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Gynecologic and Obstetric Implications of the Joint Hypermobility Syndrome (a.k.a. Ehlers–Danlos Syndrome Hypermobility Type) in 82 Italian Patients

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Joint hypermobility syndrome (JHS) emerges as likely the most common clinical form of Ehlers–Danlos syndrome. Given the striking predominance of affected women, practitioners often face gynecologic and obstetric issues. However, their decisions are still based on personal experience rather than literature due to the lack of a consistent body of evidence. We collected a set of gynecologic and obstetric features in 82 post-puberal women with JHS attending two Italian centers. Common gynecologic findings were dysmenorrhea (82.9%), meno/metrorrhagias (53.7%), irregular menses (46.3%), and dispareunia/vulvodinia (31.7%). Forty women were nulliparous and 42 had one or more pregnancy for a total of 93 diagnosed conceptions. Of them, 16.1% were spontaneous abortions, 6.5% voluntary interruptions, 10.7% preterm deliveries, and 66.7% deliveries at term. Overall outcome of proceeding pregnancies was good with no stillbirth and fetal/neonatal hypoxic/ischemic event. Non-operative vaginal delivery was registered in 72.2%, forceps/vacuum use in 5.5% and cesarean in 22.3%. Local/total anesthesia was successfully performed in 17 pregnancies without any problem. Major post-partum complications included abnormal scar formation after cesarean or episiotomy (46.1%), hemorrhage (19.4%), pelvic prolapses (15.3%), deep venous thrombosis (4.2%), and coccyx dislocation (1.4%). Prolapses were the most clinically relevant complication and associated with episiotomy. Gathered data were discussed for practically oriented considerations. © 2012 Wiley Periodicals, Inc.

Key words: delivery; dysmenorrhea; Ehlers–Danlos syndrome; joint hypermobility; prolapse; pregnancy

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INTRODUCTION

Joint hypermobility (JHM) is a common, heritable trait observed in up to 10–30% males and 20–40% females [Hakim and Grahame, 2003]. Generalized JHM is considered the physical marker of various hereditary connective tissue disorders (HCTDs). Among them, the joint hypermobility syndrome (JHS), alternatively named Ehlers–Danlos syndrome (EDS) hypermobility type (EDS-HT), is likely the most common HCTD, possibly transmitting in an autosomal dominant pattern and with a presumed prevalence of 0.75–2% [Hakim and Sahota, 2006]. The apparent clinical overlap between JHS and EDS-HT induced an international group of experts to consider these two conditions the same entity [Tinkle et al., 2009]. However, this assumption is not shared by all researchers [De Paepe and Malfait, 2012] and only future molecular studies will solve the conundrum.

JHS/EDS-HT is an exclusion diagnosis based on specific diagnostic criteria [Beighton et al., 1998; Grahame et al., 2000]. Until

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now, the association of non-inflammatory widespread arthralgias, generalized JHM, and minor skin signs has been considered the core phenotype of JHS/EDS-HT. However, recent studies highlight a much wider spectrum of functional derangements virtually affecting all major systems and including dysautonomia, gastrointestinal functional disorder, fibromyalgia, and chronic fatigue syndrome among others [Castori et al., 2011a]. These findings indicate the need to revise existing diagnostic criteria [Remvig et al., 2011].

Among the multifaceted clinical implications of JHS/EDS-HT, there are some gynecologic and obstetric aspects [Dickson et al., 2011; Molloholli, 2011], which are noteworthy due to the unexpected predominance of female patients [Castori et al., 2011b]. Actual knowledge is essentially limited to a handful of case reports [Atalla and Page, 1988; Thornton et al., 1988; Rochelson et al., 1991; Sakala and Harding, 1991; Morales-Roselló et al., 1997; De Vos et al., 1999; Jones and Ng, 2008; Dutta et al., 2011] and case series mixing various forms of EDS, mainly EDS-HT, EDS classic, and vascular types [Sorokin et al., 1994; McIntosh et al., 1995; Lind and Wallenburg, 2002]. The resulting thought is that pregnancy and delivery appear relatively safe in JHS/EDS-HT. Nevertheless, unsupported generalization with other forms of EDS at significant risk of potentially life-threatening complications in the pregnant woman still influences the daily activity of the practitioner [Volkov et al., 2007].

We present a review of selected gynecologic and obstetric features in a representative series of post-puberal JHS/EDS-HT women. The aim of this study is to present a consistent body of details on the gynecologic and obstetric implications of JHS/EDS-HT and extract some generalizations for the clinical practice.

PATIENTS AND METHODS

In our practice, we are not sure to differentiate JHS and EDS-HT based solely on clinical grounds, as many patients fulfill both set of diagnostic criteria (see below) and pedigree study commonly demonstrates intrafamilial segregation of JHS and EDS-HT as a single genetic trait. For these reasons, we grouped together patients affected by JHS and EDS-HT. Individuals were enrolled from those attending the multidisciplinary "joint hypermobility" clinic at the "Umberto I" and "San-Camillo-Forlanini" Hospitals in Rome (Middle-South Italy) and the "Ehlers–Danlos syndrome and inherited connective tissue disorders" clinic at the "Spedali Civili" University Hospital of Brescia (North Italy). Although not all Italian EDS patients have been evaluated in these centers, collected data are well representative of the Italian patients' and practitioners' experience in gynecologic and obstetric aspects of JHS/EDS-HT. All patients were originally assessed by physical examination and questionnaire administration focused on collecting information about selected aspects of their gynecologic and obstetric history. Applied questionnaire consisted of 30 self-developed questions (10 open and 20 closed). In most cases, data were gathered retrospectively on clinical records, telephone calls, and follow-up evaluations. In a minority of them, information was collected directly at time of first assessment. Only post-puberal women were included in this study.

Diagnosis was based on published diagnostic criteria including the Brighton criteria for JHS [Grahame et al., 2000] and the Villefranche criteria for EDS-HT [Beighton et al., 1998; Table I]. Patients were included if they met at least either one of these two sets. In our clinical practice, the Brighton criteria are the most stringent for young-adult, adult, and elder patients, while the Villefranche criteria are the best for individuals in the pediatric age. For this study, JHM was mainly assessed applying the Beighton score [Beighton et al., 1973]. Other joints were equally evaluated although, at the moment, their status do not influence diagnosis establishment. Beighton score is a nine-point evaluation with attribution of one point in the presence of any of the following: (a) Passive apposition of the thumb to the flexor aspect of the forearm (one point for each hand), (b) passive dorsiflexion of the V finger beyond 90° (one point for each hand), (c) hyperextension of

TABLE I. Applied Diagnostic Criteria in Our Patients' Sample

Brighton criteria (JHS)	Villefranche criteria (EDS-HT)
Major criteria	Major criteria
Beighton score ≥4/9	Beighton score ≥5/9
Arthralgia for >3 months in >4 joints	Skin involvement (hyperextensibility and/or smooth, velvety skin)
Minor criteria	Minor criteria
Beighton score of 1–3	Recurring joint dislocations
Arthralgia in 1–3 joints	Chronic joint/limb pain
History of joint dislocations	Positive family history
Soft tissue lesions >3	
Marfan-like habitus	
Skin striae, hyperextensibility, or scarring	
Eye signs, lid laxity	
History of varicose veins, hernia, visceral prolapse	
For the diagnosis: Both major, or 1 major and 2 minor, or 4 minor criteria and the exclusion of other heritable connective tissue disorders.	For the diagnosis: Both major features; presence of one or more minor features is useful for the differential from partially overlapping heritable connective tissue disorders.

the elbow beyond 10° (one point for each arm), (d) hyperextension of the knees beyond 10° (one point for each leg), (e) forward flexion of the trunk with the knees extended and the palms resting flat on the floor. Skin/superficial connective tissue features were assessed qualitatively on the basis of accumulated experience by palpation and gentle stretching of the skin at the volar aspect of the palm (at the IV metacarpal) and/or forearm. Other HCTDs were excluded clinically. As the diagnosis of JHS/EDS-HT is clinical in essence and, at the moment, no molecular confirmation is available, genetic studies were guided by evidence in selected cases for excluding partially overlapping conditions, such as classic and vascular EDS, Loeys–Dietz syndrome(s), and arterial tortuosity syndrome. Investigated genes included *COL5A1*, *COL5A2*, *COL3A1*, *TGFRB1*, *TGFRB2*, and *SLC2A10*. Individuals with incomplete diagnosis were equally excluded. This implied that a group of patients with features of JHS still insufficient for a firm clinical diagnosis based on available diagnostic criteria, but likely destined to develop full-blown JHS, were not included in this study.

RESULTS

Eighty-two (44 from the "Umberto I" and "San Camillo-Forlanini" Hospitals in Rome and 38 from the "Spedali Civili" University Hospital in Brescia) patients were identified. Diagnosis confirmation needed exclusion of partially overlapping HCTDs by molecular testing in 14 individuals. *COL5A1* and *COL5A2* screening was performed in patients with a clinical diagnosis of JHS/EDS-HT and affected relatives with one or a few widened scars, while analysis of *COL3A1*, *TGFRB1*, *TGFRB2*, and *SLC2A10* was carried out in case of first-degree relative died by sudden death and/or asymptomatic vascular anomaly (such as, carotid and/or focal intracerebral vessel kinking and/or coiling, and mild dilation of the aortic root) in the patient. Age at evaluation and general systemic features for diagnosis assessment and overall evaluation are itemized in Table II.

TABLE II. Systemic Features

Feature (# of patients = 82)	Frequency (%)
Mean age at evaluation (range)	38.74 yrs (15–71 yrs)
Chronic (>3 months) arthralgias in >4 joints	60 (73.2)
Chronic/recurrent myalgias	65 (79.3)
Chronic (>6 months) fatigue	69 (84.1)
Poor sleep	54 (65.8)
Memory/concentration problems	50 (60.9)
Congenital joint hypermobility	67 (81.7)
Residual joint hypermobility (Beighton score ≥4)	58 (70.7)
Recurrent joint dislocations	62 (75.6)
Recurrent (>3) soft-tissue lesions	33 (40.2)
Soft/velvety/mildly hyperelastic skin	56 (68.3)
Easy bruising	54 (65.8)
Eye findings according to Brighton criteria	28 (34.1)
Varicose veins	11 (13.4)
Gastrointestinal symptoms	59 (71.9)

Gynecologic Findings

Physiologic data concerning the gynecologic history of the patients' sample is summarized in Table III. In brief, in our patients' cohort, 62 (75.7%) women were fertile at the time of examination while 20 (24.3%) were post-menopausal. Forty-two (51.8%) patients have had at least one pregnancy with two as the most common number of diagnosed pregnancies per woman. In the remaining, common reasons for the nulligravid status were (i) too young age (17 women aged ≤25 years), (ii) disease-driven psychological distress influencing social relationships, and (iii) medically induced fear for pregnancy complications and/or risk of transmission. Additional gynecologic features are summarized in Table IV. Many women experienced dysmenorrhea (82.9%), which is in according to previous studies showing that pain is a common finding in JHS/EDS-HT [Sacheti et al., 1997; Voermans et al., 2010]. Intensity of dysmenorrhea-associated pain was investigated by an 11-point scale (numerical rating scale; 0 = no pain, 10 = the most intense pain). Results ranged from 3 to 10 with a mean of 7.9 (severe pain). Possible causes for dysmenorrhea included polycystic ovaries (13.4%), endometrial cysts (4.9%), uterine fibromas (8.5%), and endometriosis (2.4%). Twenty-six (31.7%) patients with dysmenorrhea also displayed dyspareunia/vulvodinia, which, in turn, was never reported in isolation from dysmenorrhea. Mechanisms leading to dyspareunia/vulvodinia were not systemically investigated. However, at least two patients reported mucosal chronic fragility/xerosis as possible cause.

Obstetric Findings

A total of 93 pregnancies were registered among the 42 women with at least one pregnancy. Overall, 15 (16.1%) led to miscarriages, six (6.5%) to voluntary interruptions, ten (10.7%) to pre-term deliveries likely due to premature rupture of the membranes (PROM), and 62 (66.7%) to deliveries at term. Most miscarriages occurred during the first trimester and were considered not related to the underlying disorder. No specific investigation was recorded in these cases, except for a single instance, in which histology of the aborted material showed molar degeneration. Among the six voluntary interruptions of pregnancy, four were performed for social/psychological reasons while two for intolerable worsening of the disease state. Of the pre-term and at term deliveries, all have had a good outcome with no registered stillbirths and fetal/neonatal hypoxic/ischemic events. Among the 72 deliveries, 56 (77.8%) were vaginal and 16 (22.2%) by cesarean. Of the former, episiotomy was performed in 36 (64.3%) and forceps/vacuum use in four (7.1%); of the latter, cesarean was indicated in two cases (14.2%) for deterioration of disease-associated symptoms. Among vaginal deliveries, twelve women had 20 (35.7%) pregnancies with precipitous delivery. Total (# twelve) and epidural (# seven) anesthesias were performed in 19 (26.4%) deliveries and were always without technique-related complications (e.g., spinal hematoma, intubation troubles, or anesthesia-induced hypotension). One total anesthesia was complicated by anesthesia-induced hypotension successfully treated with hypertensive drugs and

TABLE III. Main Gynecologic Features

Feature (# patients = 82)	Frequency (%)
Mean age at menarche (range)	12.18 yrs (9–16.5 yrs)
Post-menopausal women	20 (24.3)
Mean age at menopause (range)	46.35 yrs (36–53 yrs)
Women with 0 pregnancies	40 (48.2)
Women with 1 pregnancy	10 (12.2)
Women with 2 pregnancies	19 (23.2)
Women with 3 pregnancies	8 (9.8)
Women with 4 pregnancies	4 (4.8)
Women with 5 or more pregnancies	1 (1.2)
Mean number of pregnancies/woman (mode)	2.2 (2)

hypothermia. The most common post-partum complications included abnormal scar formation (either delayed wound healing with atrophic scar or keloid formation) after episiotomy or cesarean (46.1%), intra- or post-partum hemorrhages (19.4%), uterine (15.3%), vesical (15.3%) and rectal (11.1%) prolapses, deep venous thrombosis (4.2%), and coccyx dislocation (1.4%; Table V). In all cases, peri- and post-partum hemorrhages were successfully treated and no further worsening of health status was registered. Any instance of uterine rupture was not registered. Relationship between prolapse occurrence and delivery modality was summarized in Table VI. We had difficulties in gathering information on the exact estimation of the time interval between (last) delivery and onset of the prolapse, mainly due to the heterogeneity of ascertainment by prolapse symptoms.

Disease-related symptoms improved in twelve (12.9%) pregnancies, while they worsened in 36 (38.7%). Features which worsened during pregnancy included: Gastrointestinal complaints (24.3%), asthenia (21.3%), limb/lower back pain (36.4%), pubalgia (6%), sleep disorders (6%), anxiety and depression (6%). Twenty (47.6%) out of 42 women with at least one pregnancy undertook various drugs (including ritodrine chlorohydrate, vasosuprin, myolene, acetylsalicylic acid, paracetamol, 17α-hydroxyprogesteron, gravibinam, and unspecific antiacids, antiemetics, and antiepileptics) during pregnancy without any significant side effects. Comparison of the prevalence of skin features (i.e., soft/velvety and/or mildly hyperextensible skin) among complementary women subgroups was not significant for occurrence of prolapses ($P = 0.9863$), need of episiotomy ($P = 0.5885$), intra- and post-partum hemorrhages ($P = 0.2862$), and abnormal scar formation after episiotomy or Cesarean ($P = 0.2259$).

TABLE IV. Other Gynecologic Features

Feature (# patients = 82)	Frequency (%)
Irregular menses	38 (46.3)
Meno/metrorrhagias	44 (53.7)
Dysmenorrhea	68 (82.9)
Dyspaureunia/vulvodinia	26 (31.7)
(Micro)polycystic ovaries	11 (13.4)
Endometrial cysts	4 (4.9)
Uterine fibromas	7 (8.5)
Endometrial hypertrophy	2 (2.4)
Confirmed endometriosis	2 (2.4)

DISCUSSION

The present study collected data on selected gynecologic and obstetric features from the largest sample of JHS/EDS-HT patients (# 82) described till date. Similar, previously published studies gathered data from up to 68 patients affected by various forms of EDS [Sorokin et al., 1994; McIntosh et al., 1995; Lind and Wallenburg, 2002] with consequent difficulties in extrapolating information by clinical subtype.

Gynecologic Aspects

In this work, fertility was overall preserved, as mean age at menarche and menopause, rate of pregnancy/woman and of spontaneous abortion were comparable with those in the Caucasian population. Despite this, fertile women often (~50%) showed minor menses disturbances with irregularity and meno/metrorrhagias. Dysmenorrhea was the most relevant feature, being observed in >80% patients with a mean intensity of ~8/10, corresponding to severe pain. Pelvic pain was also complicated by dyspareunia and/or vulvodinia in nearly 1/3 of the cases. The mechanism(s) leading to pelvic pain is largely unknown in JHS/EDS-HT. This study identified possible underlying causes, including polycystic ovaries, endometrial disease, uterine fibromas, and dry mucosae, only in a few cases. The rate of at least some of these features, such as endometriosis and vaginal dryness, is underestimated in our sample compared with previous studies [Sorokin et al., 1994; McIntosh et al., 1995]. In our cohort, this was likely due to incomplete methodology of data collection which did not include systematic gynecologic examination.

Pregnancy Planning

In managing fertile women with JHS/EDS-HT, every gynecologist faces the unsolved conundrum of encouraging rather than discouraging pregnancy. In our sample, ~40% patients referred worsening of the disease state during pregnancy. Interaction between constitutionally lax joints and weight increase was traditionally considered the underlying cause of symptom amplification, which mainly involved the musculoskeletal system [Grahame and Keer, 2010]. In our sample, the spectrum of exacerbated complaints was wider than expected and included gastrointestinal findings, asthenia, anxiety, depression, and sleep disorder, in addition to pubalgia and limb/back pain. Conversely, general health improved in 13% patients while it remained unchanged in the remaining (47%). Therefore, the relationship between JHM and pregnancy-related homeostatic changes appears more complex than previously thought and, at the moment, disease evolution during pregnancy seems unpredictable. Nevertheless, symptom worsening prompted to therapeutic abortion in two instances and elective Cesarean in other two cases. Therefore, while at the moment there is no

TABLE V. Pregnancy, Delivery, and Post-Partum Findings

Feature (# pregnancies = 93)	Frequency (%)
Pregnancy	
Miscarriages	15 (16.1)
Voluntary interruption pregnancies	6 (6.5)
Bleedings/spotting	49 (52.7)
Worsening of symptoms	36 (38.7)
Improving of symptoms	12 (12.9)
Delivery	
Mean duration of labor (range)	10.58 hr (0.33–72 hr)
Mean gestation week at delivery (range)	38.5 (26–42)
Deliveries at term	62 (66.7)
Preterm deliveries	10 (10.7)
Livebirths	72 (77.4)
Stillbirths	0 (0)
Fetal/neonatal hypoxia/ischemia	0 (0)
Vaginal deliveries	56 (77.8)[a]
Operative deliveries	4 (7.1)[b]
Precipitous deliveries	20 (35.7)[b]
Episiotomies	36 (64.3)[b]
Cesareans	16 (22.2)[a]
Anesthetic procedures	19 (26.4)[a]
Post-partum	
Abnormal scar formation after episiotomy/Cesarean	24 (46.1)[c]
Manual placental removal	4 (7.1)[b]
Intra- and postpartum hemorrhages	14 (19.4)[a]
Uterine prolapses	11 (15.3)[a]
Bladder prolapses	11 (15.3)[a]
Rectal prolapses	8 (11.1)[a]
Deep venous thromboses	3 (4.2)[a]
Coccyx dislocation	1 (1.4)[b]

[a]Pregnancies which reached 3rd trimester (i.e., total without miscarriages and voluntary interruptions) only (total = 72).
[b]Vaginal deliveries only (total = 56).
[c]Deliveries requesting cesarean or episiotomy only (total = 52).

reason to contraindicate pregnancy in JHS/EDS-HT, the risk of intolerable symptom amplification should be considered and preventive strategies, hopefully within a multidisciplinary approach, are expected in every woman with JHS/EDS-HT planning motherhood. Such strategies may include gentle, experienced manual therapy, stress management, sleep hygiene, and relaxation techniques for preventing/early treating pelvic pain and gait abnormalities [Nelson et al., 2012], and application of non-pharmacological measures for contrasting dysautonomia [Mathias t al., 2011] among others.

Timing of Delivery

Preterm delivery due to PROM has been repeatedly reported in JHS/EDS-HT [Thornton et al., 1988; De Vos et al., 1999]. In our sample, preterm delivery likely due to PROM was registered in ~10% pregnancies, but none of them led to major complications (e.g., stillbirth and cerebral hypoxia/ischemia). Therefore, while PROM is a possible manifestation of HCTDs, this does not likely need special care in JHS/EDS-HT. In addition, the registered rate of preterm delivery may be of doubtful relevance in consideration of the small size of the patients' cohort. Conversely, precipitous delivery occurred in more than 1/3 of the cases. Such a possibility should be considered by pregnant women as well as practitioners at the time of delivery planning.

Delivery Modalities and Complications

There are still unresolved controversies on the choice between Cesarean and vaginal delivery in JHS/EDS-HT. Accordingly, the summation with specific disease features including dysautonomia, and soft tissue and vascular fragility may lead to possible complications in both. These controversies are mainly caused by the paucity of studies on consistent numbers of patients with homogenous phenotypes. Anecdotally, normal vaginal delivery can be encouraged in JHS/EDS-HT [Jones and Ng, 2008]. On the other side, aggravation of musculoskeletal and/or systemic symptoms during pregnancy might necessitate Cesarean [Atalla and Page, 1988; Golfier et al., 2001]. In addition to the general risk of hemorrhage, a series of theoretical complications may be identified for all delivery options: (i) Abnormal response to Valsalva maneuvers in case of dysautonomia for non-operative vaginal delivery, (ii) perineal injury and poor wound healing for instrumental (vaginal) delivery, and (iii) increased risk of internal and cutaneous post-operatory complications for Cesarean. Our findings indicate a risk of ~1/5 of intra- and post-partum hemorrhages irrespectively to the delivery modality, and an high rate of abnormal scar formation in both Cesarean and vaginal delivery with episiotomy. In all cases, hemorrhages, although causing hypovolemia in some instances,

TABLE VI. Prolapse(s) Per Woman (# 42) in Relation to Delivery Procedure(s)

	Uterine prolapse(s)		Vesical prolapse(s)		Rectal prolapse(s)	
Women	Absolute (%)	Relative (%)	Absolute (%)	Relative (%)	Absolute (%)	Relative (%)
Total	11/42 (26.1)	—	11/42 (26.1)	—	8/42 (19)	—
Natural without episiotomy or cesarean	0/42 (0)	0/11 (0)	1/42 (2.4)	1/11 (9)	0/42 (0)	0/8 (0)
Cesarean only	0/42 (0)	0/11 (0)	0/42 (0)	0/11 (0)	0/42 (0)	0/8 (0)
Episiotomy only	9/42 (21.4)	9/11 (81.8)	8/42 (19)	8/11 (72.8)	6/42 (14.2)	6/8 (75)
Episiotomy + cesarean	2/42 (4.8)	2/11 (18.2)	2/42 (4.8)	2/11 (18.2)	2/42 (4.8)	2/8 (25)

were always successfully managed without life-threatening complications and no internal organ/vascular accidents were registered after Cesarean. Consequently, all delivery options showed a very limited numbers of local and systemic short-term complications.

Prolapses

Interestingly, we demonstrated that pelvic prolapses represented common late-onset complications. As expected by previous studies in the general population [Handa et al., 2011, 2012], the chance of developing uterine/vesical/rectal prolapse were associated with delivery modality. However, partially in contrast with what observed in unselected women in whom prolapses correlated with operative vaginal delivery but not episiotomy [Sigurdardottir et al., 2011; Handa et al., 2012], in JHS/EDS-HT, the highest risk for prolapses was registered in women requesting episiotomy in at least one pregnancy (including the four instances of operative delivery). In particular, most (90.9%) prolapses occurred in women with positive history for episiotomy, except for a single occurrence of vesical prolapse after spontaneous vaginal delivery without episiotomy and a further one in a nulliparous woman.

The reason(s) as to why episotomy associates with prolapses in JHS/EDS-HT is unknown. However, in a practical perspective, elective Cesarean and non-operative vaginal delivery without episiotomy appear the best choices in JHS/EDS-HT. Anedoctically, a reduced rate of perineal tears has been described in JHS pregnant women due to the inherently stretching skin. Then, JHS/EDS-HT patients might need episiotomy less frequently than general population [Grahame and Keer, 2010]. Our findings are apparently in contrast with this assumption as episiotomy was registered in >1/3 of the deliveries. However, in our sample, we are not sure that all episiotomies were guided by a real clinical problem. Therefore, in any given pregnancy, all efforts should be applied to avoid both forceps/vacuum use and episiotomy; the former as a general recommendation, the latter as a specific need in JHS/EDS-HT. Spontaneous vaginal delivery without preventive episiotomy should be considered the first line choice followed by elective Cesarean in case the former cannot be predicted and/or in presence of instrumentally confirmed dysautonomia.

Anesthetic Considerations

Uniform anesthetic guidelines are still lacking in JHS/EDS-HT [Kuczkowski, 2005]. In our sample, we did not find any life-threatening complication related to local and total anesthesia, performed in 12 and seven instances, respectively. We were not able to collect accurate data about anesthetic procedures in all cases, but our results outline the absence of any major contraindications for total and regional anesthesia in JHS/EDS-HT. Other groups discussed the pros and cons of spinal versus epidural anesthesia in JHS/EDS-HT in relation with hemodynamic changes in case of dysautonomia, local anesthetic resistance for epidural procedures, and risk of hematoma [Jones and Ng, 2008]. The authors proposed a combined spinal-epidural with a moderate spinal dose as the best initial technique with early fluid loading and phenylephrine infusion in presence of dysautonomia. We agree with such recommendations.

CONCLUSIONS

Overall, our study first outlined that, according to the reinforced concept that pain is a widespread and highly debilitating feature in JHS/EDS-HT [Sacheti et al., 1997; Voermans et al., 2010], pelvic pain is nearly universal and represents the most severe gynecologic feature in women with JHS/EDS-HT. Secondly, motherhood is generally accepted and should not be contraindicated in this condition. Thirdly, special care, supported by highly specialized consultation, should be posed in strategies for preventing symptom worsening during pregnancy and in planning delivery and anesthesia. Prospective and more focused studies, hopefully including investigations on the long-term complications of pregnancy in JHS/EDS-HT, are expected in order to investigate the many unsolved questions raised by our preliminary results and to define more tailored prevention and therapeutic strategies.

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