolute and relentless addition of aging population and another from the definerisk pronomodifiable factors like plump and belly population are on the rise for the world . Though, there are heterogenous causes for OA, some well known non modifiable and modifiable high risk factors collectively leads to increase in the volume of osteoarthritis cases. Therefore, I have carried out this epidimiological study on osteoarthritis of various joints from those who were attending as out-patient and in-patient in rheumatology department of Government Mohan Kumaramangalam Medical College and Hospital, Salem, where I have been as Senior Assistant Professor of Rheumatology and K. A. P. Viswanatham Government Medical College, Mahathma Gandhi Memorial Hospital where I have been promoted as Associate Professor of Rheumatology, Tiruchirappalli and from Akitha Hospital, Centre of Excellence for Autoimmune Diseases, Seelanaickenpatti, Salem, Tamil Nadu State, India from August 2009 to August 2019.

Another world bank sponsored and WHO collaboration ongoing study in Harvard university on global mortality and burden of disease from 2002 to 2030, states that musculoskeletal disorders represent the most frequent cause of disability in the world (Colin D Mathers et al 2002). The demand for primary hip and knee arthroplasty in the United States is expected to increase by 174% and 673%, respectively, by 2030. Pain control is often inadequate when OA progresses to a severe stage. The identification of individuals at high risk of OA, to be identified at early and intervene with appropriate management of the disease or else, in future, across the globe the job of the care giver for these ailments are going to be more demanding. Direct costs attributable to arthritis and other rheumatic conditions total more than \$100 billion in the United States, of which more than half of the direct costs are going to be incurred in the outpatient setting itself. As per Indian planning Commission 2011, osteoarthritis (OA) accounts for half of all chronic conditions in persons aged over 65 with about 25 % of people over the age of 60 having significant pain and disability from osteoarthritis. As per a recent statement quoted by Piramal Healthcare Limited in a nationwide campaign against chronic diseases, India is expected to be the chronic disease capital, with 60 million people with arthritis, by 2025. Prevalence increases with age, so that about 11% of all women over the age of 60 years have symptoms due to knee OA. Knee osteoarthritis is the most common condition which represents a major contribution to the burden of physical disability (Felson DT et al, 1987).

OA is due to failure of repair of damages that have been caused by excessive mechanical stress on the joint tissues. Without attempting to contain or correct the mechanical insult, any attempt at healing is bound to fail. When the joint in the same adverse environment, it is unlikely that any drug can inhibit the pathogenic cytokine pathways of cartilage breakdown. Further, it adversely increases the synthesis of cartilage matrix molecules by the chondrocytes. In the backdrop, the subchondral bone is playing a critical role in containing the mechanical abnormalities that damage the cartilage, thus, mere emphasis on cartilage repair is useless. Therefore, when abnormal stress is reduced, then, the so called disease modifying OA drugs (DMOAD) are likely to be unnecessary.

In nutshell, like any internal organ's structural failure, synovial joints also can fails. Naturally, at an initial stages, there will be asymptomatic phases of heart, liver and kidney failures. Thus, at an early phase, osteoarthritis per se can be quite asymptomatic, but only to precipitate with profound symptoms after sometime. Though, there are multi-pronged joint insults which can trigger OA, but the joint response could varies differently. The affected joint tissues can release proteoglycans and it quickly increases the expression of genes for stromelysin, aggrecanase and tissue inhibitor of matrix metalloproteinases (TIMP) by chondrocytes, leading to degradation of joint tissues.

In osteoarthritis, the weight bearing joints like hip and knee are not affected by weight of the body but due to load across these joints by the powerful muscular contractions. Likewise, the powerful flexor digitorum profundus muscular contactions and repeated load across theminimum load bearing thin metaphyseal trabecular bones, which having lesser surface areas at the distal interphlangeal jointsare the principal reasons for the OA at the DIP joints whereas maximum load bearing and less powerful flexor digitorum brevisand maximum surface areas overMCP and PIPjoints arelesserprone for OA.^{1,2}

Almost in all cases of osteoarthritis, osteophytes can be seen and it is prudent that, the word osteophyte to be used selectively for marginal new bone arising from peripheral bones and joints and whenever it is appear in the degenerative osteoarthritis of spine, it is better to be called as spondylophyte but, the term syndesmophytes are only to used be in inflammatory arthritides of spine.³

Epidemiology

Osteoarthritis, worldwide statistics reveals, over 100 million people suffer from OA, and it is one of the most common cause of disability (Hinman RS et al 2010; Heiden T et al 2009). In India, the prevalence of osteoarthritis is reported to be in the range of 17-60.6% (Sharma MK et al 2007). Epidemiological profile of this disease in India is not clear but it is estimated that osteoarthritis (OA) is the second most common rheumatological problem and is most frequent joint disease with prevalence of 22% to 39% in India (Chopra A et al 2001). The reported prevalence of OA from a study in rural India is 5.78% (Lone AH et al 2011). Eleventh

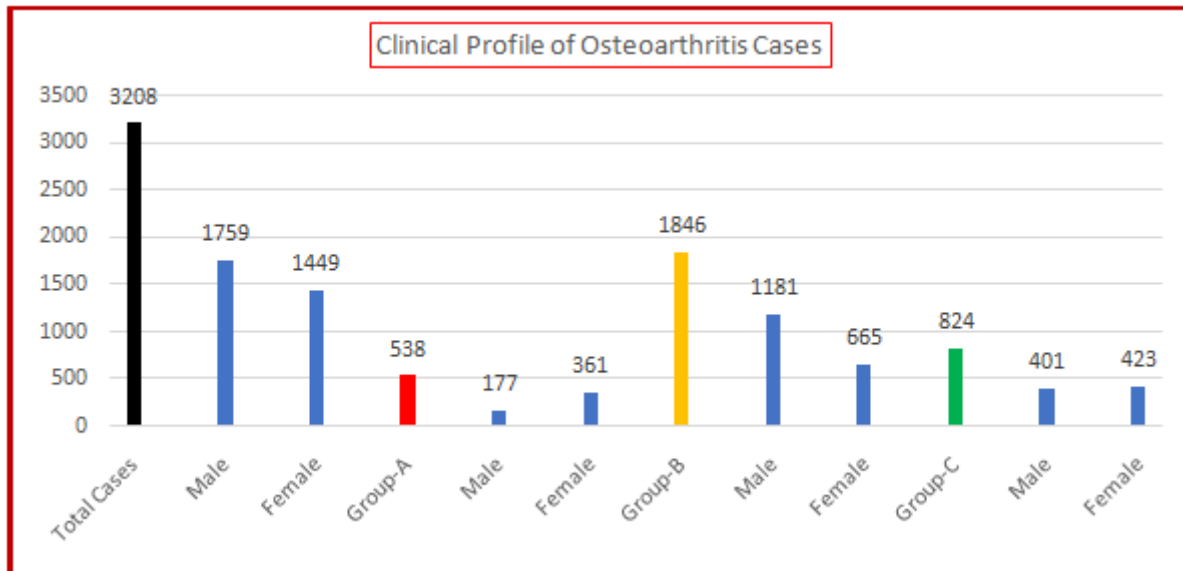
COPCORD (Community Oriented Program for Control of Rheumatic Disorders) reports showed, the pooled prevalence of knee OA is 8%. In the Bhigwan population in India, six percentages of the respondents had chronic knee pain without clinical evidence of OA (Syed A et al, 2011). Marita Cross et al 2010 study shows that, OA knee and hip is the 11th leading cause of disability and 38th highest in disability adjusted life years (DALYs). The Years of life lived with disability (YLDs) for hip and knee OA increased from 10.5 million in 1990 to 17.1 million in 2010. Currently, in America, OA is the most common form of arthritis, and second to ischemic heart disease. It affects more than 52.5 million people (Barbour KE et al, 2013 & Hootman JM et al 2016), and OA is the common disability after 50 years of age for admission than rheumatoid arthritis and probably this number will swell with the aging of the existing plump and bellies population. Another world bank sponsored and WHO collaboration ongoing study in Harvard university on global mortality and burden of disease from 2002 to 2030, states that musculoskeletal disorders represent the most frequent cause of disability in the world (Colin D Mathers et al 2002). The demand for primary hip and knee arthroplasty in the United States is expected to increase by 174% and 673%, respectively, by 2030. Pain control is often inadequate when OA progresses to a severe stage, and identification of individuals at high risk of OA and early detection and intervention are essential for the improved management of this disease, or else in future, across the globe the job of the care giver for these ailments are going to be more demanding. In US alone, the direct costs attributable to arthritis and other rheumatic conditions are more than \$100 billion, in this more than half of the direct costs are going to be used in the outpatient setting itself. Indian planning Commission 2011, osteoarthritis (OA) accounts for half of all chronic conditions in persons aged over 65 and among them, 25 % of people over the age of 60 are having significant pain and disability from osteoarthritis. As per a recent statement published by Piramal Healthcare Limited, after nationwide campaign against chronic diseases, India is expected to be the chronic disease capital, with 60 million people with arthritis, by 2025. The true prevalence of OA, however, varies greatly depending on the kind of definition used, age, sex and geographical area studied. When radiographic case definition applied, the prevalence of OA can be very high. Prevalence increases with age, so that about 11% of all women over the age of 60 years have symptoms due to knee OA. Knee osteoarthritis is the most common condition which represents a major contribution to the burden of physical disability (Felson DT et al 1987). Studies have shown that knee osteoarthritis in men aged 60 to 64 is more commonly found in the right knee (23%) than the left knee (16.3%), while its distribution seems to be more evenly balanced in women (right knee, 24.2%; left knee, 24.7%). The heterogeneous etiology of OA contributes to the real challenges for the physician's to treat and to find an effective disease-modifying drugs. Cross-sectional studies have shown that the risk of knee osteoarthritis is 1.9 to 13.0 times higher among underground coal miners than in a control population;

presumably, the main risk factor in this occupational groups are due to frequent kneelings or squattings.

Incidence and Prevalence

In the US, the incidence of knee OA is between 164 and 240 per 100, 000 patient per year, hip OA is between 47 per 100, 000 patient per years and hand OA ranges from 2% to 4% per year. The incidence rate of In the Asia-Pacific region, the prevalence of Knee Osteoarthritis was 7.50% in China (Wigley RD et al 1994), 5.78% in rural India (Chopra A et al 1997), 22.00% to 28.00% in urban and 25.00% in the rural population of north Pakistan (Farooqi A et al 1998), and 10.20% in Bangladesh (Haq SA et al 2005). The overall prevalence of OA rises from 1% in people <30 years to almost 10% in those >40 years, and 50% in those > 60 years. The Beijing Osteoarthritis Study showed that the prevalence of hip OA was lower in men than in women, and that the prevalence of knee OA in Chinese women was higher when compared with US cohorts. Many countries in Asia are witnessing rapid increases in aging population. In Asia, it has been estimated that the percentage of people with ages over 65 years will double in the next two decades, from 6.8% in 2008 to 16.2% in 2040. In most of the developed world's, demographic change was a gradual process following steady socio- economic growth over several decades. In many Asian countries, the change is being compressed into two or three decades. For example, during the period 2008– 2040, it is estimated that Singapore will increase the proportion of people aged 65 and over by 316%, India by 274%, Malaysia by 269%, Bangladesh by 261%, and the Philippines by 256%. In 2008, Japan had the huge world's oldest population (21.6% aged 65 years and over) and China and India were ranked the top two countries in the absolute number of people aged 65 and over (106 and 60 million, respectively).

The prevalence of OA, however, varies greatly depending on the definition used, age, sex and geographical area studied. A levelling off or decline occurs at all joint sites around the age of 80 years. The age and sex standardized incidence rate from the Fallon Community Health Plan in Massachusetts (USA) was highest for knee OA 240/100, 000 person/years, with intermediate rates for hand OA (100/100, 000 person/years) and lowest observed rates for hip OA (88/100, 000 person/years). For hip OA, the reported prevalence was 0.9 and 1.6 per 1000 per year in men and women respectively and for knee OA the corresponding Figure s were 1.18 and 2.8 per 1000 per year in men and women respectively. By 2020, worldwide OA is expected to be the fourth leading cause of disability. In our study, there are 3208 cases (M-1759 & F-1449) have been enrolled and based on the age of presentation, they were categorized into 3 groups. Ages from 35-50 years are in Group-A, (in 538, M-177 & F-361), 51-70 years of ages in Group-B, (in 1846, M-1181 & F-665) and from 71 years and above are in Group- C (in-824, M-401 & F-423).



Causes and Risk Factors for OA

There are some modifiable and non modifiable risk factors for osteoarthritis are exists. It is our duty to identify the possible treatable causes to prevent or at least to reduce the burden to these huge population of our society.

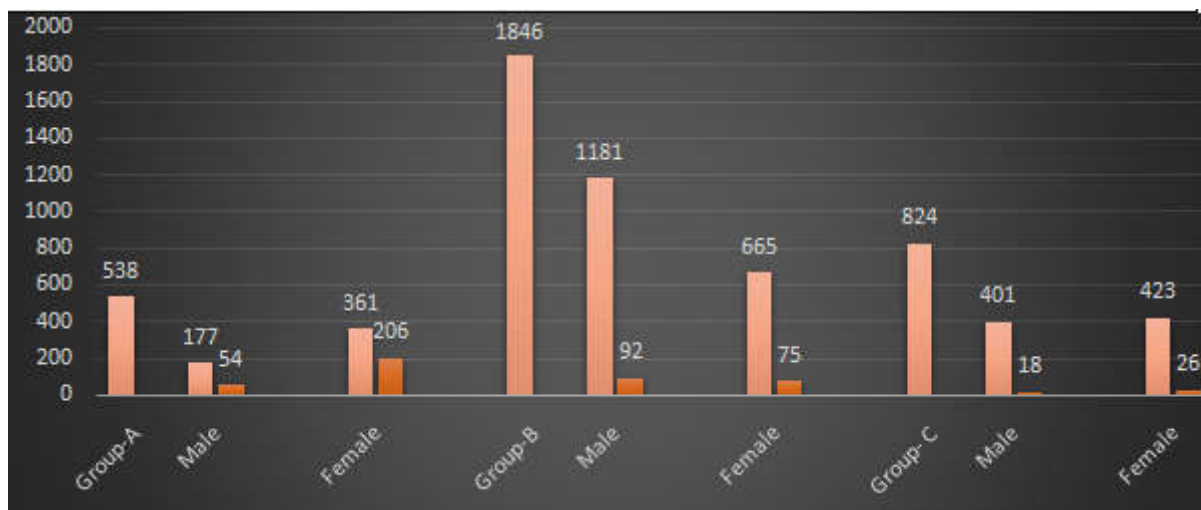
Modifiable Risk Factors

Obesity

Obesity is the most significant and greatest modifiable risk factor for an OA, leads to decreased mobility and negative impact on quality of life.⁴Coggon et al reported that BMI > 30kg/m² is associated with 6.8 times risk for OA knee. It is directly related to OA, both by excessive joint loading, and altered biomechanical patterns. Rise of 2 units of BMI,

leads to 36% chances of OA knee. Leptin is a 16- kd protein product of the obese gene (ob) and is produced primarily by adipose tissue. It acts centrally in the hypothalamus to regulate food intake and energy expenditure. Plasma leptin levels will be high in overweight individuals and it falls once they reduce weight. As per the article, leptin affects subchondral bone and it can theoretically play an important role in pathogenesis of OA. This constitutes the rationale behind disease modifying therapy through therapeutic strategies to counteract dysregulation of this proinflammatory adipokine production.⁵⁻¹⁰In our study, obesity was found as a significant cause in age group less than 50 years and it was predominantly seen in female (57.06%) than male (30.50%), whereas in other two groups, it was found as equal as in both sexes.

The Direct Relationship of Obesity and Incidence Osteoarthritis



Among the joint replacements population, more than 60% are obese, and the rate of post operative complications also are high in these groups. Weight loss improves both symptoms of %OA and it can slow the progression of OA. Study has proved that elimination of overweight could

reduce the incidence of OA knee by about 25% to 50% and OA hip by 25%.

Occupation

Farmers affected with OA knee and hip, whereas house wives are affected more often with knee and hand OA. Drillers are found to have OA of hand and shoulders. Ballet dancers have ankle OA and the sports persons, due to frequent injuries and micro fracture of cartilages, they usually develop knee and ankle OA. Avoiding frequent injuries to shoulders and hands can be minimized by periodical and paced manner of rest while operating heavy drilling machines and masons who working on high ceiling and gold smith and silver smith, respectively.¹¹⁻¹⁷ Likewise knee OA can be reduced by avoiding prolonged knee flexion manouvere and stop the habit of taking food in sitting posture with folded legs as we practice in Indian subcontinent. Do not carry, over head weight and persistent bending of spine and hip to avoid spondylosis and hip OA and incidentally, people with sedentary life style have markedly reduced hip OA.

Non Modifiable Risk Factors

Age

Age is the predominant non modifiable risk factor. As age advances, the incidence of OA are increases. This is best explained by inherent increases in systemic and local factors, obesity, ligament laxity and impaired neuromuscular joint protective mechanism in old ages. In

more than 80% of people after the age of 60, radiological evidence of OA are present. In the Framingham study, the prevalence was 30% between ages 65 to 74 years. It is thought that, increased incidence of microdamage to articular cartilages is the probable reasons for OA in the elderly population. But the incidence of OA in both sexes appear to be the same at and after 80 years of age.¹⁸

Over more than a decade of my experiences on osteoarthritis patients from three different centres from August 2006 to August 2019 (Rheumatology OP in Govt. Mohan Kumaramangalam Medical College Hospital, August 2006 to August 2019 and it was conducted in three different centres, namely in rheumatology out-patient department of the Government Mohan Kumaramangalam Medical College and Hospital, Salem where I have been there for more than a decade as Senior Assistant Professor of Rheumatology and K. A. P. Viswanatham Government Medical College, Mahathma Gandhi Memorial Hospital where I have been promoted as Associate Professor of Rheumatology, Tiruchirappalli and from Akitha Hospital, Centre of Excellence for Auto Immune diseases, Salem, TN State, India) are have been used for this study. There are 3208 cases (M-1759 & F-1449) have been enrolled for this study and based on the age of presentation, they were categorized into 3 groups. Ages from 35-50 years are in Group-A, (in 538, M-177 & F-361), 51-70 years of ages in Group-B, (in 1846, M-1181 & F-665) and from 71 years and above are in Group- C (in-824, M-401 & F-423).

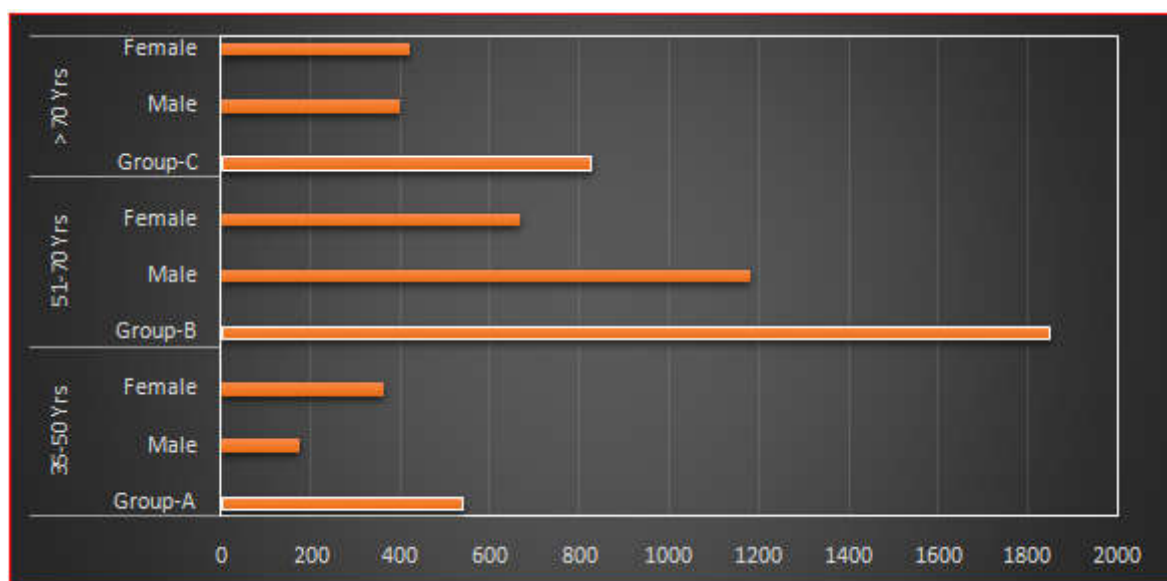
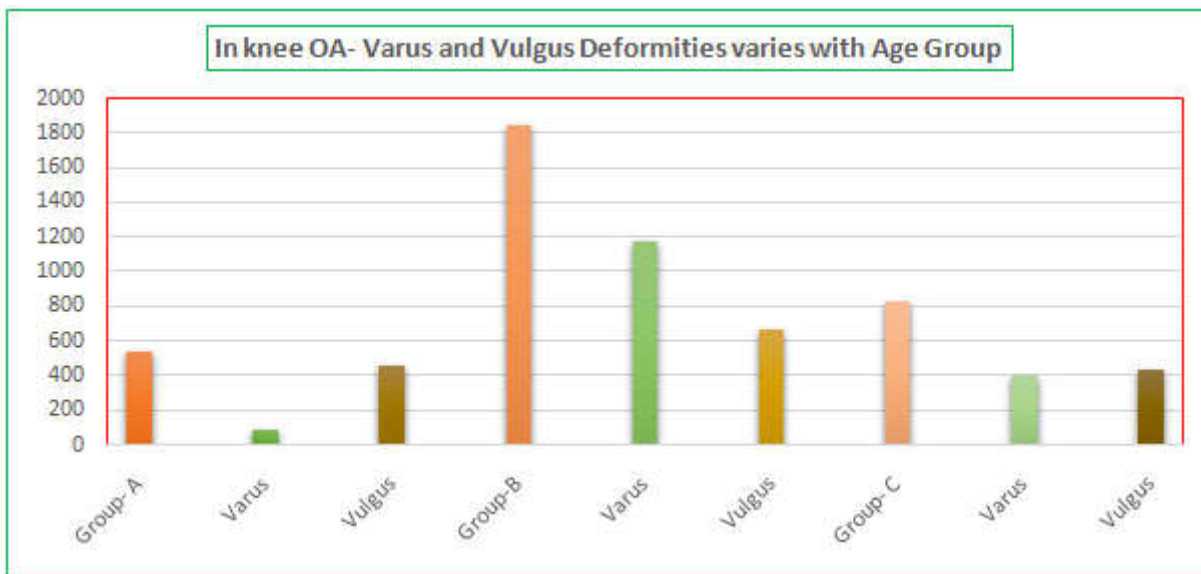


Figure 1: Age and sex wise incidence of osteoarthritis

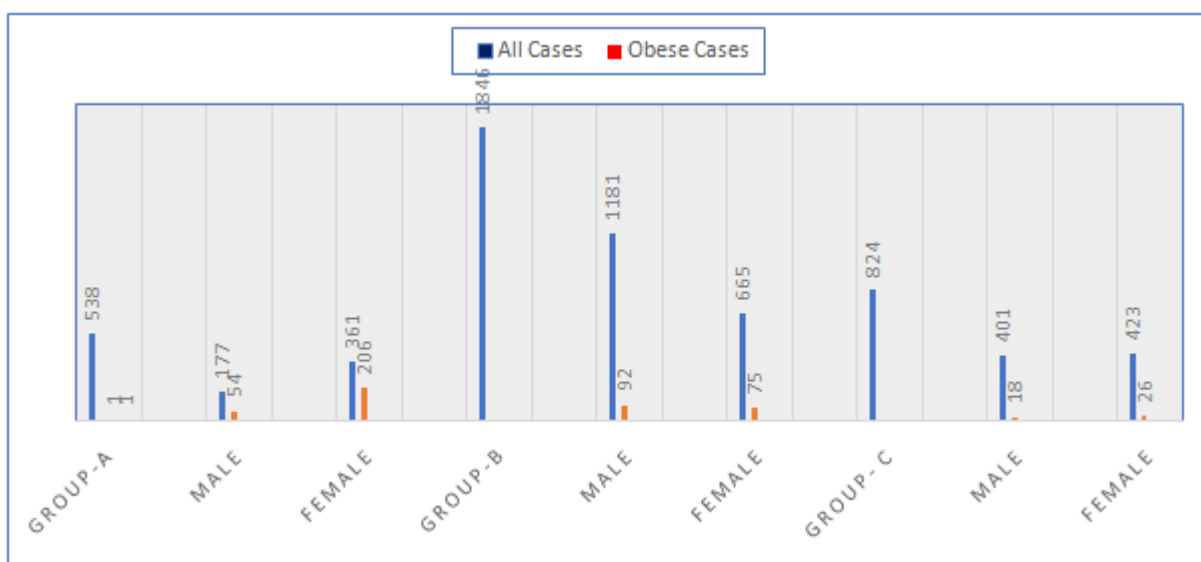
The youngest and oldest ages was seen, 35 and 92 years old, female and male, respectively. In Group-A, female outnumbered the male (female 67.10% (n-361) and male 32.89% (n-177) and in Group- B, male with OA are higher than female (male 63.97% and female 36.02%, whereas, more or less equal in both sexes in Group-C, as 48.66% and 51.33%, in male and female, respectively. Among both sexes, knee is most commonly involved joint. Unilateral

OA knee is the usual clinical presentation in age group less than 50 years but after fifty, bilateral knee involvement was noted. In our study, interestingly, in knee OA, genu varus and vulgus deformities varies with population age group. Genu vulgus deformities are commonly seen in group-A, and genu varus deformities are predominantly noted in group-B, and whereas in group-C, the varus and vulgus deformities have been observed equally.



Next to knee, OA hand was found and least was found in elbow joint. Another interesting features was observed that obesity has strongest association with OA and it was the predominant cause for the OA in young female. In our

study, obesity was found as a significant cause in age group less than 50 years and it was predominantly seen in female (57.06%) than male (30.50%), whereas in other two groups, it was found equally in both sexes.



(Figure 1) (Figure 2) (Figure 3) and likewise obesity, osteoarthritis and flat foot association was found in 36.96% of female and 11.82% of male.

Age and sexes are the most powerful risk-factor for OA (Cicutini FM et al 1997; Brown KS et al 1974). The prevalence of knee OA increases with age (Maurer K 1979); therefore, even the impact of this disease become more substantial with the aging of the population. Studies have shown that knee OA can greatly diminishes health status in the elderly population (Dominick KL et al 2004; Fryback DG et al 1993). Lawrence et al 1966, showed that, not only the marked increase in the occurrence of severe OA (equivalent to Kellgren and Lawrence system - Kellgren JH et al 1963 grades 3 and 4) with advancing age, but also that this age related increase is appeared to be exponential after 50 years of age. Mohamed Ahmed et al 2012, in a study on prescribing patterns in the management of arthritis in the department of orthopaedics, his study

reveal that out of 75 osteoarthritis patients, about 60% are in the age group between 51-65 years. Dinesh Bhatia et al 2013, study reveals that the prevalence of osteoarthritis is between the ages of 30 to 65 years. The prevalence of OA increases indefinitely with age, because the condition is not reversible. Men are affected more often than women among those aged over 55 years. A community-based cross sectional study was carried out in an urban resettlement colony in South Delhi to study the prevalence of knee osteoarthritis in women aged 40 years and treatment seeking behavior of women suffering from osteoarthritis, found 47.3% of women (123/260) are suffering from knee osteoarthritis.¹⁹⁻²⁰

Ethnicity and Race

The prevalence of OA differs with ethnicity and race. In USA, knee OA is common in African American than Caucasian (Dillan et al, 2006; Braga et al, 2009) whereas

Chinese and Caucasians are seem to have similar, but Chinese women have significantly higher prevalence (Zhang et al, 2001). Both hip and hand OA are less common in Chinese than Caucasian (Nevitt et al, 2002; Zhang et al, 2003). In general, OA knee is more common in Indians whereas hip OA in European populations with a sharp distinction that OA hip also can be seen in poor Indian farmer, due to the habit of carrying weight on head.

Sex

Sex hormones might have role, either in onset, initiation or progression of OA. This can be better explained by the presence of oestrogen receptors in chondrocytes and women who use HRT has less prevalence of OA than the counterpart.²¹⁻²³ However, study results are conflicting and this relationship was never clearly observed (de Klerk et al, 2009). Whatever it is, OA knee and hand OA are affecting women twice than men whereas more often, hip OA was seen more in men.

Injuries and recurrent stress on the joint

Injuries and recurrent mechanical stress on the joints are thought to be the causes for OA. Ankle injuries with trimalleolar fracture almost certainly result in OA. The human and animal model studies has shown that loss of ACL (anterior cruciate ligament), injuries to meniscus or surgical meniscectomy often leads to knee OA. Even though, there was no cartilage damage after an injury, cartilage may degenerate rapidly, if the joint is malaligned or unstable.

The pattern of occurrences of OA of joints are directly related to the type of occupation they entertain. Case controlled studies have shown that jackhammer operators, shipyard workers, drillers, coalminers and others in these similar groups of activities lead to OA due to repetitive vibrating injuries. Likewise OA knee is due to repeated kneeling, squatting, bending and lifting heavy weight or carrying load over head as often the practices by our own Indian villagers and farmers. Comparatively, hip OA are common in Indian farmers whereas westerners suffer more with OA hip and knee. Obesity is a major determinant of OA knee. If major injuries are excluded, long distance running and jogging do not appear to increase the risk of OA knee. Players who participate in highly competitive sports or in athletics sustain more joint injuries, and thereby they develop OA than low risk sports. As per the study, long distance runner and tennis players are found to have 2 to 3 fold increased risk of developing OA knee and hip.²⁴⁻²⁶

Effect of Anatomical Changes in Shape of Joint

Even when there is a subtle structural anatomical change in the shape of joints, it becomes subjected to repetitive mechanical stresses. Thereby, these joints prone for OA. Murray has reported that preexisting asymptomatic subtle anatomic abnormality can result in primary hip OA, and he noted that simple osteotomy in such cases, can achieve positive outcome. In support to his observation, the pistol grip deformity (non spherical shape) of femoral head and

abnormally low neck shaft angle is the predisposing risk factor for OA hip. Likewise, another observation by Cooke and Colleagues has found that abnormal geometric force can perpetuate into OA knee.²⁷⁻³¹

Effect of overweight on OA

Obesity seems to be an independent and strongest risk factor for OA. There are two mechanisms that can explain the role of overweight in OA. First, overweight increases mechanical stress on weight bearing joints and these overweight persons have higher bone mass, which may cause stiffness of subchondral bone and break down of cartilage. Second, overweight individuals, have increased expression of insulin like growth factor type-1 and visfatin, which has damaging effect on overweight bearing joints. When the body mass index (BMI) is highest quintile at the initial stages of examination itself, the risk of developing OA knee incidence could be 1.5 times for men and 2.1 times for women. When the weight increases further, risk burden will raise to 1.9 times for men and 3.2 times for women. It is certain overweight plays a role in OA knee.

Periarticular Muscle Weakness

When there is a muscle weakness around the knee joint, like quadriceps wasting or atrophy, the brake on the pendular action of lower limb is lost or reduced. When this stabilizing effect of knee is lost, the mechanical stresses on the joint will increase, which result in OA knee.

Genes and Osteoarthritis

Like any other inflammatory arthritis, OA too has genetic role in the disease onset and pathogenesis. Number of epidemiological, linkage genome wide association studies are found to have genetic influences on OA. These studies lead us to probe into molecular mechanism involved in onset and progression of OA and thereby we can find potential treatment option or it can help us to recognize the person at risk for OA.^{32, 33} Studies have found that, mother of women with DIPJ OA has two times increased risk of OA in her and likewise, the proband sister, three times as likely as the mother and sister of an unaffected women. It appears that autosomal dominant transmission is involved in female and recessive inheritance in male. Heberden's nodes are 10 times more commonly present in female than male that too more on dominant hand. Type II collagen point mutation was identified in the cDNA coding. This results in switching of arginine to cysteine at position 519 in the fibrillar α II chain. The presence of this abnormality is found to be associated with familial chondrodysplasia and secondary OA in several generations of families. Likewise, genetic abnormalities of the type II collagen gene (COL2A1) which is located in chromosome 12 are being associated with OA and spondyloepiphyseal dysplasia (Ala-Kokko et al, 1990).³⁴ Pseudoachondroplasia and multiple epiphyseal dysplasia are present in early onset OA with short stature. In this, gene defect have been localized to short arm of chromosome 19. The clinical picture in these genetically predisposed individual can have OA in uncommon joints than primary OA (eg, Elbow

joint) and therefore OA can occur in adolescent age itself. Another recent study has shown IL1 gene cluster is associated with development of hip, knee and hand OA. The group of genes appears to be involved in early skeletal development and maintenance of cartilage and bone are GDF5 (growth/ differentiation factor, by Miyamoto et al, 2007), FRZB (frizzled related protein β , by Loughlin et al, 2004 & Lories et al, 2007 & 2009), TGF β (transforming growth factor β / SMAD3, by Valdes and Spector, 2010) and DIO2 (type 2 iodothyronine deiodenase, by Meulenbelt et al, 2008). Among all these genes, GDF5 (also known as cartilage derived morphogenic protein 1-CDMP1, is a member of BMP) has strongest role in development of OA. The lack of reduction in GDF5 gene result in abnormal ligament laxity, joint instability, or it can lead to abnormal collagen network and subchondral bone modeling and remodeling, thereby, culminate in OA (Danns et al, 2011). Another GWAS study has proved that genetic variant in the DOT1L- like, histone H3 methyltransferase (DOT1L) gene is strongly associated with joint space width and hip OA. Since DOT1L is an enzyme and hence in future, pharmacologically, we can target it in the management of OA (Barry et al, 2010).

Effect of Density of Bone and OA

Actually, an inverse relationship is being appreciated in OA and osteoporosis, that is; the bone mineral density is much stronger in OA joints. There was an indirect evidence to support this point that, OA prevalence is higher in patients with osteopetrosis than in those people with higher bone mineral density.

Effect of oestrogen hormone and OA

The incidence of OA seems to be greater and rapidly progressive in menopausal age group of women than men and this suggests that post menopausal oestrogen deficiency increases the risk of OA. In these records, studies have proved that women who have used the HRT (Hormonal Replacement Therapy) are at lesser risk for developing OA knee and hip than the women have not used HRT. Yet, there were no randomized controlled trials to say that oestrogen should be used for prevention and treatment of OA. As per clinical trials, HRT may prevent pathological changes in OA but not the symptoms of OA.

Role of Vitamin-D3 and other Vitamins in OA

Nowadays, deficiency of vitamin- D3 is associated with increased risk for OA than those who have normal or high vitamin- D3. The disease progression is three times more worsened and progress rapidly in people with low vitamin D3.³⁵⁻³⁷ Antioxidant effects are being conferred by other dietary sources like vitamin- C, beta carotene and vitamin E. They appear to have an inhibitory effect on progression of OA. However, prospective, randomized controlled trials are necessary to confirm the role of vitamins and other antioxidant in OA.

Factors Worsening the Progression of OA

Events which initiate the joint damages are different from the joint worsening factors of OA. Once pathological tissue damage is occurred in the given joint, and if the relevant atmosphere of further structural damages are present like obesity, old age, women, presence of Heberden's nodes, constant or repeated and perpetual injuries to the joint and of course, the presence of dietary deficiency of vitamin C & D can precipitate OA.

Factors Worsening the Pain and Disability of OA

Disability gets worsened when patients have more anxiety and depression about the disease and further worsened by periarticular muscles weaknesses. The degree of disability and the pathological severities are more in females than males, because male seek medical advice early than female.

Often there won't be any correlation between the amount of pain and radiological signs of OA. Some have severe degenerative changes, osteophytic overgrowth, subchondral sclerosis and JSN (Joint Space Narrowing), but they are asymptomatic. On the contrary, quite number of patients, report to clinician with severe pain in knee or hip, but nothing abnormal seen radiographically. Liang precisely expressed this issue in few words "X-ray don't weep but patient weep."³⁸

Pathology

Chondrocytes are responsible for the production, maintenance, remodeling and eventually destruction of the cartilaginous matrix. Metabolic activities of chondrocytes are low and it can survive even in low hypoxic state. Hypoxic stimulus regulate the intracellular expression of hypoxia inducible factor-1 α (HIF-1 α), which support the survival of chondrocytes. The nutrients for the cellular activities of chondrocytes are obtained from synovial fluid and subchondral bone. Perhaps, chondrocytes per se has limited regenerative capacity and so whenever, significant injuries are there, it often predispose to OA (Dell'Accio and Vincent, 2010).³⁹

In early stages of disease, chondrocytes appear to adapt to local stress, by proliferation of chondrocytes in clusters, which alter the ECM by expressing markers of inflammation like collagen type X, VEGF and matrix metalloproteinase 13. Chondrocytes go for progressive destruction, cell death by apoptosis and necrosis by release of the matrix degrading enzymes and cytokines. Even before clinical symptoms start, the smooth surface of the articular cartilage becomes roughened with small irregularities and superficial clefts. When the disease is unchecked, the cracks become deeper, extend up to middle zone of cartilage. When these lesions grow and connect each other, damaged surface area is increased. Cleft becomes eroded and ulcerate and finally exposing the underlying subchondral bone. Subchondral bone is a global term that includes the subchondral bone plate, underlying trabecular bone and bone marrow space. Subchondral bone remodels itself and appears like an

ivory, dense substance with a smooth surface and it is called eburnation. Further, it progresses with formation of new bone at the joint margin (osteophyte). Subchondral cysts are formed either by influx of synovial fluid or by local necrosis of bone and bone marrow oedema.⁴⁰⁻⁴² Though the insult, starts in articular cartilage, and ends up in bone, these two processes mutually influence each other and co-contribute to the progression of disease (Karsdal et al, 2014).⁴³

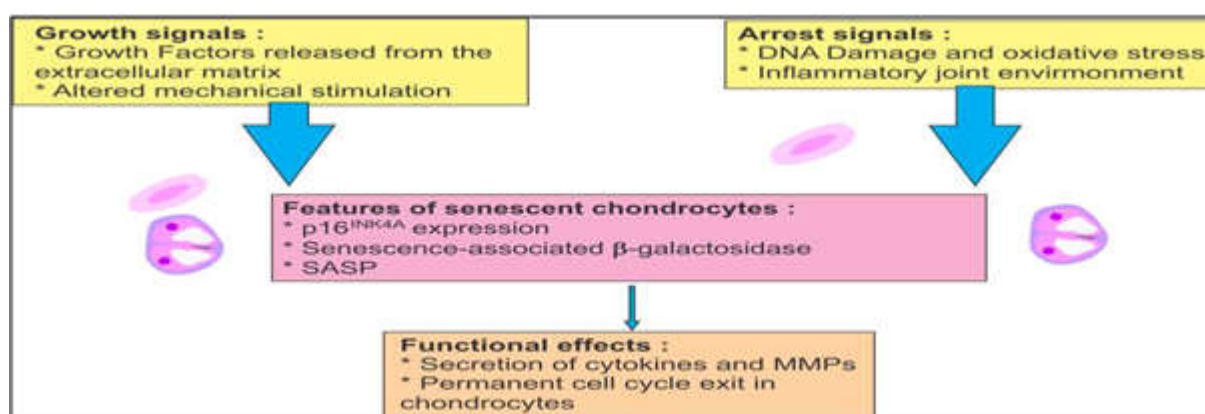
Pathogenesis

In the early stages of the disease, water content is increasing, leading to tissue edema and weakening of the collagen network. Type II collagen synthesis decreases and is replaced to some extent by type I collagen. Likewise, proteoglycan content strongly decreases and shorter glycosaminoglycans appear. The concentration of type 6 keratan sulfate increases during the osteoarthritic process to the detriment of type 4 keratan sulfate. These changes modify the capacity of the ECM to retain water, changing the distribution of force in the weight bearing zone and the transmission of load to the subchondral bone.

Pauli et al, 2016 study, shed light on the connection between aging changes in chondrocyte of articular cartilage and the way that can promote development of OA. Eventhough, age and OA is inter-related, there must be several independent processes can contributing to this chronic disease. The age-related inflammation is aptly

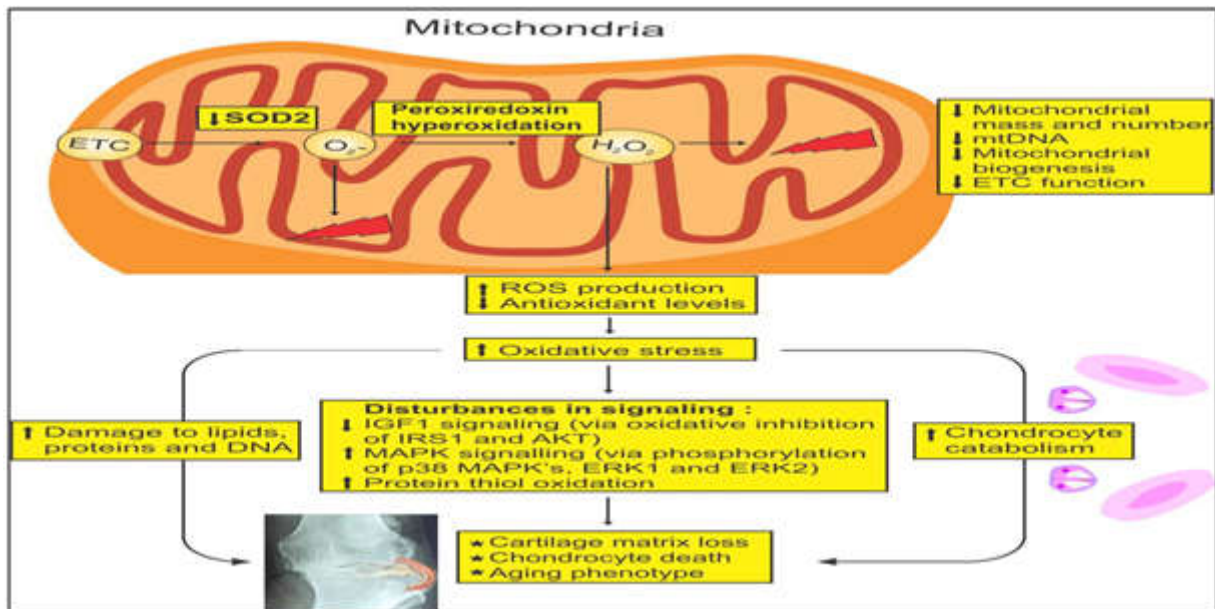
called as 'inflamm-aging'. The cell of senescence may negatively affect the local environment by SASP (senescence associated secretary phenotypes). This proinflammatory cellular phenotype, can be induced by simultaneous stimuli from growth factors from ECM, altered mechanical pressure and arrest signals like mitochondrial DNA (mtDNA) damage, and increased oxidative stresses (reactive oxygen species) with decreased antioxidants contribute to release of proinflammatory cytokines (IL1 β , IL6, IL8 and TNF α) and proteases like MMP 3, & 9, causes disturbances in cell signaling with decreased IGF1 natural growth factors, reduced activity of 5'-AMP- activated protein kinase and finally it is associated with loss or defective function of autophagy. Therefore, there will be loss of cartilage matrix and chondrocyte cell death. These various processes can contribute to the development of OA by promoting a proinflammatory, catabolic state accompanied by increased susceptibility to cell death, that together lead to increased joint tissue destruction and defective repair of damaged matrix. Improved understanding of aging-related inflammatory mechanisms that can lead the discovery of new targeted therapies with an aim to slow or stop the progression of this disabling condition. (Figure 5.1 and 5.2)

Pathogenesis of Osteoarthritis by the Phenomenon of 'Inflamm-aging' by Senescent cells
Inflammation caused by aged cells (Figure 5-1)



DNA, deoxyribonucleic acid; SASP, senescence-associated secretary phenotype; MMPs, matrix metalloproteinases.

Figure 5.1a: Pathogenesis of osteoarthritis by the phenomenon of 'inflamm-aging' by senescent cells



mtDNA, mitochondrial deoxyribonucleic acid; ETC, electron transport chain; ROS, Reactive oxygen species; IGF, insulin-like growth factor; IRS, insulin receptor substrate; MAPK, mitogen-activated protein kinase; ERK, extracellular signal-regulated kinase.

Figure 5.1b: Pathogenesis of osteoarthritis by the phenomenon of 'inflamm-aging' by senescent cells

In aging cartilage, advanced glycation end products (AGE) get accumulated, which lead to protein modification by non enzymatic glycation and it leads to alteration of biochemical properties. Moreover, AGE can bind to specific receptors present on the surface of chondrocytes, called receptors of advanced glycation end products (RAGE). The AGE/ RAGE system is involved in the catabolic activity of the chondrocytes (Loeser et al, 2016).⁴⁴ It changes the properties of the ECM, making the collagen structure more susceptible to degradation by collagenases. When these changes occur in collagen network, it becomes irreversible.

After stimulation either by mechanical stress or by cytokine, MMPs can be synthesized by chondrocytes, synoviocytes and osteoblast. These MMPs are zinc dependent endopeptidases and are capable of degrading all kinds of ECM proteins. OA chondrocytes produce a variety of matrix degrading enzymes including MMP-1, MMP-3, MMP-9, MMP-13, MMP-14 and aggrecanases, ADAMTS-4, ADAMTS-5 (a disintegrin and metalloproteinase with thrombospondin motifs), thus demonstrating that cartilage cells contribute to the degradation of their own tissue. Their effect can be controlled by tissue inhibitors of metalloproteinases (TIMPs) and by the inhibitor of plasminogen activator. Hence, the balance between the amounts of MMPs and TIMPs in the cartilage determines the level of degradation (Cawston and Young, 2010).⁴⁵

Breakdown of the type II collagen is mainly due to collagenase-1 (MMP-1) and collagenase-3 (MMP-13), which are localized in the superficial zone and deep zones

of cartilage respectively. Stromelysin -1 (MMP-3), Stromelysin-2 (MMP-10) and Stromelysin-3 (MMP-11) are also involved in the degradation of cartilage (Okada et al, 1992). Likewise, Matrilysin (MMP-7) can degrade the ECM components of proteoglycans (Ohta et al, 1998). In rapid destructive hip OA, MMP-3 and MMP-9 are elevated in synovial fluid and plasma (Masuhara et al, 2002).⁴⁶

TGF β is considered an anabolic factor for cartilage. Despite its physiological role in healthy cartilage, the pathway and its downstream effects appear dysregulated in OA (Vincent T, et al and Van der Kraan et al, 2010).^{47, 48} In aging or in stressed cartilage, there appears to be a critical shift in TGF β - receptor interaction, with preferential activation of the activin-like kinase (ALK)-1 receptor over the ALK-5 receptor. This process stimulates chondrocyte hypertrophy and it contributes to osteophyte formation and synovial fibrosis. Likewise, BMPs (bone morphogenic protein), also plays a role in osteophyte formation (Van der Kraan et al, 2007 & 2010; Lories et al, 2011).⁴⁹⁻⁵¹ Wnt (wingless protein) signaling plays a potential role in cartilage and bone homeostasis. Activation and suppression of the Wnt- β catenin cascade can lead to OA in rodent models. Activation of β - catenin leads to chondrocyte hypertrophy and chondrocyte death by suppression of β - catenin.

Cartilage breakdown products increase synovial inflammation. The inflamed synovium produces catabolic and proinflammatory mediators that lead to increased production of proteolytic enzymes responsible for cartilage breakdown. The most common histological feature of inflammation of synovial tissue is hyperplasia, with an increased number of lining cells and a mixed cellular infiltrate (Myers et al, 1990; Smith et al, 1997; de Lange Brokaar et al, 2012).⁵⁴ Macrophages and T cells are the most common cells in OA synovial tissue (Benito et al, 2005; Bondeson et al, 2006; Diaz- Torne et al, 2007; Pessler et al, 2009; Scanzello et al, 2009; Ogdie et al, 2010),⁵⁵ although there is little evidence of a fully developed adaptive immune response. Inflammatory cells

and their cytokines are present in both early and late OA (Benito et al, 2005). In addition, these cytokines can stimulate chondrocytes to release cartilage degrading enzymes. Chondrocytes have inherent capacity of producing these kinds of cytokines and they can act via autocrine and paracrine pathways (Golding, 2000; Martel-Pelletier et al, 1999).⁵⁶ Likewise, mechanical forces can activate chondrocytes to induce inflammatory cytokines. Sometimes, oxidative stress may induce the chondrocytes to release cytokines (Kurz et al, 2005).

Synovial inflammation in OA

Inflammation of synovium in OA can occur by the following reasons. When degraded cartilage fragments fall into the joint cavity, they act as foreign bodies, thereby synovial cells react and start producing inflammatory mediators or else synovial cells per se may act as primary trigger for OA. Another reason, it could be initiated or aggravated by the presence of systemic inflammatory mediators or by the release of inflammatory mediators from aging joint cartilages. The synovium undergoes variable degree of hyperplasia, and inflammatory changes may sometimes be observed, although to a much lesser extent than in RA and other inflammatory arthropathies. Osteochondral bodies commonly occur within the synovium, reflecting chondroid metaplasia or secondary uptake and growth of damaged cartilage fragments. The outer capsule also thickens and contracts, usually retaining the stability of the remodeling joint. The muscles surrounding affected joints commonly show evidence of wasting and non specific type II fibre atrophy.

Infra- Patellar Fat Pad and OA

In OA, infra- patellar fat pad may have an association with inflammation (Ioan- Facsina and Kloppenburg, 2013).⁵⁷ The IFP is composed of adipocytes and stromal vascular cells like macrophages, T cells and mesenchymal stem cells. Cellular interactions between these cells and OA have been described.

IL1 β and TNF α are the prominent cytokines in cartilage catabolism (Ushiyama T, et al, 2003).⁵⁸ IL 1 can induce the expression of MMPs and other degradative genes. In OA cartilage, IL 1 is found to be co-localized with TNF α , MMP-1, MMP-3, MMP-8, MMP-13 and type II collagen. In addition, IL1 appears to induce ADAMTS-4, whereas TNF α induces both ADAMTS-4 and ADAMTS-5. IL 1 and TNF α increases the synthesis of PGE2 by stimulating the gene expression and or by activating COX-2 microsomal PGE synthetase-1 (Mpges-1) and soluble phospholipase A2 (sPLA2). Moreover, these can produce excessive amount of nitric acid via inducible nitric acid synthetase (iNOS or NOS2) and induce other proinflammatory cytokines like IL 6, leukocyteinhibiting factor (LIF), IL 17, IL 18 and chemokine IL 8.

In obese individuals, adipose tissue secretes many soluble mediators, like adipokines. These adipokines (resistin, leptin and adiponectin) are found in synovial fluid (Schaffler et al, 2003) and it has multiple functions.⁵⁹ Therefore in obese individuals, in addition to weight

bearing joints with OA, non weight bearing joints like Hands are also affected by these systemic effect of adipokines. Some studies have demonstrated that metabolic syndromes like hypertension and type 2 DM have an adverse effect on cartilage homeostasis and hence association with OA.

Chondrocytes divide to produce nests of metabolically active cells. Initially, matrix components are produced at an increased rate, but at the same time, there is increased degradation of the major structural components of cartilage, including aggrecan and type II collagen. Eventually, the concentration of aggrecan in matrix falls and makes the cartilage vulnerable to load bearing injury. Fissuring or fibrillation of the cartilage surfaces then occurs, leading to the development of deep vertical clefts. Localized chondrocyte death and decreased cartilage thickness; this is focal rather than generalized in nature and mainly affects the maximum load bearing part of the joint, although, eventually, large parts of the cartilage surface can be damaged. Calcium pyrophosphate and basic calcium phosphate crystals often become deposited in the abnormal cartilage.

The subchondral bone is also abnormal, with osteosclerosis and subchondral cyst formation. Fibrocartilage is produced at the joint margin, which undergoes endochondral ossification to form osteophytes. Bone remodeling and cartilage thinning slowly alter the shape of the OA joint, and increasing its surface area. Patients with OA also have higher BMD values at sites distant from the joint, and this is particularly related to osteophyte formation. The reason for this is not completely understood but it may reflect the fact that common signaling pathways are involved in the regulation of bone and cartilage metabolism.

The real understanding of the cellular and molecular processes and mediators involved as well as communication between cells and tissues can lead to the identification of therapeutic targets and the development of specific strategies to prevent, treat and of course, in future we can even sincerely aim for cure of OA.

Clinical Features of Osteoarthritis

OA is the most common musculoskeletal disease-causing high rate of physical and functional disability. Occurrence of OA is on the rise due to addition of aging population every year and they are already almost equal to the middle age population. Unfortunately, across the globe, due to increase in the plumps and bellies population, the OA is no longer considered as diseases of old, but of middle aged too. As a result of these, we see lot of OA segment of patients even below 50 years and they often find difficult to accomplish their own jobs of daily needs, work day absenteeism, loss of works and income or women with household chores, which directly or indirectly affect quite large number people and in addition, they are also have disturbed sleep, depression and other psychosocial disorders. Added to this, chronic and persistent pain in OA and sometimes, even in post joint replacement patients are experiencing joint pain due to recently recognized,

enhanced central neuronal signalling which are arise remote from the affected joint.

Osteoarthritis of Hand

As our early ancestors were evolved from quadrupeds to bipeds, changes have occurred in hands as like what happened in pelvis, spine and hip joints which have increased the risk of osteoarthritis. The pinch grips of human hands are not tuned like apes, which result in hand OA at base of thumb, and walking upright, which make them prone for OA knee and hip OA.

Hand OA is most common osteoarthritis and it frequently affect female than men with sex ratio of 10:1 and familial aggregations are usually present (Spector et al 1996). Hand OA begins after 40 years, disease course usually insidious, but sometimes, acute in onset and it affects multiple joints like DIP, PIP and 1st CMC joints (Kloppenburger and Kwok, 2011). When MCP joints are involved, it should prompt us to investigate for inflammatory and metabolic causes of RA and iron storage diseases. As the disease progresses, there is characteristic loss of mobility and flexion and deviation of distal phalanx. When patients present with polyarticular hand OA, always look for OA in other joints. If there is involvement of OA hip, knee or other joints, it is called generalized OA. Hand OA can present as nodular OA, erosive OA and a selective involvement, at the base of the thumb (1st CMC).

Nodular Osteoarthritis

This is the most common type of primary osteoarthritis, usually in female during 5th decade of life with sex ratio of 10:1. Familial clustering is often present There is a strong genetic role in NOA, with possible polygenic mode of inheritance. This disease often coincides with the menopause with an unpredictable sudden onset of acute arthritis involving DIP, PIP and CMC joints, with simultaneous onset of OA knee and other peripheral joint. Hands appear stiff with synovial swelling and often it is associated with either Heberden's or Bouchard's nodes. Before developing knobblies swelling or bony bumps over the fingers, it can present as inflammatory arthritis. When bony nodularity's are present in DIP and PIP, it is called Heberden's and Bouchard's nodes respectively, and often these can be more marked in dominant hand. These nodes are responsible for subluxation, dislocation and malalignment of fingers, thereby poor hand grip. Nodular hand OA corresponds to generalized polyarticular OA. Occurrences of nodular OA in middle ages are one of the predictors of osteoarthritis of knee in future. DIP OA may cause confusion with psoriatic arthritis, to ascertain PsA (Psoriatic Arthritis), just look carefully; we can pick up features of nail psoriasis, plaque psoriasis, asymmetrical arthritis of other joints, with special predilection to cause arthritis of IP joint of thumb but selectively sparing CMC joints of thumb. Radiologically, both these entities have different manifestations, such as, sea gull wing appearance in OA and pencil in cup in PsA.

Erosive Osteoarthritis of Hand

One third of patients develop, acute or subacute onset of OA in both hands with morning stiffness, and present with rapidly progressive painful and erosive OA mimicking as inflammatory arthritis. However, systemic symptoms are relatively absent. Typically occurs in postmenopausal women with sex ratio of 12:1. Pathologically has combination of degeneration of cartilages and proliferative synovitis, narrowing of joint spaces, subchondral erosions are present. But unlike RA, there will be no marginal erosion and osteopenia.

First Carpometacarpal Joint Osteoarthritis of Hand

(Trapeziometacarpal OA or Osteoarthritis of Base of Thumb)

As mentioned earlier, as against apes, human thumb not at all well designed for pincer grip and grasp. Because of its relative instability, and daily routine repetitive use of this joint for every action, it is left with no choice but to proneness for OA. This multifunction CMC saddle joint is formed by the trapezium bone of wrist and the first metacarpal bone of thumb. CMC OA is occurred when the cushioning cartilage is eroded or slips away. Dahaghin et al, showed that about 15% of women and 7% of men between 50 and 60 years of age suffer from CMC OA.⁷⁸ In another study, Armstrong et al, reported a prevalence of 33% in postmenopausal women, and 11% in men older than 55 years.⁷⁹ Hard manual labourers, gold & silver smith, rope puller, manual coir makers, carpenters, house wife, hand drill user are prone for CMC OA. De-Quervain's tenosynovitis can be associated with CMC OA and it can exacerbate or limit the functional ability of thumb.

Symptoms of Hand OA

Most commonly present with pain and usually the EMS lasts less than half an hour. Range of motion of fingers will be reduced, and crepitus are present. Due to presence of Heberden's and Bouchard's nodes, joint subluxation or malalignment, hand grip and pinching of objects and opposition will be affected. In acute onset, erosive hand OA typically can mimic acute synovitis of RA and PsA. In CMC OA, pain at the base of thumb, initially worsened on movement, giving pressure to thumb and whilst tying a knot or holding a saucepan, the domestic act of lifting a grinder, and when gold or silver smith doing precision works etc, and later on felt even at rest.

Signs of Hand OA

DIP and PIP are swollen, tender, soft and fluctuant at early stages and later become bony hard. There will be Heberden's and Bouchard's nodes in DIP and PIP respectively. Chronic disuse wasting can result in prominent appearance of PIP and DIP joints and it looks like inflamed joint but actually, the bone which appear prominent due to wasting of small muscles around the joint. Dislocation, subluxation and malalignments of fingers can be present.

Typical image of Hand OA



clinically bony hard PIP and DIP joint and X-ray hand showing DIP & PIP joint narrowing and erosion in second and third DIP and third PIP

Figure 6.1: showing typical hand OA with DIPJs and PIPJs arthritis and narrowing of joint spaces

Erosions are noted in 2, and 3 DIPJ & PIPJ. CMC OA is also noted. (Courtesy: Samikrishnan.P)

Swelling and sometimes, redness at the base of thumb can be noted in CMC OA. In advanced stages of CMC osteoarthritis, squaring of hand, and zigzag deformity of thumb with deviation of thenar eminence towards the middle of hand, whilst the thumb phalanges extended. FIGURE 6.1

Osteoarthritis of Knee

Overall prevalence in the elderly population is about 24%, and at least about 8% could be seen in middle age and obese people. In young and middle ages, obese females are more affected than male. By 2050, as per North American literature, about 66 to 100% of people above 70 to 80 years are going to develop OA knee. Indians and Chinese have increased incidence of severe OA knee. Farmers, miners, people carrying excess weight on head and other jobs which require frequent bending of knees are more prone for OA knee. It can involve either one of medial and lateral tibiofemoral compartment and the patellofemoral compartment. The precise location of pain can be helpful for locating the compartmental OA, like, when pain is present in outer aspect of knee in obese female or male with genu valgus, they will be having lateral TF OA. Likewise, when pain is present on medial aspect of knee with genu varus and anterior knee, it is probably due to medial TF and patellofemoral OA respectively. The patellofemoral OA pain usually presents during climbing or descending stairs or while get down from buses and it occasionally leads to buckling of knees and falls. Valgus and varus deformities can directly affect the range of movement and accelerate the cartilage injuries, subchondral sclerosis and joint space narrowing.

Symptoms

Pain and Stiffness (Pain in OA, “worsened by work and relieved by rest”)

Pain is the troublesome symptom. In early OA, they often feel pain after brief exertion. Later, they will notice pain while getting up from squatting, climbing stairs, and running and followed by pain even at rest. They feel period of gelling (stiffness) of joint for some time, before becoming relieved from pain, and it last only for about 30 minutes. This is often called as “first movement pain”. Pain disturbs the sleep by hitting of condyles by muscular relaxation or by increases in joint effusion at rest. Pain usually presents on both sides of knee, sometime, one side more than other. There will be difficulty in kneeling, and difficulty in sitting and getting up from Indian style sanitary ware. Female with OA, they have difficulty in performing household chores. Frequently, there won't be any correlation between painful limb and radiological signs of OA. Sometime, patient stance will aggravate the joint pain, that is, if they stand on one leg, that side of joint will receive 2/3 of body weight; therefore, the pain, damage, disability and deformities are further worsened. Frequent locking of knees and difficulty in extending the flexed knees due to loose bodies or fragments of cartilage in the joint space. Sometimes, they feel friction or grunting sounds in knees while walking due to meeting of roughened and irregular cartilages. Buckling or “giving way” feel in knees can be appreciated by patients, which can be due to quadriceps wasting, meniscus lesions, ligamentous laxity or slip of patella from intercondylar fossa due to condylar displacement by uni-compartmental OA knee. Occasionally, pain may be present, much lower than knee joint, and over medial side, that is due to anserine bursitis. Posterior knee pain can be due to tense effusion or by ruptured or infected baker's cyst. Their gaits become altered by bowing of legs, knock knees, shortening of limb or disparity in limb height, and by fixed flexion

deformity. OA may be associated with depression and disturbed sleep due to pain, cost of treatment and foresee huge expenditure for surgery etc. Articular cartilages are anerve structure and it is insensitive to pain, but there are reasons for pain in OA.

Common causes of pain in OA Joints	
Periostial inflammation	subchondral bone inflammation
Pressure on subchondral bone	Venous engorgements
Intramedullary joint cavity Hypertension	Capsular distension or stretching
Synovitis	Osteophytic outgrowth
Tendonitis	Fasciitis
Bursitis	Stretching of Nerves by pressure
Entrapment of Intraarticular ligaments	Central sensitization of pain

Swelling

Mild to moderate swelling of knees are present, usually one side more than the other. They often have suprapatellar effusion and with baker’s cyst, patellar tap can be elicited. About 20 to 30% of patients come to us with severe and tense swelling of one leg, with warmth and tenderness of calf muscle, which is due to ruptured baker’s cyst. It often misleads to think as DVT. Why it is

important, because, Moses sign and Homan sign are also positive in this condition, thus there will be error in clinical judgements. Just look for crescent sign (semilunar shape swelling around medial and lateral malleolus) with subcutaneous oedema. If present, that is probably due to ruptured baker’s cyst.

Signs

There will be reduced range of movement, and pain on extremes of joint mobilization. Mildly warm and is tender. One can appreciate patellar tap, fluid thrill, joint crepitus (sometimes audible) or locking of knee whilst moving due to presence of loose bodies in joint cavity. Patella may get jetted out from intercondylar fossa. Knee looks enlarged due to condylar enlargement, synovitis and partly due to osteophytic growth.

In secondary OA, condylar enlargement is not usually present, but effusion, deformity and subluxation of joints may appear as enlarged joints. Decreases in anterior and posterior laxity of joint are associated with reduced joint space. 80 - 90% of patients have bow (varus) knee due to medial femorotibial compartment OA, whereas 10 – 20% has knock (valgus) knee, due to lateral tibiofemoral compartment OA. (Figure 6.2, 6.3, 6.4 and 6.5)

Varus and Vulgus of deformity knee



Reduction of vulgus knee after brace and footwear with lateral insole

Figure 6.2: shows vulgus and varus deformities of knee joints, and appreciable reduction in varus deformity by knee brace and with footwear modification. (by Samikrishnan. P)



FIG. 6.3

FIG. 6.4

FIG. 6.5

Figure 6.3: shows bil. medial TF JS narrowing, subchondral sclerosis, osteophytes and varus deformity.

Figure 6.4: shows bil. lateral TF JS narrowing, subchondral sclerosis and valgus deformity.

Figure 6.5: shows bil. patellofemoral JS narrowing, protuberant spiking osteophytes. (bySamikrishnan.P)

Periarticular structure examination can aid in identifying anserine bursitis, infrapatellar and prepatellar bursitis. Instability of knee may be present, due to damages to protective mechanism of muscles and ligaments. Always look for quadriceps wasting and when Lachman's test and posterior drawer tests are positive it denotes, injuries had happened to ACL and PCL respectively. Altered gait patterns can be caused by a conscious or subconscious attempt to protect the joint or to minimize the pain. (FIGURE 6.6)

Prevalence of hip OA is about 11%. Incidences of hip OA are common in western than in Asian and particularly in Chinese. Whites and African Americans are anatomically prone for OA hip than African and Caucasians. An Indian farmer has OA due to their occupational nature. Men and women are equally affected by OA hip, it can be unilateral or bilateral (Srikanth et al, 2005).⁸⁰ Unilateral OA hip have increased chances of involving opposite hip due to change in gait and pressure effect (Cooper et al, 1996).⁸¹ People with congenital anomalies, like Legg- Calves Perthes, coxa vara, and slipped femoral epiphysis, avascular necrosis are prone for OA hip. Though obesity is not a direct cause for hip OA, however, recent theories have proved that obese people can release more adiponectin from fat mass, and it has a pathogenic role in osteoarthritis, but once OA developed, it can worsen pain.

Symptoms

Sharp and stabbing or dull aching pain in groin is the usual description in OA hip, it radiates down on anterior thigh to knee and in male, and they occasionally feel pain in testis. Pain usually develops slowly and worsens over time. Pain and stiffness will be more in morning or sitting or resting for a while. In patients with central and medial axial OA,

they feel pain in deep buttock. There will be difficulty in completely lying supine with resting of spine, with an extended leg whilst during sleep. They feel comfortable to lie in decubitus position or by flexing knee to 50° to 90° to get resting of spine over bed for sleeping. Difficulty in getting out of bed and first move stiffness are usually present. Patients often describe their friction or grating or crunching of hip joints as 'Corn flake breaking sounds' deep inside his or her buttock. There will be difficulty in sitting and abducting thigh over western commode, and also similar difficulties for getting in and out of car. There will be displeasure in sexual act in both men and women. Task of cutting one's own toenails and for putting on socks are difficult. Occasionally, patients may present with referred pains to knees and often it is true that, origin of pain from hip is overlooked. Simple manoeuvres can easily pick up disease of hip by flexion, internal rotation are reduced and severely painful whereas in knee, did not have any signs of inflammation and its range of movements are full and painless. Likewise, other causes elsewhere can produce pain in the hip joints that are prolapsed lumbar disc, spinal canal stenosis, sacroiliitis, meralgia paresthetica, gluteal vascular claudication or intrapelvic pathology.

Signs

Before you touch on the patient, just watch for their gait. They walk with antalgic gait with lurching of spine and body stance towards abnormal and painful side (FIGURE 6.7) as against in neuromuscular diseases, patients tend to lurch the spine and body stance towards normal side.

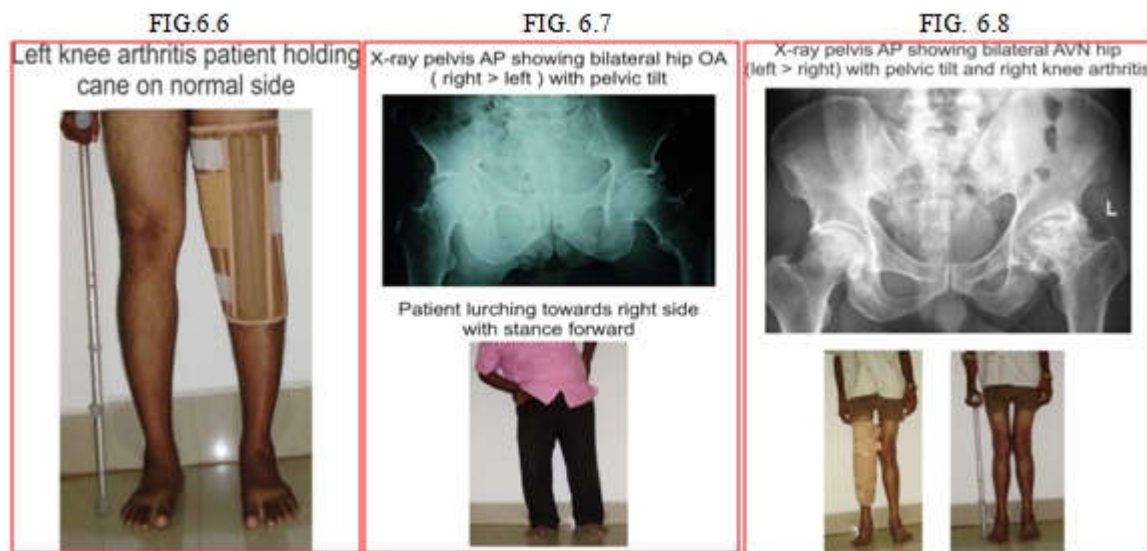


Figure 6.6 showing left knee OA patient, holding walker stick on normal side for an additional support for walking.

Figure 6.7 Bil. hip OA (R>L) and see the patient is lurches with stance forward to same side of pain and supporting his hands for walking.

Figure 6.8 Bil. AVN hip with secondary OA with grade 4 on left and grade 3 on right side and patient is leaning to more painful right side and he has right knee arthritis but it is not referred pain, and left hip is in external rotation and in adduction. (Courtesy: Samikrishnan Perumal)

Altered gait patterns are caused by either conscious or subconscious attempt to protect the joint or to minimize the pain as they give maximum mobilization to normal side joint and then use their normal limb as fulcrum and slowly lift the leg without giving rotational movements to the painful joint whereas in neuromuscular diseases, stance to normal side and the entire movements depends on normal side muscle power. The way they use cane, can be assessed during walk examination. If you give cane or walking stick to them, they hold it on normal side and walk with lessened pain whereas if you provide them axillary crutch, they hold and keep it on the diseased side of arm pit, and put all their weight on the axillary crutch and walk without much mobilizing the painful hip. (FIGURE 6.8) While lying supine, they often keep their hip flexed, adducted and partially everted foot to reduce the pain. Tenderness over groin can be present. Reduced internal rotation is earliest sign in OA hip, later; there will be difficulties for all movements of extension, flexion of hip and rotation. In young individual with femoroacetabular impingement causes pain while internally rotating and adducting the hip in the flexed position. Deep inside hip, crepitus or grating sounds are usually present on mobilizing joint. Pain over lateral aspect of thigh is usually due to trochanteric bursitis.

Osteoarthritis of Cervical and lumbar Spine

Most common and yet another age-related osteoarthritis of spine. According to Mayo clinic, more than 85% of people

over 60 years of age are affected but disease processes can begin in relevant structures around 40 years. Following structures are involved in spinal OA, posterior facet joints, apophyseal joints, intervertebral fibrocartilaginous discs and vertebral bodies. It is better to call new bony outgrowth, spur or spike lesions of spine as spondylophytes than osteophyte, as this term osteophytes, exclusively can be used for peripheral skeletal OA. Both spine and peripheral OA shares anatomical similarities and pathophysiological processes. Males predominate over females, and although some people may have severe disease, they never experience any symptoms and vice versa also speak well. Spinal cord can be affected either by disc degeneration, herniation or prolapse, and vertebral subluxation by disease per se, or by wrong manipulation of spine by traditional bone healer and occasionally by whiplash injury leading to cervical or rarely dorsal spinal OA. Similar lesions of lumbar spinal OA can cause cauda equina syndrome with bowel and bladder dysfunction.

Symptoms

Pain and stiffness of neck or back is present, which is worsened by flexion, extension and lateral bending whereas in inflammatory arthritis, pain will be more on side to side movement. Mechanical spinal pains and discomforts are worsened by work and relieved by rest and by lying down. When discovertebral joints are affected by disc herniation or spondylophytes causing root compression can cause tingling, numbness and weakness of arms, thighs and legs. Dizziness or vertigo can occur when spur or spondylophytes extend into vertebral foramina, disturbing vertebral arteries. Sometime, dysphagia can be experienced by patients, when large anterior spondylophytes from cervical spine compromising the oesophagus.⁸² (Figure 6.9 & 6.10)



Figure 6.9 and **6.10** showing large and irregular spondylophytes compromising the oesophagus.

Figure 6.11 showing various mode of onset of cervical pain syndrome. (Courtesy: Samikrishnan Perumal)

Driving can be difficult, due to restriction of cervical spinal movements. Audible grinding noise or crepitus sounds can be heard or felt by patient. Coughing and sneezing can exacerbate the root pain. (vide. Figure 6.11) Locking of lumbar spine, when you rotate torso to grab grocery bags from car, and when picking object from floor causes sharp or nagging pain in waist. Sometimes, patient may feel intermittent, radicular, claudication lower limb pain on extension of lumbar spine or while on walking, which is typically relieved by flexion of spine that is probably due to neuro claudication as against vascular claudication pain which gets reduced after brief period of rest. Rarely posterior occipital headache can also occur, when C1, C2 nerve root gets compromised by spondylophytic lesions. Unsteady gait or difficulty in getting up from squatting or differential weakness like quadriplegia or tetraplegia can be the presenting symptoms of cervical spondylosis, due to high cord compression.

Signs

Restrictions of movements of cervical, and lumbar spines are present, more for lateral bending than for side to side. Look for muscle wasting or twitching of muscles in the

selective distribution of dermatomes, caused either by root or radicals' compression or by irritation of nerve root respectively.

Look for 'stepping in' of spine; while patient in standing and after minimal flexion, if it is present, it is strongly suggestive of spondylolisthesis. An easy way of remembering the dermatomes sensory disturbances are as given below, C1 is rarely represented or if at all affected, sensory loss in vertex of scalp (area of tuft of hairs in vertex), C2 in cap area of Pope, C3 in gentle man collar area, C4 in nurse collar area, C5 in upper, outer sleeve area of shirt, C6 in lower and outer full sleeve area of shirt, C7 in middle of full sleeve area of shirt, C8 in inner full sleeve area of shirt and D1 in sleeveless shirt area of arm pit, and likewise, D2 collar bone area, D3, D4, D5 and D6 gentle man shirt pocket area, D7 and D8 women blouse border area (subcostal area), D10 over umbilical area, D9 between blouse border and umbilical area, D11, D12 at gentle man belt or women's waist fold saree area and for L1 in penoscrotal area, L2 and L3 in gentleman pant pocket area, L4 in half pant area (up to knee), L5 in outer and inner full pant area of leg, and S1 in gentle man shoe area, S2 in rear area of pant, S3, S4 & S5 are in perianal area.

Spurling's test or cervical compression test is useful clinically to assess the spondylophytic or discovertebral lesions causing root compression and it is an attempt to practically reproduce pain.



It can be done in three ways, in Spurling's test A, keep head and neck in straight position and give pressure by interlocked palm on top of head, when pain get worsened, it indicate, apophyseal joint causing root compression, (Figure 6.12) and in Spurling's test B, ask patient to keep the head and neck in semi flexed position, and give pressure to head, when pain get exaggerated, indicative of spondylophytic lesions compressing on exit root, (Figure 6.13) and lastly in Spurling's test C, keep the head and neck in semi extended position, and give pressure, if pain gets worsened, posterior facet joints are affected. (Figure 6.14)

Haffman's sign

Involuntary flexion of thumb and index fingers occurs when cervical spondylosis causing C5 and C6 radiculopathy, but normally it does not happen.

Sometimes, elicitation of deep tendon reflexes are useful in localizing the involved root in the spinal cord by osteoarthritis of cervical or lumbar spines.

Inversion of Supinator reflex

While eliciting supinator jerk, instead of flexion at elbow, it elicit finger flexion and is associated with an absent biceps jerk and brisk triceps jerk is indicative of spinal cord lesion at C5 or C6.

Absent knee reflex

When knee jerk absent, there should be discovertebral or spondylophytic compression of (L3) L4.

Absent ankle reflex

When patient is unable to extend the great toe with an absence of ankle reflex is indicate S1 root compressed by spondylophytic changes or by spondylolisthesis.

Lasegue's test or Leg Rising test or Lazarevic's sign

While patient lying down on his back on an examination table, ask him to relax the spine, and then lift the patient leg while the knee fully extended and ankle in dorsiflexion. If patient experiences sciatic pain at an angle between 30° and 70°, then test is positive, and it indicate discovertebral or spondylophytic root compression and herniated or prolapsed disc in L4, and L5 is the possible cause for the pain.

Lasegue's Sign

Like Lasegue's test, lift the leg to 30° and flex the knee, then straighten the flexed knee to up to 70°, and if patient develop back pain, is indicate L4 and L5 root compression.

Osteoarthritis of Shoulder

Comparatively, OA of shoulder is less common than other large weight bearing joints but when affected, is more debilitating and leads to depression, anxiety, limitation of

activities, and poor job performance. Usually, osteoarthritis of acromioclavicular joint (ACJ) is more commonly affected than glenohumeral joint (GHJ). Among these, acromioclavicular OA is noticed more in men whereas glenohumeral OA predominates in women. Overhead sports activities, workers of heavy constructions, masons, heavy drill machine operators, recurrent shoulder dislocation, repeated injuries to shoulders and poorly controlled diabetes are other common risk factors for OA shoulder.

Symptoms

Pain is the predominant symptom and it is relentlessly progressive. In acromioclavicular OA, pain worsens on shoulder abduction, internal rotation and reaching of hand to opposite shoulder, as a result, there will be discomfort or difficulty in taking bath, combing hair, catching ball in cricket field, difficulty in defending in basketball game, difficulty in pole-vault game, disc throws, carrying weight above head in weight lifters and in rock music's, the upside down walking and dancing by both hands. Masons, waiters and housewives may experience difficulty in holding objects in hand at 90° angle of elbow joint for long time and they may feel that objects may get dropped or slip down from hand. In glenohumeral OA, initially they feel soreness or mild pain deep inside and posterior aspect of shoulder on usage and later pain can be felt by the patient even at rest and interfere with sleep and followed by all range of movements can cause pain and rotation becomes impossible. Throwing of ball and lifting objects from high cupboard, professional dancing, chopping of wood, and steering a car are difficult. While sleeping, pain gets worsened by keeping arm under their head and even wakes them up by excruciating pain. Crepitus or grinding sounds can be heard and felt when the sphericity and congruity of joint is lost or by deposit of calcific bodies in joint cavity. Sometimes, shoulder may have large effusion, warm and tender with prolonged morning stiffness, and it indicate, it is not by OA, but it could due to RA or Milwaukee's shoulder, gout, pseudogout and infective arthritis. Cervical spondylosis can cause pain in and around the shoulder, by careful history and physical examination, we can easily rule out this pathology, because neuropathic symptoms can be present in these cases. Sometimes, bursitis, rotator cuff disease, adhesive capsulitis can mimic as OA shoulder, but in these conditions, pain is not observed or felt by patients on passive movement and on palpation. Night pain is the usual presenting symptom in shoulder impingement syndrome and while emptying water from mug or can (emptying Can sign).

Signs

On inspection, look for swelling of joint, wasting of muscles around the shoulder, twitching of muscles, prominence of bone and winging of scapula. During palpation, assess for passive and active movements of shoulder for restriction of movements, painful arc syndrome and crepitus etc. When signs of inflammation are present, it is probably due to RA, PsA, Milwaukee's shoulder, gout, pseudogout and or post traumatic

haemarthrosis. Bony enlargement can be seen in OA, or it may look prominent due to disuse wasting of muscles around shoulders. Presences of pain, paraesthesia in outer aspect of shoulder and with twitching of muscles, indicate C4, C5 root irritations or cervical cord lesions.

Osteoarthritis of Ankle and Foot

During standing, walking, and running, the foot and ankle provide support, shock absorption, balance, and several other functions that are essential for our motion. Three bones make up the ankle joint, primarily enabling up and down movement. There are 28 bones in the foot and more than 30 joints that allow for a wide range of movement and it forms arches in feet to enable us to transmit weight of the body to the ground without damaging underlying structures by chief characteristics of its elasticity and cushioning effect. In addition, ankle and foot have multiple tough ligaments and tendons that provide natural protection to the underlying structures, maintain the typical ankle mortise with a medial malleolus at higher position or level than lateral malleolus and it aiding to form the arches of foot and thereby osteoarthritis is less common. Osteoarthritis of big toe is often caused by kicking or jamming, or by dropping weight on the toe. Osteoarthritis of first MTP can result in hallux valgus, hallux rigidus and cock up toe. Hallux valgus, hallux rigidus are the common presentation in OA whereas hallux varus is mostly seen in RA with an overriding of second toe over great toe. Tight footwear can cause varus deformity and further lead to

bunion over the medial aspect of MTP. In real sense, ankle and foot are often prone for repeated injuries or sprains. Injured joints are 7 times at risk for osteoarthritis than the normal. Again, there are weakest parts (talonavicular joint) in arches of foot, either by birth or by collapse of medial longitudinal arch, by weight falling on midfoot, primary or secondary obesity, misfit foot wears (high heels) leads to pes planus or flat feet's (stand and walk with pronated, inverted foot) leads to plantar fasciitis or OA of talonavicular and tarsometatarsal bones. The collapse of transverse arch can cause stress on base of metatarsal bones and on metatarsophalangeal (MTP) joints. Likewise, pes caves or club foot (stand and walk with supinated and everted foot) is causing stress on tibialis anterior, tibiotalar joint, hind foot pain and plantar fasciitis.

In ankle and foot, the most common joints affected by OA are tibiotalar, subtalar, talonavicular, talocalcaneal, calcaneocuboid, metatarsocuneiform and first metatarsophalangeal joints. Varieties of neurologic diseases, including tabes dorsalis and diabetes can cause a neuropathic joint, that is often seen in ankle and foot than hand (hands in syringomyelia). Chronic inflammatory arthritis like rheumatoid, spondyloarthritis, and uncared chronic primary or secondary flat foot, causes collapse of ankle mortise, that leads to slipping or displacement of tibiofibular joints, and as a result of this, medial malleolus displaced down than lateral malleolus, that leads to ankle OA. (Figure 6.15, and 6.16)

FIG. 6.15



FIG. 6.16



Figure 6.15 and 6.16 showing ankle mortise collapse with loss of an arches resulting into callosity of foot. See medial malleolus is displaced down than lateral malleolus, and ankle vulgus (courtesy: Samikrishnan Perumal).

Symptoms

Reduced ability to stand, walk and bear weight. Swelling and stiffness of ankle joint with difficulties in up and down walking, especially in uneven surface or terrain. Pain can be worsened on standing after a brief period of rest. Hind foot walk will be difficult. There can be difficulties in rugby, football, dancers and soccer players. Hallux rigidus patients can have trouble in standing on toes, dancing and initiation of running. Wearing shoes and chappals are the real task for the patients with hallux valgus and varus

deformities. Bunion can be present over the medial aspect of MTP.

Signs

Look for warmth, tenderness, and effusion in anterior aspect of ankle crease and it appear as springy fullness. Dorsiflexion and plantar flexion can be reduced; inversion and eversion can be painful and restricted. In chronic inflammatory arthritis, collapse of ankle mortise can be noted with displacement of tibiofibular alignment. Presence of tophi gives an evidence of gouty arthritis. In standing examination, if tibial varus present, it is probably due to Paget's disease with secondary ankle arthritis. In the era of chikungunya, as this virus is known to critically attack already damaged joints, many patients of existing

subtle ankle OA is reported to outpatient department with severe debilitating arthritis. Presence of pretibial oedema and tenderness goes in favour of chikungunya, because this virus is known to replicate in subperiosteal region of tibia. When flat feet present, gently dorsiflex the great toe, medial longitudinal arch will appear to form, is called Jack's test. In hallux rigidus, dorsiflexion is completely absent and painful.

Osteoarthritis of Temporomandibular Joint

As any other joints, TMJ can be affected by OA, but it is the end point of long-standing TMJ dysfunction. It is a common finding incidentally on base of skull imaging, and indeed pain from TMJ dysfunction is often self-limiting. It is the only joint that the dentist and faciomaxillary surgeons predominantly must deal with. Though, several disorders can affect TMJ, correct diagnosis is important for the appropriate treatment. Sex ratio could be anywhere between 3:1 or 6:1. It can present either with unilateral or bilateral OA.

Symptoms

Present with orofacial pain or preauricular pain while opening the mouth, on side to side movements, on chewing, clenching and during yawning and pain can be worse on awakening. There will be difficulty in biting, initially for hard object and later even for semi soft. Coarse grinding noise or crepitus can be heard and felt. Ultimately jaw may get locked or deviated to one side. Sometime, TMJ OA, can produce referred pain to ear, or lateral aspect of neck.

Signs

Maximum unassisted inter-incisal opening 35 mm and it admits 3 fingers in vertical plane, but in TMJ OA, it becomes reduced. Tenderness on palpation, decreased range of side to side movements, flattened condyle or occasionally palpable osteophytes can be felt. Heavy occlusion of second molar on affected side or traumatizes the posterior molar on same side. Minimal blow to chin causes severe pain on affected side. Crepitus or popping sounds of TMJ can be heard by stethoscope. Ultimately there won't be any pain or sounds from TMJ when it is destroyed.

Osteoarthritis of Elbow Joint

Unlike other joints, the elbow is one of the least affected joints by OA, because of its well matched articulating joint surfaces and with strong stabilizing ligaments. It can withstand enough forces across the joint without becoming unstable. Men are affected more than women after 50 years of age. OA of elbow joints can be due to traumatic injuries to bone, cartilages, ligaments, or by fractures and dislocations. Because of failure or absence of chances for stabilization of ligaments due to repetitive injuries as in baseball players and vibrating machinery users, they are likely to be prone for elbow OA.

Symptoms and Signs

Pain, stiffness and loss of range of movements of elbow are the usual presenting complaints. Difficulties are noted during pronation and supination of elbow when hand has some weight or mug full of water, and difficulties in carrying weight with semiflexed elbow. Throwing ball and twisting movements becomes impossible. Patients report about grating or locking sensation of elbow. Occasionally, they may feel tingling and numbness in ring and little fingers, due to entrapment of ulnar nerve in groove of medial epicondyle, or by joint effusion or osteophytic compression.

Calcium Pyrophosphate Dihydrate Deposition Disease (CPPD Arthritis)

CPPD disease is the second most common form of crystal arthritis. It is an autosomal dominant familial crystal deposition disease, often involving joints uncommonly affected by primary OA such as MCP, WJ and elbow joints. Our understanding of the pathophysiology of CPPD remains rudimentary, and consequently no specific therapies for this arthritis exist. The chondrocalcinosis including asymptomatic disease progressively increases in prevalence with aging, but it is rare before 55 years, and that does not get noticed before an injury. Indeed, in majority of elderly patients with CPPD of knee also have detectable chondrocalcinosis in other joints. In studies of UK, radiographic survey was done on hands, wrist, pelvis and knees of patients admitted to a geriatrics wards, and found that, there was 44% prevalence of chondrocalcinosis in patients older than 84, 36% prevalence in the 75 to 84 year olds, and a prevalence of 15% in 65 to 74 year olds and 4.5% in those older than 40 years old. In another study, an association was seen with diuretics use with hypomagnesemia, and chondrocalcinosis.

The loose avascular connective tissue matrix of articular hyaline cartilage, menisci, and ligaments and tendons are susceptible for calcification. The levels of ambient magnesium and the composition of the chondrocyte extracellular matrix influence the dynamics of CPPD crystal formation, and it helps us to determine whether predominantly monoclinic or triclinic CPPD crystals are formed. Significantly, monoclinic CPPD crystals are more inflammatory than triclinic CPPD.

Alteration of the concentration of calcium, inorganic phosphate (P_i), inorganic pyrophosphate (pp_i), and the solubility products of the iron are clearly at work in promoting CPPD and BCP crystal formation. Noxious effects of excess PP_i on chondrocytes including induction of MMP 13 expression and promotion of apoptosis leads to cartilage degenerative manifestation of CPPD disease. The relatively unique capacity of chondrocytes to produce copious amounts of extracellular PP_i is double edged, as supersaturation of cartilage extracellular matrix with PP_i is a major factor in promoting CPPD crystal deposition. The rising of cartilage PP_i is the common mechanism as well in hypophosphatasia, hypomagnesemia, hemochromatosis and hyperparathyroidism of all these secondary causes of CPPD arthritis. Chondrocyte hypertrophy and

inflammation can jointly drive chondrocytes calcification and progression to OA by hypoxia inducible factor- 2 α , Indian hedgehog, calgranulins, oxidative stress, P₁ transport, varieties of cytokines (IL 1 β , TNF), receptor for advanced glycation end products (RAGE) signalling and it is modulated by transglutaminase 2 (TG2) release. Sometime, the CPPD crystal per se, can trigger joint inflammation by sub clinically traffic into joint fluid and synovium and it directly stimulate chondrocytes, synovial lining cells and intra articular leukocytes thereby contribute to cartilage degradation and worsening of OA. In this regard, CPPD crystals activate cells partly via mitogen activated protein kinase activation and induce cellular release of cyclooxygenase and lipoxygenase derived arachidonic acid and TNF, IL1 and CXCL8. The ingress of neutrophils and its effects on neutrophil endothelial interaction likely a major locus for therapeutic effects of colchicine in acute CPPD arthritis like pseudogout.

Common Clinical Presentation of CPPD Deposition Disease are as follows, I.Asymptomatic CPPD* (Lanthanic), II. Acute recurrent monoarthritis (pseudogout, EULAR-> acute CPPD crystal arthritis*), III. Pseudoseptic arthritis, IV. Acute recurrent haemarthrosis, V. Chronic degenerative arthritis (pseudo- osteoarthritis, EULAR-> osteoarthritis with CPPD*), VI. Chronic symmetric polyarthritis mimic as rheumatoid (EULAR->Ch. CPPD inflammatory arthritis*), VII. Systemic illness as Pyrexia of unknown origin, or as PMR, VIII. Destructive arthritis- in haemodialysis dependents, IX. Carpal tunnel syndrome, X. Pseudo tophaceous, XI. CNS complicating CPPD arthritis. (* EULAR – revised the name and avoided term pseudogout).

Clinical Features

The clinical manifestations of CPPD crystal deposition disease are protean. Idiopathic chondrocalcinosis appear only after the fifth decade of life whereas familial chondrocalcinosis, may cause arthritis even before fourth

decade. Likewise, secondary forms of CPPD arthritis by haemochromatosis, hyperparathyroidism can manifest before third and fourth decades of life. Mere hypothyroidism is not causing chondrocalcinosis, but initiation of thyroxine replacement can precipitate CPPD arthritis. It can just present as asymptomatic chondrocalcinosis to oligoarticular, polyarticular, destructive OA and rarely with neurological complications. It has special predilections to involve knee, wrist, MCP, elbow and glenohumeral joints. Occasionally, it can involve hip, ankle, symphysis pubis and mid foot but does not involve first MTP joint. It can cause cervical cord compressive myelopathy by ligamentum flavum thickening or transverse alar ligament calcification and odontoid fracture.

Acute Gout like Attacks (Pseudogout)

About 25% of people with CPPD will experience acute inflammation of knees, wrists and ankle joints, mimicking as acute gouty arthritis. But it never involves 1st MTP. It can present as episodic attacks lasting few days to weeks, in the form of mono or oligoarthritis. These acute inflammatory symptoms occur because of lysis of polymorphonuclear white cells that have ingested CPPD crystals. The onset of acute arthritis can be precipitated by surgical or minor trauma or sometimes by intraarticular hyaluronic acid. The affected joints are red, swollen, warm, stiff and severely tender. Fever may accompany an acute attack. Pseudoseptic arthritis clinically is difficult to differentiate, unless synovial fluid aspiration is done to confirm CPPD crystals.

Chronic Polyarthritis mimic as Rheumatoid Arthritis

About 5% of people with CPPD can present with symmetric polyarthritis of small and large joints, lasting for several months and mimic as rheumatoid with usual morning stiffness and fatigue and it can also lead to joint deformities and is often misdiagnosed as RA. (Figure 6.17 and 6.18)

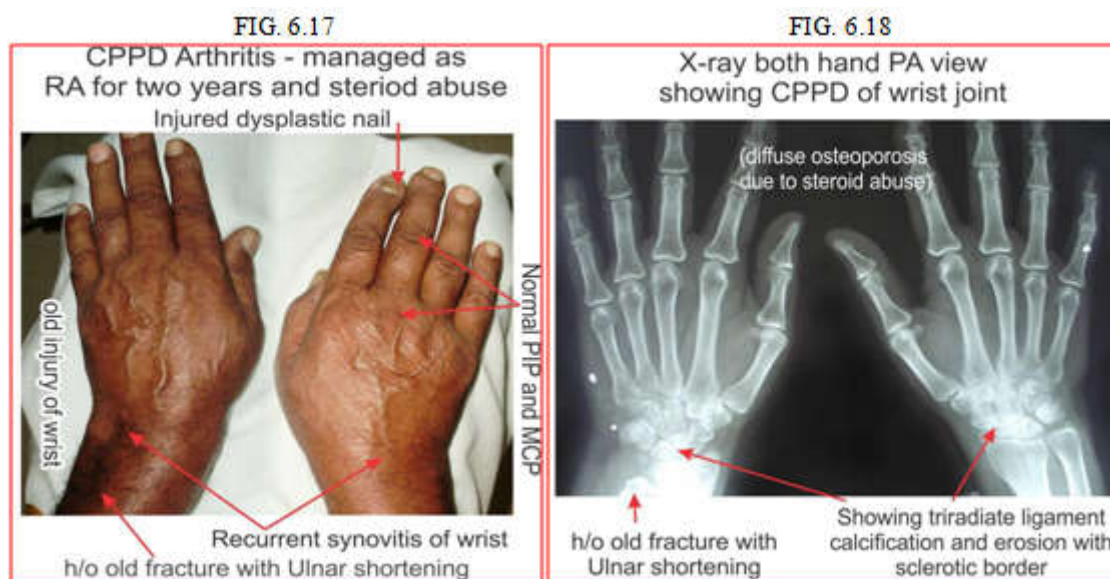


Figure 6.17 presented with recurrent synovitis of wrist and II, and III MCPJs and shortening of left ulnar bone and post traumatic dysplastic nail in right index.

Figure 6.18 shows diffuse osteoporosis, triradiate ligament calcification and erosions and narrowing of radiocarpal joints space and shortened ulnar bone by an old injury. (by Samikrishnan. P)

Chronic Degenerative Arthritis

Nearly almost about 50% people with CPPD crystal deposition will progress to degenerative and destructive osteoarthritis. (Figure 6.19 and 6.20) It can involve several joints ultimately resulting in deformities of large and small joints.



Figure 6.19 CPPD linear calcification of cartilage, wrapping of patella and osteophytes

Figure 6.20 severe destructive CPPD arthritis, subchondral sclerosis, osteophytes and calcinosis. (Courtesy by Samikrishnan. P)

Diagnostic Criteria for CPPD Disease

Criteria	
I	Demonstration of CPPD crystal in biopsy or synovial fluid or by X- ray diffraction powder pattern
II	A Identification of mono or triclinic crystals showing weak positive birefringence
	B Presence of typical calcification on radiograph (punctuate or linear calcification)
	C Presence of typical findings for CPPD in articular cartilage by Ultrasound
III	A Acute arthritis (in knee, wrists or other large joints)
	B Chronic arthritis (in knees, hip, wrist, carpus, elbow, shoulder and MCP)

Diagnostic Categories

- A. Definite: criteria I or IIA must be fulfilled
- B. Probable: criteria IIA or IIB or IIC must be fulfilled
- C. Possible: criteria IIIA or IIIB suggests possible CPPD disease

Milwaukee Shoulder

Milwaukee shoulder is relatively uncommon, distinct and destructive arthritis seen in elderly individuals. Women are affected more than men in the ratio of 4:1. The shoulder and knees are frequently involved but it can also attack wrist, hip and mid tarsal joints. It is characterized by intraarticular or periarticular hydroxyapatite crystals and rapid destruction of the rotator cuff and the glenohumeral joint. Unilateral shoulder joint involvement is more common and is seen in the dominant side, however, even in case of bilateral shoulder involvement, it is almost always more advanced on dominant side. Etiology of this disease is unclear. Pathophysiologically, abundant cartilage NO production may promote mitochondrial dysfunction, chondrocyte extracellular ATP depletion, and lowering of extracellular PP_i, favouring HA crystal

deposition whereas reverse will happen in CPPD arthritis with an increase in PP_i.

They clinically present with sudden onset of pain and swelling in a shoulder with large effusion and it may lead to rapid destruction, subluxation and or upward migration of shoulder joint. Joint fluid aspiration yields large volume of cloudy white fluid and sometimes frank haemorrhagic, with a normal or mildly increased inflammatory cell counts and HA crystals can be demonstrated with Alizarin red stain.

Power doppler US examination can pick up calcific periartthritis or tendonitis and it usually seen in avascular area of tendon and it is about 1 cm away from the joint. Radiographs show evidence of upward migration and destruction of humeral head with negligible osteophytes or no remodelling of bone.

Diffuse Idiopathic Skeletal Hyperostosis (DISH / Forestier's Disease)

DISH is characterized by ossification of anterior spinal ligaments producing tortuous, thick, flowing candle wax

like mass, distinctly anterior to and without niching with vertebral bodies and it is characteristically present more on right side of spine.

Clinical Features

Onset of disease after 50 years of age and about 20% of male and 5% of female are affected. Present more often in diabetics. Usually asymptomatic, only less number of patients report with back pain but without spinal mobility restriction. Rather involvement of lumbar spine is protective against the onset of low back pain. Dysphagia can be present when anterior cervical spinal ligament goes for large mass like thickening and causing oesophageal compromise.

Quite often, it is found by routine investigation for some other disease. It is easy to differentiate from lumbar spondylosis by the presence of restriction of spinal mobility and radiculopathy and radiologically by readily demonstrable spondylophytes. The differential diagnosis is spondyloarthritis and AS, wherein the affected individuals are young with inflammatory back pain, buttock pain, asymmetrical peripheral arthritis and enthesitis, but radiologically, AS/ SpA presents with thin, marginal syndesmophytes which closely niches with vertebral bodies, often fuse and ossify with complete loss of spinal movements. Sacroiliitis is the hallmark for SpA and AS whereas presence of sacroiliitis rules out DISH. Unless it produces mass effects by ligament calcification with pressure symptoms, no specific treatment is required for DISH and physiotherapy can be advised.

2. Conclusion

There are some situations where difficulty can arise in differentiating primary osteoarthritis from secondary inflammatory arthritis. The meticulous history, physical examination, elicitation specific joint features can surely yield the clinical diagnosis of osteoarthritis. Thus, correct clinical diagnosis of primary osteoarthritis is mandatory before initiating basic investigations to confirm the diagnosis and instituting proper treatment.

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