Hypermobile Ehlers-Danlos Syndrome during Pregnancy, Birth and Beyond: A Review of Midwifery Care Considerations

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Abstract

The Ehlers-Danlos Syndromes (EDS) are an underdiagnosed group of conditions with implications and risks associated with childbearing. Those with EDS suggest that healthcare professionals have a lack of awareness in this area, and consequently describe delays in access to appropriate healthcare services. This paper draws on the existing international evidence available to present evidence-based care considerations for childbearing women with hypermobile Ehlers-Danlos Syndrome (hEDS) throughout the antenatal, intrapartum and postnatal periods. Care considerations are also offered in relation to the care of the newborn infant. The management of hEDS in childbearing women and babies can be complex. Findings point to the need for a multidisciplinary approach to formulating individualised care plans in partnership with women. In understanding the evidence in relation to this issue, midwives will be better able to practice evidence-based and woman-centred care.

Key phrases

- Pregnancies associated with hypermobile Ehlers-Danlos Syndrome are considered to be complex with increased maternal and neonatal risks.
- Those with all types of Ehlers-Danlos Syndrome report a lack of awareness among healthcare professionals and therefore delayed access to appropriate care.

- The risks associated with hypermobile Ehlers-Danlos Syndrome in childbearing include higher rates of infertility, preterm labour, preterm rupture of membranes, problems with anaesthesia, atonic uterus, bleeding, tears during birth, wound dehiscence, skin hyperextensibility, poor healing, fetal malpresentation, bruising, cardiac anomalies, mental health issues, pelvic prolapse, cervical tissue abnormalities, unstable joints and tissue fragility.
- Individualised approaches to maternity care planning made in partnership with the woman and multidisciplinary teams are indicated.

Introduction

The Ehlers-Danlos Syndromes (EDS) are a group of multisystemic, inherited conditions that affect connective tissue (Malfait, Francomano et al. 2017). The various subtypes of EDS can share symptoms such as joint hypermobility and hyper extensible and/or fragile skin (Bloom, Byers et al. 2017). Yet many EDS subtypes also include clinical characteristics relating to pain, extreme fatigue, irritable bowel, sleep disturbance, depression, anxiety and other cardiovascular, gastrointestinal, orthopaedic, oromandibular, neurological, allergic/immunological, and psychological aspects of health (Tinkle, Castori et al. 2017). The prevalence of EDS was historically estimated to be 1 in 5,000 for all subtypes (Beighton, De Paepe et al. 1998), although other work suggests a much higher prevalence of 0.75-2% (Hakim, Sahota 2006). There has been no high-quality prevalence study carried out since EDS received a major reclassification in 2017 (Tinkle, Castori et al. 2017).

Despite these estimated prevalence rates, EDS is considered to remain largely underdiagnosed (Castori 2012, Gazit, Jacob et al. 2016). This is concerning for those

receiving maternity care, as it is also associated with a number of complications relating to pregnancy and birth. Such complications can include precipitate labour, preterm rupture of membranes, scoliosis (problems with anaesthesia), atonic uterus, bleeding, vaginal and/or perineal tears during birth, wound dehiscence and tissue fragility (Lawrence 2005, Castori, Morlino et al. 2012). This presents a unique opportunity for midwives and other members of the multidisciplinary team to understand, raise awareness of and more effectively support undiagnosed pregnant women, and those suspected of having or diagnosed with EDS.

Those diagnosed with EDS perceive a lack of awareness among healthcare professionals and describe delays in access to appropriate healthcare services (Terry, Palmer et al. 2015). If EDS remains poorly understood by the multidisciplinary team, this may significantly compromise maternity care (Ross, Grahame 2011). Consequently, this paper draws from wider literature and a number of key contemporary reviews to present evidence-based care considerations for both the mother and the neonate during the antenatal, intrapartum and postnatal periods. However, this field of research is at early stages of building an evidence base and much more research into this area is needed.

The International EDS Consortium recognises thirteen EDS subtypes. Whilst the much rarer Vascular Ehlers–Danlos syndrome (vEDS) holds the most significant risks for childbearing women, such as arterial dissection/rupture, uterine rupture and haemorrhage (Murray, Pepin et al. 2014), care considerations in this paper will primarily focus on hypermobility EDS (hEDS) as the most common form of EDS (Volkov, Nisenblat et al. 2007). hEDS is part of the most recent reclassification (Tinkle, Castori et al. 2017), but in previous classification systems it was known as either Ehlers–Danlos Syndrome Type III or Ehlers–Danlos syndrome hypermobility type (Malfait, Francomano et al. 2017, Smith 2017). The recent

reclassification also introduced a new hypermobility-based diagnosis; Hypermobility Spectrum Disorder (HSD). Treatment for this group of HSD and for those with a historical diagnosis of Joint Hypermobility Syndrome will be the same as for hEDS. Whilst Chetty and colleagues have recently provided guidance for obstetric care in women with genetic disorders (Chetty, Norton 2017), to our knowledge, this is the first paper to draw on the existing evidence available to explore midwifery care considerations for this unique subgroup of childbearing women.

Antenatal care considerations

Firstly, those with a variety of EDS subtypes report significantly higher rates of infertility than the general population (Hurst, Lange et al. 2014). As such, families may wish to access genetic counselling services, where individual hereditary factors can be explored more thoroughly. Additionally, as with other conditions, some women may take medication. Therefore, a pre-conceptual review would be advisable, as prescribed medications may need to be stopped or changed.

As one of the key features of EDS and its many subtypes is disordered collagen synthesis, it is considered reasonable to offer additional monitoring to women, beginning with earlier ultrasound scanning to confirm the pregnancy and to monitor cervical length as the pregnancy progresses (Hurst, Lange et al. 2014). It is also prudent to note that striae atrophicae (stretch marks) are common in those with hEDS and may well be present before a pregnancy occurs (Castori 2012). This also becomes significant when assessing maternal parity, where stretch marks may be taken as an indication of a previous pregnancy.

Following conception, increased levels of the relaxin hormone during pregnancy can exacerbate pre-existing joint elasticity and pain in those with hEDS (Atalla, Page 1988, Volkov, Nisenblat et al. 2007, Lind, Wallenburg 2002). As such, these women are three times more likely to require referral for intervention due to Pelvic Girdle Pain (PGP) and instability than the general population (Lind, Wallenburg 2002, Tinkle 2010). Consequently, the identification of excess joint mobility, joint dislocations, pelvic pain and/or instability may prompt an early referral to both physiotherapy and general practitioner (GP) services. Appropriate maternal positioning should also be led by the mother throughout routine examinations, to minimise the risk of joint dislocations or excess pain.

The elasticity of soft tissues means there is an increased risk of profound varicose veins in the legs and the vulva during pregnancy (Tinkle 2010). Should this occur, compression hosiery and/or a referral to a vascular service may be advisable (Marsden, Perry et al. 2013). Likewise, whilst gastroesophageal reflux is a common complaint of pregnancy, those with hEDS can experience symptoms of this more frequently (Castori, Camerota et al. 2010a). This is again thought to be due to the elasticity of soft tissues. In such cases, symptoms can be routinely managed with diet and lifestyle changes such as avoiding fatty or spicy foods, remaining in an upright position, and taking antacids and/or alginates. It is worth trying to avoid opioids, as gastric symptoms can be exacerbated by their use (Levy 1993).

Women with hEDS often also experience postural orthostatic tachycardia syndrome (POTS) (Grigoriou, Boris et al. 2015). One study exemplifies this, where 78% of participants with hEDS also displayed symptoms of POTS (Gazit, Nahir et al. 2003). POTS is defined by a rise in heart rate of >30 beats/min or a heart rate of >120 beats/min reached within 10 min of head-up tilt when moving from supine to an upright position (Kanjwal, Kosinski et al. 2003).

Whilst this is significant to those with hEDS, it is also a significant consideration for maternity services, as POTS predominantly occurs in women of child-bearing age (Kanjwal, Kosinski et al. 2003).

During pregnancy, cardiovascular changes such as peripheral venous pooling and inferior vena cava obstruction may exacerbate the symptoms of POTS, such as episodes of dizziness, nausea, palpitations, fatigue and fainting (Kanjwal, Karabin et al. 2009). Allowing for and predicting such changes during routine antenatal examinations and intrapartum care could avoid misdiagnoses and/or unnecessary intervention, as maternity care and postural positioning becomes tailored to the individual. Furthermore, it is useful to note that those with POT frequently also experience episodes of hypotension, or of orthostatic intolerance (Jones, Ng 2008). They may also experience dysautonomia, a term used to describe a malfunction of the wider autonomic nervous system (Tinkle 2010). As such, adequate salt and fluid intake is considered especially important in POTS, particularly if vomiting in early pregnancy. Nevertheless, some symptoms associated with POTS are reported to improve or remain stable during and after pregnancy (Kimpinski, Iodice et al. 2010, Blitshteyn, Poya et al. 2012).

In caring for the psychological wellbeing of women receiving maternity care at all stages, it is important to recognise that those with hEDS are more likely to experience depression and anxiety than the general population (Baeza-Velasco, Gély-Nargeot et al. 2011, Castori, Camerota et al. 2010a). The mental wellbeing of those with all subtypes of EDS can also deteriorate further in conjunction with exacerbated fatigue and pain (Voermans, Knoop et al. 2010, Rombaut, Malfait et al. 2011). As such, it is important for the multidisciplinary team to manage pain and fatigue effectively in partnership with any mental health

management strategies. For midwives, this means proactively making early and appropriate referrals to local services in partnership with the mother.

Intrapartum care considerations

Whilst those with hEDS should not be discouraged from vaginal birth as a birth preference (Sundelin, Stephansson et al. 2017), there are other specific care considerations to be made for this unique subgroup of childbearing women. For example, due to the hypermobile nature of hEDS, it is practical to consider appropriate maternal positioning throughout labour and birth. In over-extending the hips via lithotomy or the McRoberts manoeuvre, excess pain and/or injury may be caused and unstable joints that dislocate easily may be loosened (Molloholli 2011). These risks of injury may be increased by the use of either local or regional anaesthetic, as pain when joints dislocate may then be eliminated. As such, accurate record keeping, and collaborative antenatal planning is advisable to reduce the incidence of such complications.

Due to the varied and changing molecular structure of collagen fibres, the skin and tissues of those with hEDS may have reduced strength and stiffness (Kaalund, Høgsaa et al. 1990). This puts those with hEDS at a higher risk of Preterm Premature Rupture Of Membranes (PPROM), which ultimately may result in preterm birth (Levy 2004, Bird 2007). This is because PPROM is specifically associated with a reduction in amnion collagen content, which is thought to relate to a disturbance in collagen metabolism (Hermanns-Lê, Piérard 2016). Consequently, conditions such as hEDS may alter the chorionic fetal membranes to more readily induce PPROM. This particular risk factor may be documented to support informed clinical decision making.

Such laxity in the soft tissues of those with hEDS has also been associated with an increased risk of fetal malpresentation, precipitous vaginal birth (<4 hours) with a frequency of 28%-36% and uterine prolapse in childbearing (Roop, Brost 1999, Golfier, Peyrol et al. 2001, Levy 2004, Bird 2007, Ross, Grahame 2011, Castori, Morlino et al. 2012, Castori, Camerota et al. 2010a). Yet whilst such known risk factors may aid clinical assessment in confirmed cases of hEDS, there is no clear advantage to vaginal vs caesarean birth or clear evidence to support the routine use of prophylactic interventions (Levy 2004, Knoepp, McDermott et al. 2013). This indicates that individual care plans should be formed in partnership with the mother and multidisciplinary teams until further evidence becomes available.

Easy bruising and bleeding is common in all EDS types (Paepe, Malfait 2004). This can manifest with mucosal fragility (Coster, Martens et al. 2005). Moreover, once a certain load is applied to the skin of those with reduced stiffness and increased fragility, greater deformation and injury can occur (Kaalund, Høgsaa et al. 1990). Therefore, if a childbearing woman feels that this is a risk, it is prudent to work with her to optimise birth positions and techniques which encourage skin collagen and the rectus abdominis muscles to adapt slowly to excess pressure and stretching during birth. As episiotomy in those with hEDS is associated with an increased risk of pelvic prolapse, birth via caesarean section may be preferred in cases where episiotomy would otherwise be clinically indicated (Wiesmann, Castori et al. 2014).

In cases where local anaesthetic is required, it is important to recognise that local analgesia may be less effective or require higher doses for those with hEDS (Arendt-Nielsen, Kaalund et al. 1990, Hakim, Grahame et al. 2005). However, spinal analgesia is generally considered to be safe and effective for those with hEDS (Wiesmann, Castori et al. 2014). Additionally, a

subarachnoid block has also been recorded as a suitable option for those with POTS (Motiaa, Doumiri et al. 2016). In order to consider individual risk factors, access to an early anaesthetic review during pregnancy may be advisable.

For those experiencing POTS, labour presents a number of problems. Firstly, pain and stress may worsen any episodes of tachycardia (Motiaa, Doumiri et al. 2016), yet epidural analgesia can worsen haemodynamic instability via peripheral vasodilatation and hypotension (McEvoy, Low et al. 2007). Moreover, during the second stage of labour, those with POTS can respond abnormally to performing the Valsalva manoeuvre ('purple' pushing, where breath is held and used to direct pushing) (Stewart, Medow et al. 2005). Here, during the early phases of a Valsalva manoeuvre, a larger decrease in blood pressure can be noted, followed by a larger overshoot of blood pressure and an increased heart rate in the late phases, revealing greater hemodynamic instability in those with POTS. In one case, to counteract this, low dose epidural, invasive blood pressure monitoring, and a forceps-assisted delivery was used to successfully diminish the Valsalva manoeuvres made by the mother (McEvoy, Low et al. 2007). Where appropriate, midwives could also usefully optimise strategies which promote spontaneous pushing in favour of directed pushing.

In other serious cases of POTS, birth via caesarean section has been recommended (Glatter, Tuteja et al. 2005), although the majority of patients with POTS are seemingly able to birth vaginally (Kanjwal, Karabin et al. 2009). In cases where excess joint pain associated with hEDS becomes intolerable, birth via caesarean section may again be indicated (Dutta, Wilson et al. 2011). Yet in all cases, midwives could usefully promote effective pain management and the use of therapeutic birthing environments to promote reductions in

stress. Where indicated, it is important to note that birth via caesarean section does not come without its individual risk factors for women with EDS in the postnatal period.

Postnatal care considerations

Major post-partum complications for those with hEDS and other subtypes of EDS can include abnormal scar formation after either caesarean section or episiotomy (46.1%), haemorrhage (19.4%), pelvic prolapses, which may be associated with episiotomy (15.3%), deep venous thrombosis (4.2%), complicated perineal wounds (8%) and coccyx dislocation (1.4%) (Lind, Wallenburg 2002, Jones, Ng 2008, Castori, Morlino et al. 2012). Whilst the majority of such complications would be managed in line with standard recommendations, there are some specialist considerations to be made for those with hEDS. For example, birth injuries and the effects of other obstetric procedures can be further aggravated by poor wound healing and a higher risk of suture dehiscence during the postnatal period (Hakim, Grahame et al. 2005, Hakim, Grahame 2003, Castori 2012). As such, the use of non-tension and non-dissolvable sutures to be used for deep double sutures, left in for at least 14 days is advisable (Chetty, Norton 2017). Additionally, since local anaesthesia can be less effective for those with hEDS (Arendt-Nielsen, Kaalund et al. 1990, Hakim, Grahame et al. 2005), it is prudent to assess pain on an individual basis prior to commencing any type of surgical repair. Midwives may need to wait longer for local anaesthetics to take effect in those with hEDS, and/or administer larger doses in line with current protocols.

Stress urinary incontinence has been found in 40%–70% of women with hEDS, (Castori, Camerota et al. 2010b, Arunkalaivanan, Morrison et al. 2009). This is thought to be associated with weakened pelvic floor, cystocele, bladder distention and pelvic prolapse caused by connective tissue abnormalities (Tinkle 2010, Castori, Camerota et al. 2010a,

Tinkle, Castori et al. 2017). Such stresses can only be exacerbated by the added physical endurances of pregnancy and birth. As such, physiotherapy-based interventions throughout the antenatal and postnatal periods may be useful for some in preventing, living with, and treating stress urinary incontinence (Sangsawang 2014). However, in other cases, a medical or surgical referral may be most appropriate. For midwives, the promotion of a healthy diet, mobility care considerations, a healthy lifestyle and pelvic floor exercises may help to improve or reduce the risk of maternal symptoms worsening (National Institute of Heath and Care Excellence 2017, Sangsawang 2014).

Neonatal care considerations

Given that those with hEDS can experience increased risks during pregnancy and birth, there can also be significant risks present for the neonate. In the first instance, it would be prudent to prepare for resuscitation and respiratory support due to prematurity and/or hypotonia if the neonate is also predicted to inherit any type of EDS (Lawrence 2005). Though the risk of premature birth has already been established here, it is interesting to note that this was found to be more related to hEDS in the infant (40%), and less prevalent for maternal hEDS (21%) (Lind, Wallenburg 2002).

There are also further opportunities presented during the Newborn Infant Physical Examination (NIPE) for midwives to initiate further multidisciplinary input where hEDS is present in either parent. Firstly, there is an opportunity to compare the infant's overall tone and appearance to expectations appropriate for gestational age, considering that joint hyperlaxity and dislocatabilty is a common feature of hEDS (Lawrence 2005). Unsurprisingly, in one cohort of children diagnosed with joint hypermobility/EDS (now classified as hEDS and HSDs), 12% had ‘clicky’ hips at birth and 4% were found to possess an actual congenital

dislocatable hip (Adib, Davies et al. 2005). This may be a significant consideration for those interpreting the findings from performing both Barlow and Ortolani hip manoeuvres (Kishta, Abduljabbar et al. 2017). As such, where hEDS is suspected, those who identify 'clicky hips' could usefully record this as being clinically significant.

It is also useful to examine the baby's skin at this time, as some babies with EDS will have skin that feels soft, velvet-like or 'doughy' (Beighton, De Paepe et al. 1998). Whilst examining the skin, it is also useful to inspect the forehead, chin, elbows, or knees for hyper extensible skin on the palm side of the forearm and observe for skin that splits easily (Lawrence 2005, Beighton, De Paepe et al. 1998). Whilst findings here may be significant for ongoing care, it is important to remain aware that subcutaneous newborn fat may impair some early assessments.

Babies suspected of having hEDS may require additional joint support during general care and clinical procedures (Lawrence 2005). In promoting the safeguarding of children, it is also important to consider that easy bruising and dislocation may be mistaken for mistreatment (Bird 2007). In such cases, the accurate documentation of any bodily markings identified is paramount along with symptoms consistent with hEDS.

The role of midwifery

The unique role of midwives lies in promoting the health of women and childbearing families in partnership with them. EDS remains underdiagnosed (Castori 2012, Gazit, Jacob et al. 2016), yet midwives have a unique opportunity to identify any potential signs and symptoms of hEDS which may require specialised clinical attention to optimise the childbearing experiences and outcomes for this unique subset of women. Where the role of

the midwife has developed an emphasis on woman-centred care, midwives also have an opportunity to recognise, acknowledge and respect the distinctive needs, ideas, thoughts, emotions and expectations of childbearing women (Borrelli 2014), including those who present with EDS symptomologies.

Whilst it is not within a midwife's remit to necessarily diagnose hEDS, the midwife is obliged to accurately assess any person receiving their care, and to make referrals where indicated (The Nursing and Midwifery Council (NMC) 2015). Those with hEDS receiving maternity care may or may not be in possession of a firm diagnosis, yet the midwife's awareness of hEDS and its impact upon pregnancy may not only instigate more timely and appropriate referrals but also improve the quality of any professional advice given.

In their professional role, midwives are required to practise in line with the best available evidence (The Nursing and Midwifery Council (NMC) 2015). Yet difficulties remain in providing evidence-based midwifery care, as there are currently no uniform management guidelines for childbearing women with hEDS. Moreover, the existing evidence available in relation to prevalence is sometimes highly conflicting (Tinkle, Castori et al. 2017). For example, in contrast to the majority of evidence presented in this paper, some studies report that the incidences of adverse outcomes in those with some subtypes of EDS are no different from those in the general obstetrical population (Sundelin, Stephansson et al. 2017, Khalil, Rafi et al. 2013, Castori, Morlino et al. 2012, Hermanns-Lê, Piérard et al. 2014). This presents additional challenges for midwives to educate others and make the best evidence-based decisions in partnership with childbearing women. Additionally, for some women with EDS, symptoms may worsen (especially gastrointestinal complaints, fatigue, and pain), whilst for others they may improve or remain unchanged (Tinkle, Castori et al.

2017, Castori, Morlino et al. 2012). It is also important to note that although many women and babies may present with joint hypermobility, not all will have a molecularly proven syndromic condition or experience symptoms which negatively impact upon their lives (Castori, Tinkle et al. 2017).

Conclusion

The management of hEDS in childbearing women and babies is complex. Yet as hEDS remains largely underdiagnosed (Castori 2012, Gazit, Jacob et al. 2016), there is opportunity for midwives, childbearing women and multidisciplinary teams to address this issue in pursuit of optimal and evidence-based maternity care. This paper has drawn on the existing evidence available to explore some unique midwifery care considerations for childbearing women with hEDS.

The evidence presented here demonstrates how the complications associated with hEDS and childbearing can be significant. Yet the absence of obstetric management guidelines for hEDS pregnancies suggests that maternity care plans should be made and agreed in partnership with women on an individualised basis. Working in partnership with a multidisciplinary team will also be crucial in ensuring that those with EDS achieve the most appropriate maternity care plans and symptom management.

In light of a paucity of evidence in this area, further high-quality research is required to address gaps in existing knowledge, facilitate evidence-based practice and formulate robust hEDS guidelines for pregnancy, birth and beyond. Midwives have an important role in the multidisciplinary team approach to caring for women with hEDS by providing routine care, identifying and reducing risk, making swift referrals where appropriate, supporting

individualised care and giving evidence-informed education to colleagues, childbearing women and the wider public.

For further information see:

https://www.ehlers-danlos.org/

http://hypermobility.org/

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