**NEW INTEGRATIVE APPROACHES OF RHEUMATOID ARTHRITIS**

Puja Kumari\*, Ankit Rai, Alok Soni, Raghvendra Dubey, Nirmal Dongre, Shashi Alok

Theitermi"arthritis"iisiassociatedifromitheiGreekiwordsiarthron,iwhichimeansi"joint,"iandi-itis,iwhichimeansi"inflammation."iItidueitoiredness,iheat,iswelling,iandisoreness.iSo,idisciplinaryiarthritisidefinesiaired,ihot,iswollen,iandisoreijoint.iArthritisiisiaipreconditionicharacterizedibyipainfuliandiinflexibleijoints.iIfitheijointsiareired,ihot,iandiswollen.i

**1.1 Types of arthritis**

 (Warhadpande, 2019)

1. Rheumatoid arthritis
2. Osteoarthritis
3. Juvenile arthritis
4. Psoriasis arthritis

**A. Rheumatoid arthritis**

Rheumatoidiarthritisiisiaichroniciinflammatoryiillnessithatimostlyiaffectsitheijointsibuticanialsoiaffectitheibloodivessels,iskin,ilungs,iandiheart.iSeveralipiecesiofievidenceipointitoitheidisease'siautoimmuneinature.iBecauseitheidisease'siprimaryimanifestations.

Theitypicaliimmuneisystemihasitheiabilityitoidistinguish'self'ifromi'non-self'ioriforeignitissues;iwheni challengediwithiaiforeigniinvadingiagent,itheihostiordinarilyirespondsiwithianiinflammatoryiresponseiwithoutiinflictingiharmitoiself-tissues.

Autoimmuneidiseases,ionitheiotherihand,iareiprimarilyicausedibyiaifailureitoidistinguishibetween'self'iandi'nonself.'iInstead,itheibodyireactsibyiimmunologicimeans,isuchiasitheipresenceiofiautoiantibodiesioriticellsipreiactivityiagainstiownitissues,ibothiofiwhichimayiorimayinoticauseitissueidamageiandithusiareinotialwaysipathogenic.i

Iniotheriwords,iautoimmunityiisitheioppositeiofitolerance.iRAifrequentlyiprogressesitoidestructioniofitheiarticulariandialkylosisiofitheijoints.iExtraarticularilesionsimayiinvolveiskiniheartibloodivesseliandilungs,iandithusitheiclinicalimanifestationicanireassembleiotherisystemiciautoimmuneidisordersisuchiasisystemicilupusierythromatosisiscleroderma

**B. Osteoarthritis**

Osteoarthritisiisidefinediasitheicontinuingidegradationiofijointiarticularicartilages.iAsiairesult,itheiextracellularimatrixiandiarticularicartilageicellsiareitheiprincipalitargetsiofiosteoarthritisitherapy.

 **C. Juvenile arthritis**

Theimostifrequentitypeiofiarthritisiinichildreniandiadolescentsiisijuvenileiidiopathiciarthritisi(JIA),ialsoiknowniasijuvenileirheumatoidiarthritisi(JRA).i(Inithisicontext,ijuvenileirefersitoistartibeforeitheiageiofi14-16,iaiconditionitoireferredibyiidiopathiciwithinoiknowniorigin,iandiarthritisirefersitoiinflam-mation.

**D. Infectious arthritis (Septic arthritis)**

Its is caused by a bacterium infecting one or more joints. The joint is normally lubricated with a tiny amount of fluid known as synovial fluid or joint fluid.

**1.2 Prevalence /Population**

Accordingitoistatistics,iRAiandiassociatedimusculoskeletaliillnessesiafflictimoreithani0.5-1%iofithe globalipopulation,iandiitiisiexpectedithationeiinieveryifiveiAmericansiwillisufferifromioneiofitheseiailmentsibyi2020.iFemale’siareaiaffectedibyiRAithreeitimesimoreioftenithanimales,ianditheidiseaseicanistartiatianyiage,iwithiaipeakiincidenceiati50–60iyearsiofiage.iTheipreivalenceiinitheiseconditoifourth idecadesiandiisitheithreeitimesimoreicommoniiniwomenithanimen.

**1.3 Pathophysiology of Rheumatoid arthritis**

Theisynovitis,iswellingiandijointidamageithaticharacterizeiactiveiRAiareitheiendiresultsioficomplexiautoimmuneiandiinflammatoryiprocessesithatiinvolveicomponentsiofibothitheiinnateiandiadaptiveiimmuneisystems.



TNF-interleukini1i(IL-1)iandiinterleukini6i(IL-6)ihaveibeeniidentifiediasiimportantimediatorsiinithe autoimmuneiillnessirheumatoidiarthritisi(RA).iInterleukini1iisiinvolvediiniboneiresorptioniandicartilageibreakdown,ihoweveriitimayinotibeiasiimportantiinijointiswellingiandiinflammation.iPathogenesis,iasiiniotheriautoimmuneidiseases,iinvolvesigeneticipredispositioniandienvironmentalifactorsithaticontributeitoiillnessionset,iprogression,iandichronicity.iItiisiproducedibyiaicomplexiinterplayibetweenigenesiandienvironment,iwhichiresultsiiniaisymmetricibreakdowniofiimmuneitoleranceiandisynovialiinflammation.iPathophysiologyiisitheistudyiofiaberrationsiininormalimechanical,iphysical,iandimetabolicifunctioniinducedibyiaidisease,iaberranticondition,ioristateithatiqualifiesitoibeidesignatediasiaidisease.iThisiincludesitheiillness'sigenesis,iprogression,iandichronicity.iItiisicausedibyiaicomplicatediinterplayibetweenigenesiandienvironment,iwhichileadsitoiaibreakdowniofiimmunologicalitoleranceiandisynovialiinflammationiiniaisymmetricipattern.iiPathophysiologyiisitheistudyiofiabnormalityiofinormalimechanicaliphysicaliandibiochemicalifunctionieithericausedibyiresultingifromiaidiseaseiabnormalisyndromeioriconditionithatimayiiknowiqualifieditoibeicallediaidiseasei.

Severalistagesiofirheumatoidiarthritisiareirecognizediasisynovitisipannusifibrousiandiankylosesiandibonyiandialkylosisiinirheumatoidiarthritisipathogenesis.i

Stage (i) Synovities during stage one including joint pain and stiffness.

Stage(ii) Pannus formation

Stage (iii) Fibrous alkyosis

Syage (iv) Bonny alkyosis

**Causative factor and risk factor-**Most types of arthritis are caused by many factors acting together. (Barbour KE, 2013)

* Genetic make-up had the possibility likely to develop a certain disorder.
* Obesity
* Female gender
* secondary arthritis
* Greater bone density
* Joint laxity
* Repetitive joint overuse
* Joint injury
* Posttraumatic joint in congruity
* Instability or malalignment
* Joint dysplasia
* Repetitive, excessive joint torsion
* Crystal deposition
* Neuromuscular dysfunction
* Articular cartilage abnormalities may lead to joint degeneration by putting stress on the articular surface and joint instability.
* Penetration of sub-chondral bone
* Joint abrasion

**Symptoms and signs**

Thereiareidifferentivarietiesiofiarthritis,ibutitheicommonisymptomsiforialliconditionsiincludeivaryingilevelsiofipain,iswelling,ijointistiffness,iandioccasionallyiaipersistentiacheisurroundingijoints.iTendernessiandiswellingiiniseveralijoints,iweightiloss,ifever,ifatigueiandisleepiness,iandiweaknessiareiallisymptoms.iLupusiandirheumatoidiarthritis,iforiexample,icanicauseiairangeiofisymptomsiinidifferentiorgans.i(Daily,i2016).i

**1.4 Biomarker of RA:-**

Biologicalimarkers,ialsoiknowniasibiomarkers,iareibiologicitraitsithaticanibeiobjectivelyitestediandiserveiasiindicatorsiofinormalioripathologiciprocessesiasiwelliasimeasurementsiofiresponseitoitherapy.

Anti-cyclic citrullinated peptides antibody, antibodies and assay.

* Positive anti CCP in other disease.
* Anti nuclear anti body test
* Anti CCP band RA prognosis
* Anti MCV Antibody
* Other Anti-cyclic citrullinated peptides antibody.

**1. Disease acting and prognosis**

Erythrocytic seddmentation value

**2. Activity and prognosis**

C –reactive protein

Multiple protein biomarkers algorithms

**3. Investigation and other biomarkers**

Immune abnormalities and auto antibodies.

**4. Genetic factors**

Other acute phase markers

Tissue specific marker

Rheumatoid arthritis susceptibility genes in RA

TheiassociationiofiparticularihumanileukocytesiantigeniHLAiallelesiwithiRAiThisiparticularisenotypeirepresentediaisetiofiallelesiatitheiHLAiDRBigenesilocus

NonicodingiRNAi(NCRNA)imoleculesiareicomposediofilonginonicodingiRNA’SismallinucleolariRNA’simicroRNAiandicirculariRNA’SiwhichiplayianiessentialiroleiinidiseaseimeetiandiprogressioniandicanibeiusediinitheiearlyidiagnosisiandiprognosticiapproachesitoiRAidieaseianditheicurrentiknowledgeionitheisubjectifocusingionirecentiadvancesiiniRNAiMCRNAiandiasidiagnpstriciandiprognosticibiomarkersifromitheibioifliuditoitheitissueileveli.

Withiallitheitestiandibiomarkersihighispecificityipresenceieearlyiinitheidiseaseiprocessiandiabilityitoiidentifyipatientiwhoiareilikelyitoihaveisevereidiseaseiandiirreversibleidamagei.

RAiwithianiemphasisiandidiagnosticiperformanceiprognosticicapabilityiandirelevanceitoipathogensiandinewitreatmentiparaidiagnoseiiniRA

**1.5 Future Prospectus of Rheumatoid Arthritis-**

DespiteialliimprovementiiniRheumatoidiArthritis.iWeiareistillinotiableitoipresentior,icureitheidisease.iThusiRAiiiisistillitheireasoniforidisabilityiandireducediqualityiofilifeiforimanyipatients.

RheumatoidiArthritisirecentiresearchiupdatesiitiisiheterogeneousidiseaseithatibasedionidataicombiningigeneticiriskifactorsiandiautoiantibodiesi,icanibeiclassifiediintoianti-icitrullinatediproteiniantibodiesi(ACPAs)-ipositiveiandinegativeiRA.

BestiphenomenaiforiRAitreatmentipreventi to itargetimayibecomeiainewitreatmentiapproachibyi combiningigeneticiandiepigastricidataiforipersonalizeditreatment.

AsigeneticiandicellibaseditherapiesiareievolvingitheicureiofiRAi.Researchersicontinueitoilearnieachieverythingiaboutitheivariousiformieverythingiaboutitheivariousiformiofiarthritisiandicomplexityiofitheimanyiwaysitheyicanidevelop.iEventually,icureiforispecificitypesiofitheidiseaseimayibeifoundiandifinditoibetteritreatmentsiandiclinicalitrialsiareikeyitoifindingisafeiandieffectiveitreatments.InicurrentiresearchioniRAipointsitoibacterialistrainiinitheigutiasiaidiseaseitrigger.iTheistrinidiscoverediinitheiliningiofitheiintestineimayiprouditheibodyitoiattackihealthyitissueiinitheijoints.

Disease modifying Anti-rheumatoid drugs and new treatments for RA latest FDA approach Biological.

|  |  |  |
| --- | --- | --- |
| S.N. | DRUGS NAME | DRUG CLASS |
| 1. | GolimumabCertolizumab | Tnf – α factor blockers |
| 2. | Tofacitinib | Janus Kinase inhibitors |
| 3. | Toclizumab | Interleukin-6 (IL-6) receptor antagonist |

**1.6 References**

Ahuja, S.C. Ahuja, S. Ahuja, U. Nirgundi (Vitex negundo) – Nature’s Gift to Mankind. *Asian Agri-History,*2015;19(1);5-32.

Danielle, E. S. Sara, W. Meghan, B. Association of Body Mass Index with Physical Function and health related quality of life in adults with Arthritis. *Arthritis.*2013;60; 1-10.doi: [10.1155/2013/190868](https://doi.org/10.1155/2013/190868)

Dawei, W. Yuping, L.  Wei, L. Huwei, L. Separation methods for antibacterial and antirheumatism agents in plant medicines*. J Chromatogr B Analyt Technol Biomed Life Sci,* 2004;812(1-2); 101-117.doi: 10.1016/j.jchromb.2004.06.049.

Derek G.WallerBSc (HONS), D. M. Rheumatoid arthritis, other inflammatory arthritides and osteoarthritis. , 2018;373-383.

Dharmendra, K. Rajesh, K. Kumari, S. Medicinal property of Nirgundi. Journal of Pharmacognosy and Phytochemistry, 2018;7(1);2147-2151.doi: 2278-4136

Harith J. M. Nurzalina Abdul K. K.  Mohd, Z. B. A. Roziahanim, M. Vikneswaran, A. L. M. In vivo anti-arthritic and anti-nociceptive effects of ethanol extract of Moringa oleifera leaves on complete Freund's adjuvant (CFA)-induced arthritis in rats. Integrative Medicine Research, *Integr Med Res,* 2018;7(1):85-94.doi: 10.1016/j.imr.2017.11.002

[James, R. O. D](https://pubmed.ncbi.nlm.nih.gov/?term=O%27Dell+JR&cauthor_id=12115219). [Robert, L](https://pubmed.ncbi.nlm.nih.gov/?term=Leff+R&cauthor_id=12115219). [Claire, H](https://pubmed.ncbi.nlm.nih.gov/?term=Haire+C&cauthor_id=12115219)*. et al.,* Treatment of Rheumatoid Arthritis with Methotrexate Alone, Sulfasalazine and Hydroxychloroquine, or a Combination of All Three Medications.*Arthritis Rheum,*1996;46(5):1164-1170.doi:10.1002/art.10228

James, W. D. Mini, Y. Sunmin, P. Efficacy of turmeric extracts and curcumin for alleviating the symptoms of joint arthritis: A systematic review and meta-analysis of randomized clinical trials. *Journal of Medicinal Food*, 201619(8);717-719. doi: [10.1089/jmf.2016.3705](https://dx.doi.org/10.1089/jmf.2016.3705)