MRI features and treatment options for Idiopathic Chondrolysis of the Hip (ICH) in children. Outcomes of a systematic review.

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Abstract

Background: The purpose of this paper is to review the MRI features and treatment for idiopathic chondrolysis of the hip (ICH) in patients aged 18 years or less.

Methods: We included studies published in English up to August 2021. We accessed major electronic bibliographic databases on ICH that described MRI features, treatment, or both. We used the Joanna Briggs Institute (JBI) Critical appraisal checklist for case reports for Risk of bias assessment.

Results: We pooled 136 hips (125 participants) from 35 studies with 11.6 ± 3.4 years mean age. We had 46, 8, and 106 hips to assess ICH's MRI, pharmacological, and operative interventions. Geometric marrow edema (GME) ($P < 0.01$), diffuse marrow edema (DME) ($P < 0.05$), diffuse cartilage loss (DCL) ($P < 0.05$), and joint effusion ($P < 0.05$), were significantly associated with time in first MRI reviews. GME ($P < 0.01$) and focal cartilage loss (FCL) ($P < 0.01$) decreased significantly between two MRI reviews at median time of 1.75 (IQR 0.93-4.25) and 12.5 (IQR 3.75-19.5) months. Diffuse cartilage loss ($P < 0.01$) and degenerative changes ($P < 0.01$) increased significantly between the two MRI reviews. Etanercept, Methotrexate, and Botulinum Neurotoxin A drugs were used by 3, 3, and 1 report to treat ICH. Capsulectomies, total hip arthroplasty, arthrodiastasis, arthrodesis, arthroscopy operations treated 45, 18, 5, 5, and 2 hips.

Discussion: GME may be the most specific and early MRI feature in diagnosing ICH. GME and DME show an inverse relationship over time. So, it is with FCL and DCL. Despite reports on the efficacy of biologics, immunomodulators, and operations, early and late ICH management remains controversial due to poor quality studies.

Introduction

Idiopathic chondrolysis of the hip (ICH) is the rapid destruction of articular cartilage of the hip joint without a known cause (1). ICH is a disease of children between 9 to 12 years old; however, cases are reported sporadically in adults (2). Known causes of chondrolysis of the hip (CH) are Perthes disease, slipped capital femoral epiphysis, Marfan syndrome, Stickler syndrome, juvenile idiopathic arthritis, and Blount's disease (1, 3). Several inciting events have been incriminated in the causation of CH (Table 1). However, ICH is a distinct clinical entity with a typical age of presentation, non-specific clinical features, rapid deterioration, and unpredictable outcomes (1). Its histological features are described at length across published series (1). Radiography, ultrasonography, and scintigraphy are non-specific investigative modalities for diagnosing ICH. Various investigators describe magnetic resonance imaging (MRI) ICH features with considerable overlap (4-6). Outcomes of treatment in ICH have been disappointing so far. Recently pharmacological interventions and arthroscopic treatment have been reported with variable success in ICH (7-11). A study described total hip arthroplasty (THA) in adolescent ICH (12). We aimed to review the MRI characteristics and treatment options for ICH in children.

Materials And Methods

The procedures followed in this review were per the ethical standards of the responsible committee on human experimentation (institutional and national). We conducted this review following guidelines in *the preferred reporting items for the systematic review and meta-analysis (PRISMA)* [13]. This review is registered with the *International Prospective Register of Systematic Reviews (Prospero ID: CRD42022295354)*

Eligibility Criteria (Inclusion Criteria and Exclusion Criteria):

We included studies/reports published in the English language on ICH that reported MRI features or treatment options or both for at least one case in patients aged 18 years. A report/study describing more than one case was defined as a case series for this review. The cases were included regardless of the completeness of the reported data. ICH was defined as a case where the study investigator (author) diagnosed a patient based on history, clinical examination, and supportive radiographic evidence. We excluded cases managed by rest, traction, and pain control. Cases or treatment reports with less than six months of follow-up were excluded. We excluded secondary chondrolysis of the hip due to Slipped capital femoral epiphysis (SCFE), Perthes disease, and inciting events (Table 1). However, ICH cases from mixed studies meeting inclusion criteria were included in this review (4, 5, 11, 14-24). A mixed study for ICH was identified when it described heterogeneous treatment methods or reported it as a cause of arthritis. We isolated and excluded duplicate cases when they originated from more than one publication from the same center, population, or cohort and similarities in the period of study and authors.

Information sources:

We searched the electronic literature to identify studies in the English language up to August of 2021 on ICH. We searched Cochrane Central Register of Controlled Trials (CENTRAL) (2021 issue 12), CINAHL (March 2008 to August 2021), Directory of Open access journals (DOAJ) (August 2021), EMBASE (1974 to August 2021), MEDLINE (February 1948 to August 2021), ProQuest (1990 to August 2021), PubMed (January 1952 to August 2021) and Scopus (1930 to August 2021) for studies on ICH.

Search Strategy:

Annexure 1 describes the search strategy for the electronic databases for this review.

Searching for other resources:

We hand-searched the references from the included studies on ICH. We excluded conference proceedings, books, and dissertations on ICH.

Selection of studies and data collection process:

Review authors JA and GK independently screened all titles and abstracts for potentially eligible studies. We obtained full-text reports where appropriate. The same two review authors independently performed study selection. Wherever possible, the review authors retrieved and handled each patient's data individually in a case report and documented when it was not possible. We resolved any disagreements about the inclusion or exclusion of individual studies and data extraction either by discussion between the two authors or with the third author (SN) for the final study selection to ensure a consensus. We did not contact the authors of included studies. The data collected had information on study design, study population, interventions, outcomes measures, and results. We did not mask the source and authorship of the trial reports. The review authors MR and NR assessed MRI features of ICH from isolated reports. Review authors MR and NR independently extracted data from MRI reports and involved review author SN in the event of a conflict.

Data Items (outcome measures):

The following characteristics from the included reports were recorded on MRI sequences: 1 Focal (geometric) or diffuse marrow edema in the pelvis (femoral head, ilium, and ischium), 2. Size of geometric marrow edema in the femoral head, 3. joint space narrowing, 4. Joint effusion, 5. Synovial thickening, 6. muscle wasting, 7. degeerative changes (flattening of the femoral head, osteophyte formation, lateral buttress formation, fibrous ankylosis, the fusion of physis), 8. Femoral head or acetabular irregularity. Since few reports described more than one MRI review for a given case in follow-up, we classified them into first and subsequent MRI reviews and estimated the outcomes (6-8,10,12, 25-27). In a given case, each MRI report constituted an MRI review. The findings on contrast enhancement were also recorded. The review authors classified MRI characteristics into early, late, and non-specific. Degenerative changes (flattening, osteophytes and lateral buttress formation of the femoral head, the fusion of the femoral physis, Protrusio acetabuli, fibrous ankylosis, femoral and acetabular remodelling, and diffuse loss of the articular cartilage) were classified under late changes in ICH on MRI (1, 5). Marrow edema, joint effusion, joint narrowing, muscle atrophy, synovial thickening were non-specific changes. However, geometric marrow edema of the femoral head and focal loss of cartilage loss in the vicinity of ligamentum teres was classified as early changes on MRI (Figure 1) (1, 4).

Assessment of Risk of bias in included studies:

Pairs of the same review authors performed independent 'Risk of bias assessment of the included trials. We used the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Reports (last amended in 2017) quality assessment tool for 'Risk of bias assessment in this review (28). The JBI checklist for case report assesses the study/case report on nine domains to determine the study's methodological quality. We modified the scale; the responses of yes and no were assigned integers 1 and 0 for each question. However, the response of cannot Determine/ Not Applicable/ Not Reported was not assigned. The summated scores from 8 domains of each study ranged from 0 to 8. Since the review authors included all the studies the ninth domain to include was not counted for rating the studies. They were rated poor, fair, and good to assess the study quality based on their score less than <25th, 25 to 75, and > 75th percentile, respectively.

Statistical analysis:

Effect measures.

Continuous data were summarized as mean with standard deviation (SD) and median with interquartile range) Categorical data were reported as the number of hips, cases and MRI reviews, and percentages. Comparison between the first and subsequent/final MRI characteristics was analyzed using Pearson's $\chi 2$ or Fisher's exact test. Similarly, MRI characteristics were also assessed for association with time of presentation or appearance and were compared using the independent-samples t-test. For each variable, comparisons between groups were made, excluding the cases with missing data. Statistical inferences were made based on a two-sided significance level of $p < 0.05$. All analyses were performed using STATAv14.0 for Windows. Review author (P) performed the statistical assessments.

Results

Outcomes of search:

We searched 731 records up to December 2021 on ICH from electronic databases Cochrane Central Register of Controlled Trials (CENTRAL) (2), CINAHL (43), DOAJ (38), Embase (36), Medline (320), Proquest (3), Pubmed (238), and Scopus (51). We isolated 34 studies meeting the inclusion criteria from electronic databases (4-12, 14-27,29-39). Another study was isolated from the references of the isolated studies (40). We assessed 35 studies in qualitative analysis. There were 13 case reports, 20 case series, one clinical image, and a letter to the editor each. We excluded eight and one case from two duplicate studies due to similarity between the author names and study settings (41- 42). Another nine duplicate cases were excluded from a study because they were part of another study (19, 23). We excluded a case from the MRI review because of the insufficient description of ICH changes (43). We excluded two studies

for operative interventions because their follow-up was less than six months (44-45). Figure 2 is the PRISMA diagram for the studies in this review. *Annexure 2* details the reasons for exclusion of studies in PRISMA

Outcomes of Risk of bias assessment:

All studies included in this review were short case series/reports with a High Risk of bias. The Risk of bias assessment outcomes for this review is presented in Table 2. Thirty-five studies scored a mean of 4.82±2.02 points on the Risk of bias assessment tool in this review. 10, 14, and 11 studies rated poor, fair, and good on the Risk of Bias assessment tool.

Demographic outcomes:

We pooled 35 studies with 125 cases (136 hips) for this review. 11, 10, 9, 4, and 1 studies were from Europe, America, Asia, Africa, and Australia. The mean age of cases was 11.6 + 3.4 Years. There were 22 (18.6%) males and 96 (81.4%) females from 30 studies in the review. There were 43 left, 52 right, and 17 bilateral ICH hips. We pooled 46 cases/ 62 MRI reviews from 17 studies (4-10,12, 25-27, 34-37,39-40) for assessment of primary outcomes. More specifically, we had 46 cases/ hips (17 studies) where MRI was reviewed at least once. However, there were 14 follow-up MRI reviews from 8 studies among these cases (6-8, 10, 12, 25-27). Two studies added a second follow-up review in one case each (8, 25). We excluded one case from two studies due to insufficient description and poor MRI (9, 37). There were 8 cases/hips from 7 studies (7-10, 25, 35, 39) and 106 cases/115 hips from 22 studies (4-5,11-12,14-24, 26, 29-33,38) for assessment of secondary outcomes (pharmacological and operative interventions) for ICH.

Observations from the first MRI Reviews:

The Median time to first MRI after the presentation from 35 cases/15 studies was 1.75 (IQR 0.93-4.25) months. One study reported outcomes of MRI in 7 reviews at < 6 months, while another study presented outcomes of MRI reviews at a median of 2 (IQR 2-24) months (6, 26). The outcome measures on review of MRI characteristics from studies that were imaged at least once are summarized in Table 3. Though there were 43 observations of marrow edema (focal/diffuse) into the femoral head, acetabulum, or both, however, there was 26 focal geometric marrow edema into the femoral head with or without adjoining edema in the triradiate cartilage or the supra-acetabular region on MRI sequences among from 10 studies (4-5,7-9, 25, 27, 34-35, 40). The mean width of the geometric marrow edema reported from nine hips/3 studies was 8.88 (SD± 2.55) mm (4, 25, 35). One study reported the width of geometric edema in 2 cases >10mm (5). The remaining 17 cases which did not have focal marrow edema had a median time to the presentation of 6 (IQR 2-18) months from 7 studies (5-6, 10, 12, 26, 34, 36-37, 39). The two studies described before had all the cases without focal marrow edema (6, 26). We observed that the cartilage loss was inconsistently reported across studies. Seven studies performed cartilage-sensitive sequences to locate the site and the pattern of cartilage loss in this review *Annexure 3* (5-6, 25-27, 36, 40). The pattern of cartilage loss was either focal or diffuse. The site of cartilage loss was acetabular or femoral head or both. Though the pattern of cartilage loss was documented, the site of loss was inconsistently reported. Seven studies comprising 26 hips (MRI reviews) did not comment on the pattern and location of cartilage loss, but 20 hips among them demonstrated joint narrowing due to cartilage loss (4-5, 7-9, 37, 39). On the other hand, two studies/hips quantified marked cartilage loss on MRI reviews (10, 36). Six studies with 17 cases had focal cartilage loss either centrally in the femoral head or superomedial weight-bearing area of the acetabulum (5-7, 26-27,40). Two studies/2 hips specifically reported no cartilage loss. However, both had joint space reduction (25, 35). We classified 25 hips/10 studies (4-5,7-8 25-27, 34-35,40) and 21 hips/ 10 studies (6, 9-10, 12, 26, 34, 36-37, 39) studies as early and late ICH in this review based on the observations of review authors.

Outcomes of Follow-up MRI reviews:

We had 14 follow-up MRI reviews from 8 studies among 46 cases (6-8,10, 12,25-27). The median time to follow-up MRI in these hips was 12.5 (IQR 3.75-19.5) months (6 studies). One study reviewed the follow-up MRI at a mean of 11 (9-16) months (4 hips) while another at less than 18 months (4 hips) (6, 26). The frequency of MRI characteristics among the follow-up MRI in these hips is given in Table 3. Eight hips demonstrated marrow edema (7 diffuse, one focal) while six did not. Four studies (4 hips) reported improved MRI characteristics, namely marrow edema and joint effusion on treatment (7-8, 10,25). These studies are discussed under the pharmacological interventions for ICH. However, four studies (10 hips) worsened in follow-up on MRI characteristics (6,12, 26-27). All except two hips which demonstrated MRI characteristics of worsening, had diffuse marrow edema or no marrow edema, to begin with.

We compared the change in the proportion of characteristics over time between the first and subsequent MRI reviews (Table 3). We observed a transition pattern from early to late changes between the MRI reviews. While early changes of geometric marrow edema and focal cartilage loss decreased significantly, the late degenerative changes into the femoral head and acetabulum, diffuse cartilage loss, and bone remodeling increased significantly between MRI reviews. We investigated the relationship between the presence of each MRI characteristic with time for the first MRI reviews.

(Figure 3). We noted that geometric marrow edema ($P < 0.01$), diffuse marrow edema ($P < 0.05$), diffuse cartilage loss ($P < 0.05$), and joint effusion ($P < 0.05$), were significantly associated across time of first MRI reviews.

Secondary Outcomes:

We divided ICH treatment into pharmacological and Operative interventions groups.

Pharmacological interventions group (Table 4): We pooled 8 cases from 7 studies of ICH under the pharmacological interventions group . These studies were summarized into Etanercept (8, 10, 39), Methotrexate (7, 25, 35), and Botulinum neurotoxin toxin (9) sub-groups. We noticed that the included studies in the subgroup of pharmacological interventions were heterogeneous and used mixed methods to manage ICH. All except one study (8) started NSAIDs as the first treatment. Two studies used corticosteroids besides principal treatment (10, 35). Four studies performed additional procedures, including biopsy, joint debridement (open and arthroscopic), muscle releases, and bumpectomy (1, 7, 35, 39). All except one study started pharmacological treatment within a year of diagnosis (39).

Operative interventions for ICH (Table 5):We pooled 106 cases/115 hips from 22 reports under operative interventions group for ICH. There were 45 subtotal/partial capsulectomies (4-5, 14, 18, 21, 26, 29, 38), 18 THA (4- 5, 12, 18, 22), 14 open arthrotomies with or without biopsy and debridement(14, 16-17, 19-20, 24, 33), five arthrodiastasis (5, 15, 32) , five arthrodesis (18-19, 21, 23,) three osteotomies (16, 19, 29), three excision arthroplasties (19, 21), one each hanging hip operation, mould, cup and resurfacing arthroplasties (14, 19, 21). Tenotomies of muscle and soft tissue releases were either isolated or combined with other surgical procedures in 25 hips (14,17-18,22, 26, 29-30). Arthroscopy with or without associated procedures of labral debridement, abrasion chondroplasty, cartilage, and joint debridement with or without synovectomy was done for seven hips (11, 29, 31).

Discussion

This paper aimed to review the MRI characteristics of ICH and its management. We found that the geometric marrow edema on various MRI sequences may be the earliest and most specific finding in ICH cases. We see a transition in MRI changes over time. While the early changes which appear at less than two months decrease over time, the late structural changes into the bone predominate beyond six months of the disease process. Late diffuse cartilage loss changes occur as early as four months in a rare case. So was applicable between the focal and geometric marrow edema across the time. We found that most of the hips with diffuse marrow edema had coexistent changes, which indicated disease progression. ICH has been shown to have a prolonged course distributed in two phases with three possible outcomes (1). It follows an acute phase up to 18 months, followed by a chronic phase lasting 3 to 5 years. The three reported outcomes after the culmination of the disease process are 1. Peak cartilage loss up to 1 year followed by radiological restoration of joint space of up to 2 mm over next few years 2. Fibrous ankylosis, and 3. Complete recovery in extreme cases (1). From the reviews of the first and subsequent MRI, we notice that transition from focal to diffuse marrow edema occurs somewhere from the second month onwards and completes by six months.

Similarly, there was an inverse relationship between focal and diffuse articular cartilage loss. While focal cartilage loss was a predictor of early ICH, diffuse cartilage loss was associated with disease progression. A study demonstrated that the cartilage loss progressed from the central third of the femoral head to the periphery (6). We predict that hips with diffuse cartilage loss on MRI develop degenerative changes over time. We also found that those hips with focal geometric edema without demonstrable cartilage loss had joint narrowing. We believe that cartilage loss starts early, even before marrow edema; however, detecting such changes requires cartilage-sensitive imaging, lacking in most included studies. We have described various cartilage-sensitive sequences used in the studies included in this review *(Annexure 3)*.

Disease-modifying antirheumatic drugs (DMARDs), biologics (Etanercept), and Botulinum neurotoxin-A (BoNT-A) are described pharmacological interventions for the treatment of ICH in the studies included for this review (7-10, 25, 35, 39). However, the included studies were biased for the treatment with the pharmacological agents. All except one study used mixed methods for the treatment. Autoimmune mediated cartilage destruction and demonstration of HLA b27 in ICH led few studies to recommend biologics and DMARDs in its management. However, as described before, ICH has a long course with unpredictable outcomes. The mean follow-up of the studies under pharmacological interventions in this review was 36 ±18 months. Given the timeline of ICH and a mid-term follow-up in the included studies for this review, it would be unwise to draw meaningful conclusions on the efficacy of pharmacological agents.

Partial/subtotal circumferential capsulectomy was the most performed operation for ICH. However, its outcomes ranged from satisfactory to poor across the reviewed studies. Total hip arthroplasty was also a commonly performed operation in the studies in this review. One study reported ceramic on ceramic arthroplasty in an adolescent patient. We expect historical operations in ICH management (excision arthroplasty, arthrodesis, osteotomies, hanging hip operation) to be replaced by THA. These operations are associated with hip instability, degeneration in the spine over time, and morbidity due to soft tissue releases. Modern arthroplasty bearing surfaces and practices of safe hip arthroplasty may be one of the reasons for THA to replace other morbid options in the management of ICH. Joint distraction and arthroscopic techniques were also reported options in the management of ICH; however, given the smaller number of cases with limited data on long-term follow-up precludes us from commenting on the efficacy of these techniques.

Implications for research:

The treatment of ICH is divided into two broad categories. In the early stage of the disease process, the management options of rest, traction, immunomodulators, biologics, joint distraction, joint debridement, and subtotal capsulectomy focus on halting the process of cartilage destruction. Among them, the pharmacotherapeutic agents are promising because they stop the process of autoimmune mediate cartilage destruction. However, future research by multicenter trials to recruit a more significant number of patients may be beneficial to draw a logical conclusion on the efficacy of these agents. When the cartilage loss becomes extensive with exposure of the underlying bone, the joint salvage options have a limited role in management. Joint arthrodesis and replacement are the options in the late management of ICH. However, the age for onset of ICH is the critical consideration for choosing joint arthrodesis or replacement. Autologous chondrocyte implantation has been attempted to treat full-thickness cartilage defects in the hip, and its use is promising (45). We had one report describing joint replacement in adolescent patients. We believe that long-term outcomes of THA in arthritis in adolescents should be explored in managing such complex to manage diseases.

Limitations of the study:

The exclusion of studies other than English was one of the limitations of this review. We excluded 14 studies with 35 hips published in languages other than English. The inclusion of these studies would have influenced the outcomes of this review. We accept that the results of this review should be interpreted with caution due to publication bias.

Conclusion

We conclude that geometric marrow edema without any evidence of degenerative changes may be the most specific and early MRI feature in diagnosing ICH. Management of early and late ICH remains controversial despite reports on the efficacy of biologics, immunomodulators, and various operative interventions due to poor quality studies.

Declarations

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Conflict of interest:

none to declare

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Tables

Table 1

Classification of Chondrolysis of the hip in children and adults.

Primary Idiopathic Chondrolysis	
Secondary Chondrolysis in childhood hip diseases and inciting factors.	Perthes disease
	Slipped capital femoral epiphysis
	Juvenile idiopathic arthritis
	Trauma (hip dislocation)
	Liver transplantation
	Septic arthritis following magnetic resonance arthrography
	Transfer of greater trochanter
	Severe burns
	Hemodialysis
	Cryoablation
	Bone cement leak
	Marfan's syndrome
	Removal of an implant (Nail)
	Hip arthroscopy
	Sickle cell disease
	Autoimmunity
	Intra-articular Infusions
	Excision of torn acetabular labrum
	Erythema migrans

Table 2

Risk of Bias assessment for studies included in the review.

Serial number	JBI[1] Risk of Bias assessment tool for case reports (Domain).	Yes (%)	No(%)	Unclear/not applicable/Cannot determine (%)
1	Were patient's demographic characteristics clearly described?	29(82)	2(7)	4(11)
2	Was the patient's history clearly described and presented as a timeline?	19(54)	13(37)	3(9)
3	Was the current clinical condition of the patient on presentation clearly described?	27(77)	4(12)	4(11)
4	Were diagnostic tests or assessment methods and the results clearly described?	31(88)	1(3)	3(9)
5	Was the intervention(s) or treatment procedure(s) clearly described?	21(60)	1(3)	13(37)
6	Was the post-intervention clinical condition clearly described?	21(60)	7(20)	7(20)
7	Were adverse events (harms) or unanticipated events identified and described?	3(8)	27(77)	5(15)
8	Does the case report provide takeaway lessons?	18(51)	14(40)	5(9)
	Total number of studies included in review	35		

1. Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Reports quality assessment tool.

Table 3

MRI characteristics at baseline and follow-up

Characteristics	Baseline	Follow up	P value
	n=46	n=14	
Geometric marrow edema in the central third femoral head	26 (56.5)	1 (7.1)	<0.01[1]
Diffuse marrow edema	17 (37.0)	7 (50)	0.38 [2]
Focal cartilage loss	28 (60.9)	1 (7.1)	<0.01[1]
Diffuse cartilage loss	6 (13.0)	11 (78.6)	<0.01[1]
Protrusio acetabuli	4 (8.7)	4 (28.6)	0.07 [1]
Degenerative changes	5 (10.9)	9 (64.3)	<0.01[2]
Fusion of physis	1 (4.8)	4 (57.1)	<0.01[1]
Fibrous ankylosis	1 (2.2)	0 (0.0)	1.00 [1]
Joint narrowing	38 (82.6)	12 (85.7)	1.00 [1]
Joint effusion	33 (71.7)	11 (78.6)	0.74 [1]
Synovial thickening	23 (50.0)	7 (50.0)	1.00 [2]
Muscle wasting	20 (43.5)	11 (78.6)	0.03 [1]
Femoral head irregularity or erosions or both	7 (15.22)	6 (42.9)	0.03 [2]
Femoral head remodelling	8 (17.4)	6 (42.9)	0.05 [2]
Acetabular remodelling	5 (10.9)	5 (35.7)	0.03 [2]

1. Fisher exact test.

2 .Chi square test.

Table 4.

Pharmacological interventions in Idiopathic Chondrolysis of Hip in Children.

Citation/year/settings	Number of participants/hips	Pharmacological modality	Time to presentation in months	Follow-up in months	Pre-intervention outcomes	Post-intervention Outcomes	Comments
Appleyard et al./2000/USA.	1/1	Etanercept 25 mg twice weekly for 36 months	18	36	a. Wheelchair ambulator with pain control medications. b. Biopsy, arthrotomy and muscle releases. c. F= 5^0 E= -45^0	Able to play basketball F= 100^0 E = 35^0 Add = 40^0 Abd = 20^0 IR = 5^0 to 10^0 ER = 5^0 to 10^0	The authors demonstrated radiological and clinical benefits of Etanercept by its action against TNF.
Vater et al. /2020/USA	1/1	Etanercept 0.8mg/kg/week for 3 months	3	32	Pain and limitation of Motion F= 90^0 IR = 10^0 ER = 30^0	No pain, normal movements at hip after intervention.	
Kampani KT/2018/(Syria)	1/1	Etanercept 50 mg weekly for 9 months	2	9	Pain 6-9/10 F= 50^0 E = -10^0 Abd = 30^0 IR=15^0 ER= 0^0	Pain 0 to1/10, FL = 80^0 E = -10^0 Abd = 30^0 IR = 20^0 ER= 15^0	The Positivity to HLA B 27 formed the basis for institution of Etanercept treatment.
Endo et al./2020/Japan	1/1	Oral methotrexate 12mg/week, for 5 years	2	60	Crutch ambulation F= 70^0 E = -10^0 Abd =15^0 Add = -10^0 IR= 0^0 ER = 60^0	After pharmacotherapy and bumpectomy F = 110^0 E = 0^0 Abd = 30^0 Add = 0^0 IR = 30^0 ER = 60^0	The study required arthroscopic bumpectomy for increasing range of motion
Sakamoto/2011/Brazil	1/1	Oral methotrexate + Indomethacin for 3 months followed by Intravenous methotrexate 20mg/week sc for 24 months.	1	24	Limitation of ER and IR	No limitation in hip mobility	Authors did not report assessment criteria for hip function before and after methotrexate treatment.
Picazo et al./2016/Spain	1/1	Arthrotomy followed by Methotrexate 10 mg/week increased to 17.5 mg /week	2	12	F= 80^0 limited ER and IR	F = 90^0 and improvement in ER	The investigators reported culture of unusual organisms from the synovial fluid.
Khoshhal	2/2	Botulinum	5	6	Pain and	Both the Colour	The presence

K/2014/Saudi Arabia	neurotoxin A injections 100 U in selected muscle (Rectus femoris, Gracilis, Adductor longus) by the neurophysician	8	6	muscle spasticity were measured on validated standardized Colour Analog scale - 9 and modified Ashworth scale - 4	Analog scale and Modified Ashworth scale were 1 each after injections	of muscle contractures among ICH cases across published literature was the basis for treatment by Botulinum neurotoxin injection.

F= Flexion, E= Extension, Abd = Abduction, Add = Adduction, IR = Internal rotation, ER = External rotation.

Table 5

Operative Interventions for Idiopathic Chondrolysis of Hip in children.

Citation/year/setting	Number of participants/hips	Time to presentation (months)	Duration of follow-up in months (Range)	Operative Treatment modality n=hips	Pre-intervention outcome measures	Post-intervention Outcome measures n= cases	Comments
Amarnath et al./2018/India Retrospective case series	14/14	2.25 (0.25 to-8)	36 to-48	Stage I NSAID/Etanercept and weight bearing Stage II Partial capsulectomy + traction and rehabilitation Stage III Arthrodiastasis and total hip replacement	a. Clinical outcomes = NA b. Radiological outcomes = Stage I=9 Stage II=3 Stage III=2	Short term (3 years) statistical improvement in stage I but deterioration in stages II and III in long term.	Authors devised a 3-stage classification based on the findings of MRI and classified 14 patients. The study also proposed treatment methods based on the classification.
Bleck et al./1983/USA Case series	7/8		73 (28 to 112)	Iliopsoas tenotomy = 3 cases Adductor tenotomy = 1 Resurfacing arthroplasty = 1 Anterior capsulotomy = 1 Arthrotomy = 7	F = 84^0 (0^0 to 120^0) E = -10^0 (0^0 to -35^0) Abd = 18.75^0 (-30^0 to 45^0) IR = 16.85^0 (0 to 60) ER = 20^0 (0^0 to 45^0)	F= 107.5^0 (60^0 to 130^0) E = -2.5^0 (0^0 to -10^0) Abd = 35^0 (20^0 to 45^0) IR = 15.6^0 (0^0 to 45^0) ER = 30^0 (0^0 to 45^0)	The authors reported 9 patients with 11 hips however, 7 cases/8 hips meet inclusion criteria
Canadell et al./1993/Spain Case series	1/1	35	13	Arthrodiastasis/joint distraction for 75 days n=1	F = 75^0 E = -50^0 IR = 0^0 ER = 0^0 Abd = -15^0 Add = 15^0	F= 45^0 Ext = -20^0 IR = 0^0 ER = 0^0 Abd = 0^0 Add = 0^0	The study evaluated pain on a scale from 0 to 4 (0 no pain and 4 severe pain). The pain intensity changed from moderate (2) to mild (1) after treatment
Daluga at al./1989/USA	1/1	5.7 (1 to–14)	84 (13to-180)	a. Subtrochanteric osteotomy n=1			The authors reported 16 hips however, 1 case meet inclusion criteria.
Dechosilpa et al./2014/Thailand	1/1	5	48	Arthrotomy and muscle releases	Restriction in range of motions of hip.	Normal gait with 15 ER deformity	The study reported 3 cases of ICH however, 1 case meet the review criteria.
Donnan et al.	1/1	3	11	arthroscopic debridement	E -20^0 Abd deformity 15^0 Stiff hip	no improvement	
Duncan et al./1975/USA Case series	3/3	Mean = 3.66 (2to-5)	57.6 (24 to-96)	Arthrotomy and biopsy = 3	E = -50^0 (-10^0 to -80^0)	E = -56.66^0 (-30^0 to -65^0) ankylosed	The authors reported 5 cases of ICH however, 3 cases meet inclusion criteria.

Garcia et al./1999/Spain. Retrospective case series.	7/8	Mean = 6.4 (2to-12)	120	a. Capsulectomy and iliopsoas and adductor Tenotomy = 8 b. Arthrodesis = 1 c. Later THR = 6	F = -60.6^0 (30^{0}to-85^0) IR = -3.7^0(0^0 to -15^0) ER = -5^0(0^0 to -15^0) Add-Abd arc = 24^0 Shortening = 3.25 cm	Due to varied operations and follow-up over study period the outcome measures were not reported.	The study reviewed 11 cases/12 hips however, 7 cases/8 hips meet review criteria.
Hoeven et al./1989/Netherlands case series	4/4	11.5 (3 to 24)	21 (12 to 36)12	Arthroscopy= 4 Tenotomy, capsulotomy, and osteotomy = 1		Compromised results in all cases	
Hughes et al./1985/UK	1/1	3	6	Arthrotomy and biopsy	E= -20^0 FL = 80^0 IR = 0^0 ER= 30^0	Ankylosed in E = -30^0 Add deformity = 10^0 IR deformity 10^0	
Jones et al./1971/South Africa Retrospective case series.	6/6	(2 to 24)	34.5 (6 to 72)	a. Corrective osteotomy in fused hip = 1 b. Cup arthroplasty = 1 c. Mould Arthroplasty = 1 d. Excision arthroplasty = 1 e. Hip arthrodesis = 2 f. Varus derotation osteotomy= 1 g. open biopsy = 1			The study reported 9cases/10 hips of ICH but we included 6 hips meeting review criteria.
Korula RJ. /2005/India Retrospective case series.	20/21	12	23.4 (4 to 121)	a. Subtotal circumferential capsulectomy=17 b. Arthrodesis = 1 c. Excision arthroplasty= 2 d. Hanging hip operation = 1	Hips were assessed in preoperative period for range of motion.	Statistically significant improvement in range of motion in hip = 15 Fibrous ankylosis =2	This study reported the largest series for the operative treatment of ICH.
Laor et al./2008/USA Retrospective case series	6/7	Mean= 1 (0.5 to 1.5)		a. Subtotal Capsulectomy + muscle release = 7 hips b. BL THR in one case at 17 years of age		a. Normal to near normal hips = 3 and b. Moderate space narrowing hips = 2	Details of study described elsewhere in paper. Study focussed on description of early MRI features in ICH
Laubscher et al./2016/South Africa Retrospective case series	5/5	Median = 2 (2 to 24)	11 (9 to 16)	Subtotal Capsulectomy, Psoas tenotomy, release of Straight head of rectus femoris and tensor fascia lata was done in all cases.	E = - 31^0(-20^0 to -45^0) Abd deformity = 22^0 (10^0 to 30^0) ER deformity = 20^0 (10^0 to 30^0). FL-E arc = 25^0 (0^0 to 60^0)	E = -26^0 (-20^0 to -30^0) Abd Deformity = 13^0 (0^0 to 30^0). ER deformity = 8^0 (0 to 30)	Study reported deterioration in all hip in long term.

						FL-E arc = 40^0 (30^0 to 60^0)	
Lim et al./2020/South Korea (Retrospective case series)	2/2	>6	Mean study follow-up = 56 (27 to 91)	a. Osteochondroplasty of the femoral bump, b. Debridement of the torn labrum and detached articular cartilage, c. labral repair, d. removal of loose body, and e. Synovectomy were the arthroscopic procedures in operated patients.	Harris hip score (HHS), the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)subjective pain assessment with visual analog scale (VAS), and range of hip motion were assessed.	Improvement in all described scores.	The study reported outcomes of arthroscopic procedures in 32 cases however, there were 2 cases of ICH which satisfied inclusion criteria for this review.
Megremis et al./2021/Greece	1/1	18	72	Ceramic on ceramic Total hip arthroplasty(THA).	a. E= - 30^0 and severe limitation of hip motion. b. Harris hip score = 38.45%	Harris hip score = 97%	The study reported outcomes of THA in an adolescent patient with ICH.
Roy et al./1988/USA	3/3	0.5 to 24	37 (13 to 55)	Subtotal circumferential Capsulectomy n=3	F = 68^0 (60^0 to 75^0) E = -26.66^0 (-15^0 to -35^0) ER contracture = 15 in 2 cases Abd = 15^0 to 20^0	Full range of motion in all patients	Retrospective case series.
Sherlock et al./1995/UK	5/5	NA	36to-108	Extensive soft tissue releases n = 5	All patients had flexion deformity ranging from 40 to 80	Painful B/L hips =2 Ankylosis = 2 Stiff painless = 1	The authors proposed ICH and protrusion-acetabuli to be same disease
Shore et al./1981/UK	7/9	2 to-18	60 (24 to-156)	Bilateral arthroplasty= 4 Soft tissue release =1			The authors reported 8 patients with 6 bilateral hips where total hip arthroplasty was needed in all bilateral hips with ICH
Sparks et al./1982/South Africa	1/1		80.8 (12 to-168) in 10 patients	Arthrodesis = 1			The authors included 9 patients in follow up from Jones series and 9 patients of their study and complied data.
Thacker et al./2005/USA	3/3		57 (24 to 73)	Hinged distraction for 3 to 4 months	Mean score on author validated scale was 4.6 for 3 patients (5, 5 and 4)	An excellent score (0) was reported in all three patients after treatment in follow-up.	The case series recruited 11 hip arthritis patients however, 3 cases/3 hips meet review criteria. Clinical Outcomes were rated on an author validated ordinal scale consisting of pain, range of motion, and Level of ambulation. The

				cumulative scores of 0, 1 and 2 were rated excellent, good and poor results respectively
Wenger et al./1975/USA	1/1	24	Arthrotomy and biopsy	The study reported 2 cases of ICH but 1 case meet inclusion criteria

F= Flexion, E= Extension, Abd = Abduction, Add = Adduction, IR = Internal rotation, ER = External rotation.

Figures

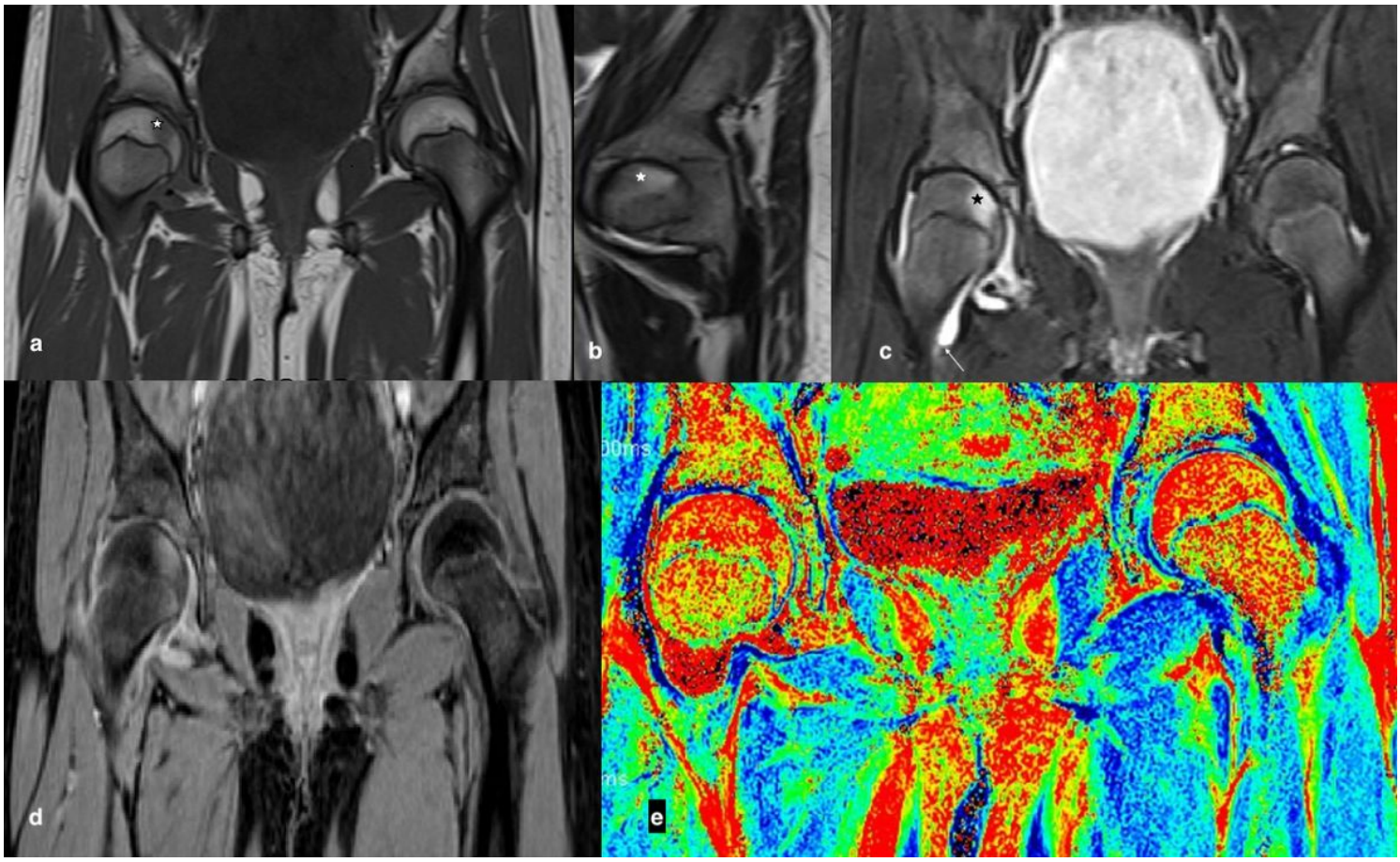

Figure 1

Images of an 11-year-old female with one month history of right hip pain and limp. MRI showed geometric area of hypointensity (star) on coronal T1-weighted image (a), hyperintensity (star) on sagittal STIR (b) and coronal T2-weighted images in the mid-third of the right femoral head. There is mild joint effusion (c, arrow). Post-Gadolinium T1 VIBE coronal image (d) showed enhancing synovial thickening (arrow), femoral articular cartilage loss and joint space narrowing. Coronal section of color coded T2 articular cartilage map(e) showed irregularity and focal chondral defects in the right hip

Kiran M, Barathi D, Sunitha VC, Sathwik D. Idiopathic chondrolysis of the hip.2019: eurorad;*Case 16388.*

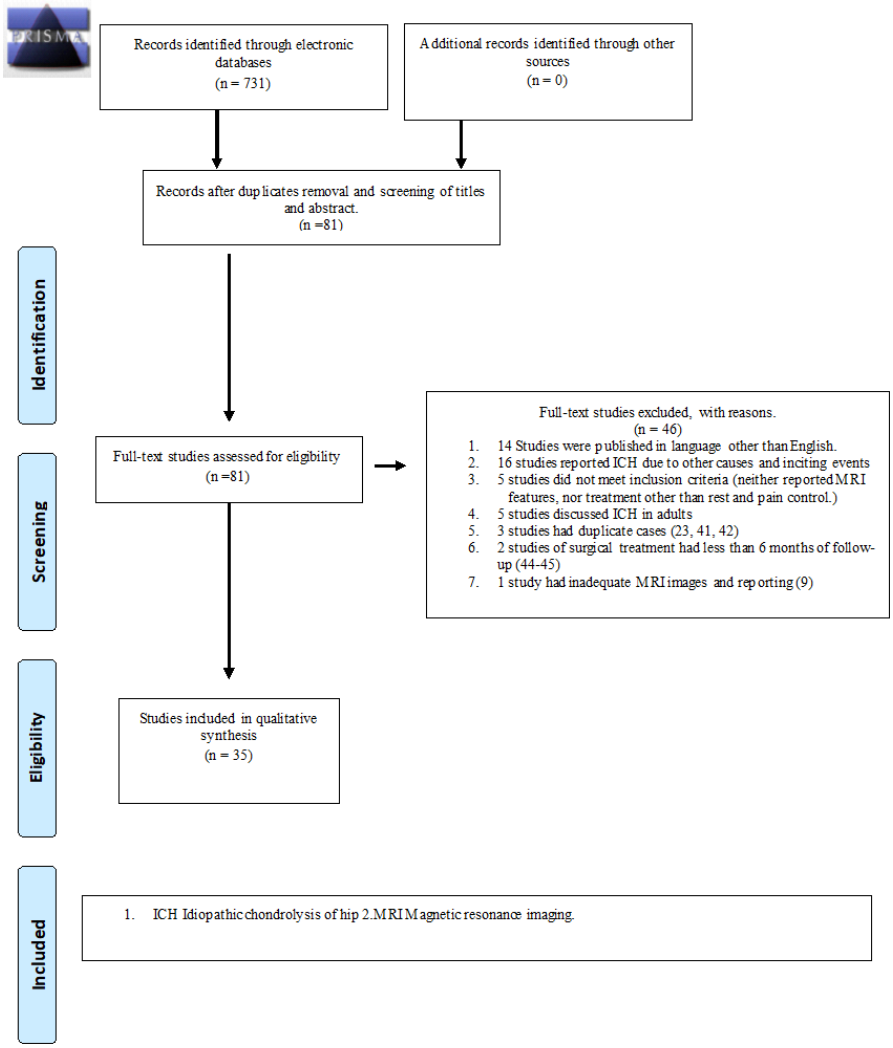

Figure 2

PRISMA flow diagram for the idiopathic chondrolysis of hip in children

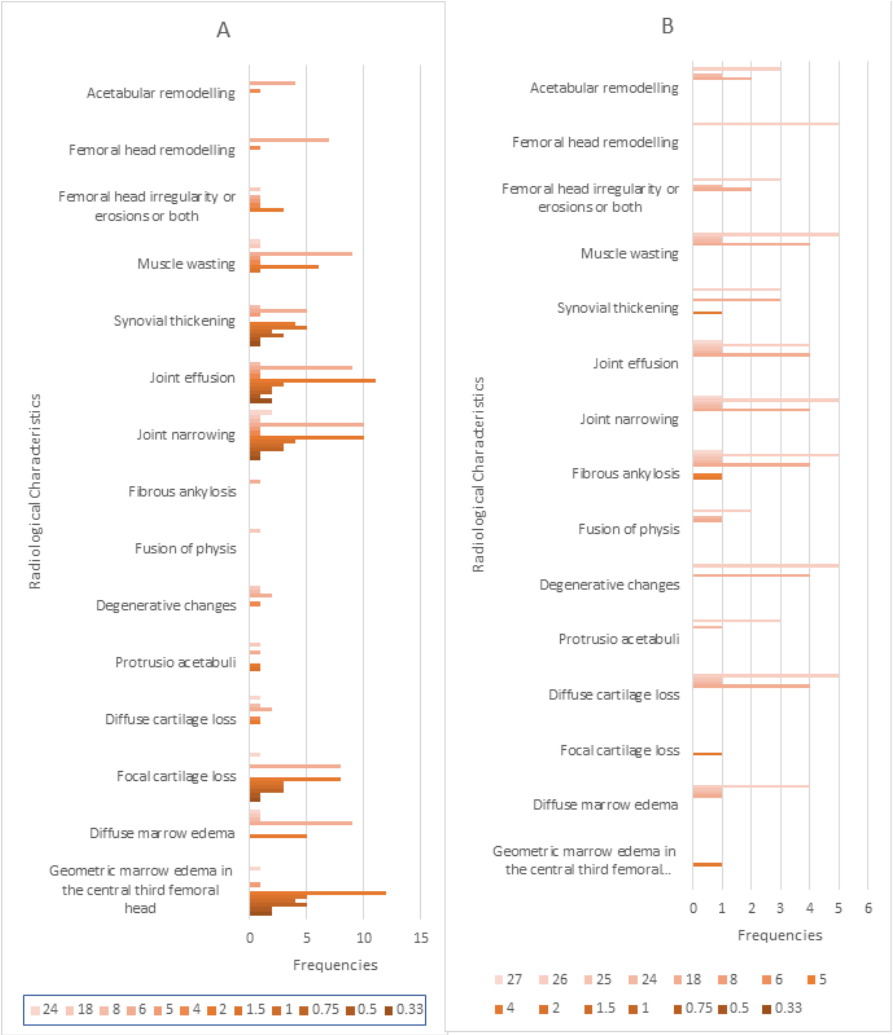

Figure 3

Distribution of MRI characteristics across first review at a median time of 1.75 (IQR 0.93-4.25) months (A) and subsequent reviews at 12.5 (IQR 3.75-19.5) months (B)

Supplementary Files

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