

Review article

Pregnancy associated transient osteoporosis of the hip (PR-TOH): A non-obstetric indication to caesarean section. A case report with literature review



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ARTICLE INFO

Article history:

Received 13 January 2021

Received in revised form 29 April 2021

Accepted 3 May 2021

Keywords:

Transient osteoporosis

Hip

Pregnancy

Caesarean section

MRI

ABSTRACT

Pregnancy related transient osteoporosis of the hip (PR-TOH) is a rare condition that manifests with sudden pain located in the groin region, anterior thigh and buttocks. It is a benign and in the majority of cases self-limiting disease, related to bone marrow oedema. It occurs during the third trimester of pregnancy or less frequently during the post-partum period. Hip movements are usually restricted by pain and it often becomes a non-obstetric indication for Caesarean delivery.

Here, we report a case of unilateral PR-TOH diagnosed by magnetic resonance imaging (MRI) and a literature review.

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Introduction

Pregnancy related transient osteoporosis of the hip (PR-TOH) is a rare condition that manifests with sudden pain located in the groin region, anterior thigh and buttocks [1]. It is a benign skeletal

disorder, related to bone marrow oedema, self-limiting in the majority of cases.

Only little is known about the underlying pathophysiology and the overall incidence. A combination of pre-pregnancy reduced bone density with the mechanical and metabolic stresses of pregnancy and lactation have been postulated to be responsible for this condition [1]. It usually occurs during the third trimester of pregnancy or less frequently during the post-partum period [1]. Hip movements are usually restricted by pain and it often becomes

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an indication for Caesarean delivery. The first described case of PR-TOH date 1959 [2].

Objective

The aim of this study, was to report the second Italian described case of unilateral PR-TOH diagnosed by magnetic resonance

imaging (MRI) and to realize a literature review of all available cases from 1959 to 2020.

Case report

A 32-year-old Caucasian, nulliparous women with a BMI of 26, was referred to the Orthopaedic clinic at 36 weeks of gestation due to severe pain (8 points on the Visual Analogue Scale-VAS) on the

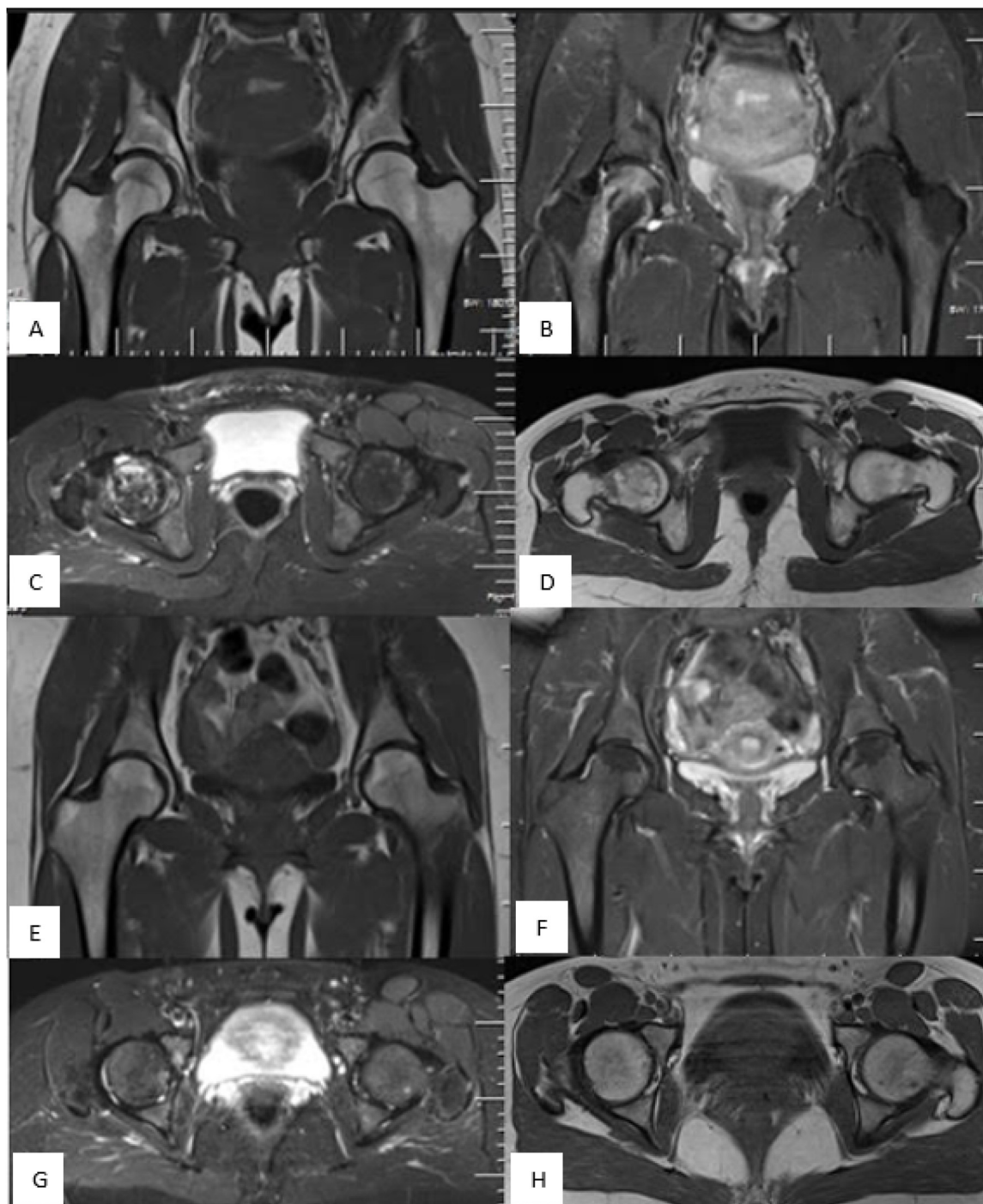


Fig. 1. A–D) MRI performed 2 weeks after caesarean delivery. A) T1 coronal sequence showing diffuse low signal of the right femoral head. B) Bone marrow oedema of the femoral head extending in the femoral neck on T2 FS sequence on the coronal plane. C) T2 FS sequence in the axial plane enhances the oedema of the right femoral head associated with a moderate joint effusion (b, c). The corresponding T1 in the axial plane showed the loss of normal fatty marrow signal. E–H) MRI performed 8 months after the first one. Evidence of resolution of the previous bone marrow oedema.

Table 1
Literature review.

Year of publication	Number of cases	Country	Maternal age at symptoms	Risk Factors	GA at Diagnosis weeks of gestation	Mode of delivery	Symptoms	Radiological exams for diagnosis	Treatment	Time for recovery
Curtiss PH 1959 [2]	3	USA	28 28 35	None	32 36 12 weeks postpartum	NA	Bilateral hip pain Left hip pain Left hip pain	X Rays X Rays X Rays	NWBPT	2.5 months 3 months 9 weeks After delivery
Longstreth PL 1973 [3]	1	USA	33	None	22	NA	Bilateral hip pain	X Rays	NWBPT	Postpartum
Nozawa S 1976 [4]	1	Japan	23	NA	36	NA	Left hip pain	X Rays	NA	NA
Beaulieu JG 1976 [5]	1	NA	NA	NA	NA	NA	NA	NA	NA	NA
Kato F 1977 [4]	1	Japan	30	NA	16	NA	Right Hip pain	X Rays	NA	NA
Chigira M 1979 [4]	1	Japan	NA	NA	Postpartum	NA	NA	NA	NA	NA
Ando K 1982 [4]	3	Japan	23 31 26	None	36 32 36	NA	Right hip pain Left hip pain Bilateral hip pain	X Rays	NA	NA
Kushi M 1983 [4]	1	Japan	27	None	24	NA	Right hip pain	X Rays	NA	NA
Kumar R 1983 [6]	1	USA	NA	NA	NA	NA	NA	NA	NA	NA
Gruber HE 1984 [7]	3	USA	NA	NA	Postpartum	NA	NA	NA	NA	NA
Lose G 1986 [8]	1	Denmark	35	None	31	ELCS TOH	Left hip pain	X Rays	NWBPT	6 weeks after delivery
Chigira M 1988 [9]	1	Japan	27	None	6	Abortion	Right hip pain	X Rays	NWBPT	3 weeks after abortion
Brodell JD 1989 [10]	2	USA	NA	NA	NA	NA	NA	NA	NA	NA
Ben-David Y 1991 [11]	1	Israel	NA	NA	NA	NA	NA	NA	NA	NA
Goldman GA 1994 [12]	1	Israel	34	None	27 Twin pregnancy	VD	Left hip pain	MRI X Rays	NWBPT	2 months after delivery
Fingerroth RJ 1995 [13]	1	USA	27	None	38	NA	Right hip pain	X Rays	NWBPT Hip fracture: surgery	3 months after delivery
Funk JL 1995 [14]	1	USA	31	None	41	VD	Left hip pain	X Rays MRI	NWBPT	4 years after delivery
Junk S 1996 [15]	1	Poland	35	None	2 weeks postpartum	VD	Hip pain	Computed Tomography Scintigraphy	NWBPT Hip fracture: surgery	4 months after surgery
Fokter SK 1997 [16]	1	Slovenia	30	None	27	ELCS TOH	Left hip pain	X Ray MRI	NWBPT Hip fracture: surgery	4 month after surgery
Siva S 1997 [17]	1	Australia	31	None	29	CS OI	Left hip pain	X Rays MRI	NWBPT	2 months after delivery
Jolliffe D.M 1997 [18]	3	United Kingdom	23 27 29	None None None	24 37 38	ELCS TOH ELCS TOH ELCS TOH	Bilateral Hip pain Right hip pain Bilateral Hip pain	X Rays X Rays X Rays	Non weight bearing physical therapy	4 months after delivery 5 weeks after delivery 2 months after delivery
Samdani A 1998 [19]	1	Japan	36	None	32	CS OI	Left hip pain	X Rays	NWBPTM	Several weeks after delivery
Sweeney AT 2000 [20]	1	America	28	None	12 weeks postpartum	NA	Right hip pain	DEXA MRI	NWBPT	4 months postpartum
Uematsu N. 2000 [21]	4	Japan	33 (mean)	None	31 (mean)	NA	2 patient Right hip pain	X Rays MRI	NWBPT	14 weeks after

Table 1 (Continued)

Year of publication	Number of cases	Country	Maternal age at symptoms	Risk Factors	GA at Diagnosis weeks of gestation	Mode of delivery	Symptoms	Radiological exams for diagnosis	Treatment	Time for recovery
Thomas E. 2000 [22]	1	United Kingdom	26	None	34	VD	2 patient bilateral hip pain Left hip pain	X Rays	NWBPT Hip fracture: surgery	18 months after surgery
AxtFliedner R 2001 [23]	1	Germany	35	None	31	ELCS	Bilateral hip pain	MRI	NWBPT	NA
Boissonnault WG 2001 [24]	1	USA	32	NA	29	TOH NA	Right hip pain	X Rays MRI	not to breast feed NWBPT	4 weeks after delivery
Wood ML 2003 [25]	1	USA	29	None	Third trimester of pregnancy	VD	Right hip pain	NA	NA	NA
Dieme C 2006 [26]	1	Senegal	41	None	28	VD	Bilateral hip pain	NA	NWBPTM	8 weeks
Laktasic-Zerjavic N 2007 [27]	1	Germany	33	None	36	NA	Right hip pain	MRI	NWBPTM Calcitonin	6 months after delivery
Cohen I 2007 [28]	1	Israel	37	None	22	VD	Left hip pain	MRI	NWBPT hip fracture: surgery	24 months after surgery
Pai WC 2008 [29]	1	Taiwan	36	None	32	CS OI	Bilateral hip pain	X Rays	NWBPT	3 months after delivery
Spinarelli A 2009 [30]	1	Italy	35	None	Third trimester	NA	Bilateral hip pain	MRI	NWBPT Hip fracture: surgery	3 months after surgery
Lamarca M 2009 [31]	1	Spain	29	None	40	VD	Left hip pain	X Rays	NWBPTM hip fracture: surgery	6 months after surgery
McWalter P 2009 [32]	1	Saudi Arabia	33	None	Third trimester of pregnancy	NA	Right Hip pain	X Rays MRI	NWBPTM	3 months after delivery
Chalouhi GE 2010 [33]	1	France	30	None	32	ELCS TOH	Right hip pain	X Rays	NWBPTM	1 year after surgery
San Juan Alvarez M 2010 [34]	1	Spain	29	None	39	ELCS TOH	Unilateral hip pain	X Rays	NWBPT hip fracture: surgery	6 months after surgery
Moltó A 2010 [35]	6	Spain	Mean GA 31	None	Third trimester Mean GA 28.8	ELCS TOH NA	NA	X Rays DEXA X Rays MRI	NWBPTM NA	9 months after delivery 8 weeks post delivery
Mirza R 2012 [36]	1	Pakistan	45	None	36	ELCS TOH	Left hip pain	X Rays MRI	NA	24 months after delivery
Emami MDJ 2012 [37]	1	Iran	24	None	28	VD	Bilateral hip pain	X Rays CT MRI	NWBPT hip fracture: surgery	6 years after surgery
Bircher C 2012 [38]	1	United Kingdom	31	None	34	ELCS TOH	Bilateral hip pain	MRI	NWBPT Bilateral Hip fracture: surgery	6 months after delivery
Patel V 2012 [39]	1	USA	34	None	Third trimester of pregnancy	VD	Right hip pain	X Rays MRI	NWBPT	NA
Anai Ta 2013 [40]	1	Japan	NA	NA	NA	NA	NA	NA	NA	NA
Lombana VEA 2013 [41]	1	Spain	29	None	39	VD	Right hip pain	X Rays MRI	NWBPT Hip fracture: surgery	NA
Izu CB 2014 [42]	1	Spain	34	None	20	NA	Right hip pain	X Rays MRI	NWBPT	2 months after delivery
Reese ME 2015 [43]	3	USA	46 44 33	None	29 Twins 33 Twins 36 Twins	CS OI CS OI CS OI	Right hip pain Right hip pain	X Rays MRI	NWBPT	1 month after delivery 3 weeks after delivery 2 months after delivery
Sachsaniadis P 2017 [44]	1	Switzerland	30	None	30	ELCS TOH	Bilateral hip pain	MRI	NWBPTM not to breast feed	4 months after delivery

Table 1 (Continued)

Year of publication	Number of cases	Country	Maternal age at symptoms	Risk Factors	GA at Diagnosis weeks of gestation	Mode of delivery	Symptoms	Radiological exams for diagnosis	Treatment	Time for recovery
Thanatsis N 2017 [45]	1	Greece	37	None	36	ELCS TOH	Bilateral hip pain	X Rays DEXA MRI	NWBPTM not to breast feed	3 months after delivery
Hadji P, 2017 [50]	52	Germany	Mean 34.6	Immobilisationteeth problems	NA	12/40 ELCS TOH 3/12 CSOI 25/40 VD	Hip pain	MRI DEXA	NWBPT 4 patients experienced Hip Fracture: Hip surgery	NA
Esteves A 2017 [46]	1	Portugal	NA	NA	Third trimester of pregnancy	NA	Hip pain	X Rays	NWBPT Hip Fracture: Hip surgery	Postpartum
Paiva F 2019 [47]	1	Portugal	48	None	Third trimester of pregnancy	ELCS TOH	Left hip pain	X Ray MRI	NWBPT	20 months after delivery
Carriles Rivero I 2019 [48]	1	Spain	NA	NA	NA	NA	NA	NA	NA	NA
Nassar K 2020 [49]	1	Morocco	38	NA	36	NA	Right hip pain	MRI	NWBPT	5 months after delivery

VD: Vaginal delivery; ELCS TOH: Elective Caesarean section for hip pain and movement functional limitation; CS OI: Caesarean section for Obstetric indication; NWBT: Non weight bearing and physical therapy; NWBPTM: NWBPT and medication; NA: not available.

right hip joint. The pain was increased by weight bearing and relieved by rest. She had no previous medical history, not assuming medication, tobacco or alcohol. No history of fractures, prolonged immobilization or teeth problems.

On the orthopaedic examination she was tender in the groin and the right upper lumbar region. She reported severe pain on the right hip abduction, flexion and extension movements. Neurological examination was unremarkable.

Laboratory analysis revealed the following results: 9.8 mg/dL of calcium, 3.9 mg/dL of phosphorus, 1.5 mg/dL of magnesium, 99 U/L of alkaline phosphatase, GOT 20 U/L; GPT 15 U/L, creatinine 0.8 mg/dl; normal thyroid functions (TSH 1.8 μ U/mL), 18.5 pg/mL parathyroid hormone, 48 ng/mL of 25 (OH) D, infective (Brucella, Lyme disease) and inflammatory parameter (C-reactive protein), rheumatoid and autoimmune markers were within the normal range. From the obstetric point of view pregnancy was complicated by a mild gestational diabetes adequately controlled by diet.

A multidisciplinary team (MDT), comprising gynaecologists, orthopaedics, physiotherapists and anaesthetists recommended: magnetic resonance imaging (MRI), analgesics (Paracetamol), thromboprophylaxis and psychological support.

The woman was admitted for induction of labour at 39 weeks of gestation that ended up to Caesarean section due to functional limitation pain related. A healthy 3200 g female neonate was delivered. After delivery symptoms got worse (10 points on the Visual Analogue Scale-VAS), 2 weeks after delivery she underwent magnetic resonance imaging of the hips (Fig. 1 images A–D)

Magnetic resonance imaging (MRI) showed diffuse bone marrow oedema involving the right femoral head, neck, and even intertrochanteric region with mild joint effusion. T1-weighted images revealed decreased signal with loss of normal fatty marrow signal, while T2-weighted images revealed matching high signal intensity in the marrow. There were also oedema along the ileopsoas muscle and quadratus femoris muscle on the right side and trochanteric bursitis probably in association with the intense effort in walking or moving to ensure neonatal care for the baby.

Because of breast feeding she did not receive additional medications. She was advised to continue in avoiding weight

bearing for at least three months, then to attend 10 physical therapy sessions, undergo 10 sessions of low dose ultrasound therapy and application of heat pads. Significant symptoms improvement has been reported at three months (6 points on the Visual Analogue Scale-VAS). A second MRI repeated after 8 month showed complete resolution of TOH (Fig. 1 images E–H)

Literature Review

The search for the systematic review was conducted using MEDLINE, EMBASE, Scopus, ClinicalTrials.gov, OVID and Cochrane Library as electronic databases. The citations were identified with the use of a combination of the following text words: “osteoporosis,” “pregnancy,” “hip,” “MRI,” and “PR-TOH” from inception of each database through December 2020. Review of articles also included the abstracts of all references retrieved from the search. No restrictions for language or geographic location were applied.

A total of 47 related studies with 123 described cases were identified [2–50] as relevant and included in the systematic review (Table 1). No guidelines were found. All available article, except one (case control study) (50), were case reports or small case series.

The mean maternal age at the occurrence of PR-TOH symptoms has been reported to be 32.1 SD 5.5. Twin pregnancies have been 4 /123, 3.2 % [12,43]. The mean gestational age at the occurrence of symptoms has been reported to be 31.43 SD 6.5, five cases had a postpartum onset [2,4,7,15,20]. According to our literature review laterality of symptoms has been specified in 51/123 cases. The left hip was involved in 15/51 (29.4 %) cases, the right hip in 19/51 (37.2 %) cases, one case have been just described as unilateral. PR-TOH has been generally unilateral in 35/51 (68.6 %) cases whereas bilateral in 16/51 (31.3 %) cases, description on Table 1 [2–50].

In the majority of cases a functional limitation of the hip has been described. The reported rate of hip fracture was 17/123 (13.8 %) [13,15,16,22,28,30,31,34,37,38,41,50].

According to our literature review X-rays have been the most used radiological technique (only after delivery). Although MRI has been progressively become the gold standard for PR-TOH diagnosis

through years, the description of each case chosen radiological examination is available on [Table 1](#).

In our analysis the mode of delivery has been described in 70/123 cases (56.9 %). Caesarean section rate in the analysed population was 50 % (35/70). PR-TOH has been the indication in 74.2 % of cases 26/35 [8,16,18,23,33–35,37,39,44,45,47,50]. In the remaining 9/35 cases (25.7 %) there was an obstetric indication for Caesarean section [17,19,29,43,50]. The offered treatment comprised: Non weight bearing and physical therapy, supportive medication, rarely it has been described the use of Calcitonine [27] and of bisphosphonate [44]. Protective weight bearing and orthopaedic surgery in case of fracture [13,15,16,22,30,31,34,37,38,41,50].

Postpartum resolution of PR-TOH occurred from 3 weeks [9] to six years [38].

Discussion

Pregnancy related transient osteoporosis of the hip is a rare condition, the first described cases by Curtiss et al. has been reported on 1959 [1].

Little is known about the underlying pathophysiology of PR-TOH. A combination of factors have been postulated to correlate with this condition [51–54]:

- Pregnancy related factors such as: immobilisation, femoral venous stasis, pressure on the obturator nerve, hormonal variation of pregnancy and moreover of lactation and
- Osteoporosis traditional risk factors such as: infective or inflammatory diseases, previous trauma, vascular lesions, neoplasia, alcoholic consumption, smoking, steroids, medications, hypothyroidism, low vitamin D or osteogenesis imperfect.

According to our literature review the majority of cases have been described without the presence of any risk factors. Peyman Hadji et al. in a case control study are the only ones that have analysed the possible specific PR-TOH risk factors. The result has been that: immobility, dental problems and lack of exercise in childhood are significantly associated to the above mentioned disease [50].

Clinical presentation is often described as a sudden onset of pain located in the groin region, anterior thigh and buttocks. It can involve one or both hips [1].

The radiologic features are osteopenia of the femoral head and neck on X Ray, low Bone Mass Density by DXA, MRI, the gold standard to diagnose PR-TOH, shows intermediate to low signal on T1-weighted images and high-signal on T2 fat saturated weighted images, MRI may also detect possible subchondral fractures [55–57].

According to our literature review X-rays have been the most used radiological technique (only after delivery). Although MRI has been progressively become the gold standard for PR-TOH diagnosis through years.

The described treatments include: conservative therapy (non-weight bearing, uses of crutches, physiotherapy), medical treatment (analgesics, Calcium carbonate, Vitamin D). Calcitonin and Bisphosphonate have been argued, while Calcitonin appears to be safe during pregnancy and has shown to reduce the duration of symptoms there are doubts on the foetal safety of Bisphosphonate that may influence foetal skeletal mineralization therefore is not recommended [58,59].

Some reports describe resolution of subcapital fractures only by protective weight bearing. In case of complete fracture, but not dislocated, an internal fixation has been performed. Whereas displaced fractures have been treated either by internal fixation or total hip replacement [1,13,15,16,22,28,30,31,34,37,38,41,50].

Symptoms usually resolve within the first 2 postpartum months, and MRI findings, in the majority of cases, return to normal over a three to six months period. Although there are reported cases resolution only after 6 years from diagnosis [38]. Recurrence in subsequent pregnancies has not been described [1–50].

No one previous paper has highlight the impact of PR-TOH on the mode of delivery, although an elective Caesarean section has been widely thought to protect women from birth-related injuries [1,60].

In the majority of PR-TOH cases the association of severe hip pain and joint functional limitation has become a non-obstetric indication for an elective Caesarean section [60,61]. According to our literature review more than 70 % of Caesarean delivery have been performed in relation to the hip functional limitation. This Caesarean section rate is well above the World Health Organization recommended ones [62].

Conclusions

PR-TOH is a rare and underreported condition, to avoid possible maternal complication such as fractures, reduce the risk of caesarean section and obtain the best pregnancy outcome it emerges as fundamental to highlight the importance of considering PR-TOH as a possible underlying cause of symptoms such as sudden, often severe and persistent pain located in the groin region, buttocks and anterior thigh. An early diagnose made up by clinical and radiological (MRI) features and subsequent multidisciplinary care team involving: gynaecologists, orthopaedics, physiotherapists and anaesthetists, will allow the best maternal outcome and reduce the caesarean section rate related to functional limitation.

Authorship conformation

- All authors have participated in (a) conception and design, or analysis and interpretation of the data; (b) drafting the article or revising it critically for important intellectual content; and (c) approval of the final version.
- This manuscript has not been submitted to, nor is under review at, another journal or other publishing venue.
- The authors have no affiliation with any organization with a direct or indirect financial interest in the subject matter discussed in the manuscript.

Financial support

No financial support was received for this study

Declaration of Competing Interest

The authors report no declarations of interest.

Acknowledgements

The authors wish to thank

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