Neonatal and Pediatric Medicine

Schaible, Neonat pediatr Med 2021, 7:2

Mini-Review Open Access

Congenital Uterine Anomalies, Preterm Birth and Cervical Cerclage: A Mini-Review

Burk Schaible*

Department of Obstetrics and Gynecology, Wake Forest School of Medicine, 475 Vine St, Winston-Salem, NC 27101, United States

Abstract

It is unknown to what degree the congenital uterine anomalies contribute to preterm birth. Even less data exists regarding what percent of these are due to cervical incompetence and if cervical cerclage improves newborn outcomes. This mini-review seeks to review of the risk of preterm birth in women with congenital uterine anomalies as a result of cervical insufficiency and the potential impact of cervical cerclage within this patient population.

Introduction

Preterm birth is one of the foremost unsolved problems in perinatal medicine with nearly one in ten pregnancies resulting in preterm birth [1]. Historical efforts made modest reductions in preterm birth [2] reaching a nadir in 2015 of 9.6% [3]. Unfortunately, the current rate of preterm birth has risen to 10.23% without a clear etiology [4].

The Burden of Preterm Birth

While nearly 25% of preterm births result from iatrogenic intervention, the remainders are a multifactorial mix of maternal and fetal conditions [5]. It is unknown to what degree the congenital uterine anomalies contributes to preterm birth. Even less data exists regarding what percent of these are due to cervical incompetence and if cervical cerclage improves newborn outcomes. This mini-review will explore the past and present understanding regarding congenital uterine anomalies, cervical incompetence and the role of cervical cerclage within this challenging population.

The Cervix: The Anatomic Gateway to Parturition

In 1947, a sentinel paper by D.N. Danforth changed the understanding of the cervix from a primarily muscular organ to a fibrous matrix responsible for retaining the conceptus [6]. Within the next decade, clinical implications were established in identifying cervical incompetence as a primary cause of spontaneous abortion and the main anatomic structure in preventing of the parturition process [7,8]. Subsequent studies have continued to focus on the structural role of the cervix in preventing preterm birth [9]. It is unknown how mechanical force placed upon the cervix change with the presence of a congenital uterine anomaly.

The Association of Preterm Birth and Congenital Uterine Anomalies

Most literature suggest an association between congenital uterine anomalies and preterm birth [10-14] In a 2014, a meta-analysis of comparative studies by Venetis et al. found eight studies correlating preterm birth with congenitally malformed uteri [15]. Despite this association, only one study identified cervical insufficiency as the potential cause of preterm birth in patients with a known uterine anomaly [16]. In 2018, the same group observed a higher rate of cervical incompetence (3.6%) in 1,099 cases of uterine anomalies compared to 279,662 controls (0.4%) [17]. While preterm birth has been associated with uterine septa, these defects tend to be more strongly associated with subfertility and spontaneous first trimester abortion [15,18]. Overall, most authorities recognize an association between fusion defects and preterm birth, but it remains unknown if cervical insufficiency is the cause of these adverse outcomes or if cervical cerclage improves outcomes.

The Role of Cervical Shortening in Congenital Uterine Anomalies

Short cervix (defined as a cervical length less than 25 mm) has been implicated in preterm delivery, yet little is known about this finding in patients with uterine anomalies [19-21]. A 2005 prospective study of 64 patients identified at 13-fold risk of preterm birth when by notifying short cervix through serial cervical lengths in patients with known uterine anomalies [22]. A more recent Australian cohort of 86 pregnancies with known uterine anomalies was unable to identify patients at risk of preterm birth through serial cervical length measurements until 24 weeks gestation [23]. This data is difficult to interpret given the different type of uterine anomalies in each group. It is also unclear if the etiology of cervical shortening is due to preterm labor or cervical incompetence within these studies.

The Efficacy of Cervical Cerclage in Congenital Uterine Anomalies

Few studies have ascertained the impact of cervical cerclage in the anomalous uterus. There are no randomized clinical trials and most of the work done exploring this comes from a limited number of case reports, case control studies or small cohorts from the 1980s and 1990s. One of the first major studies was in 1983 by Abramovici et al. noting the adverse composite pregnancy outcomes of 15 women with known uterine anomalies [24]. This cohort had a combined 45 pregnancies over two years resulting in only two live births (both preterm). The same group was then treated with cerclage placement at 11 to 12 weeks in subsequent pregnancies, resulting in a 100% live birth rate with only two preterm births. In a widely cited paper, Golan et al. identified cervical incompetence in 29 of 98 women with congenital uterine anomalies [25]. Cervical cerclage placement significantly increased term deliveries, decreased late abortions and reduced prematurity. The

***Corresponding author:** Burk Schaible, Department of Obstetrics and Gynecology, Wake Forest School of Medicine, 475 Vine St, Winston-Salem, NC 27101, United States, E-mail: bschaibl@wakehealth.edu

Received: Febuary 05, 2021; **Accepted:** Febuary 19, 2021; **Published:** Febuary 26, 2021

Citation: Schaible B (2021) Congenital Uterine Anomalies, Preterm Birth and Cervical Cerclage: A Mini-Review. Neonat Pediatr Med 7: 205.

most notable impact of cerclage was seen among bicornuate uterus. The authors concluded cervical cerclage should be placed prophylactically in al pregnancies complicated by bicornuate uterus and should be considered in all pregnancies complicated by a CUA. In 1991, Seidman et al. noted nearly double the rate of newborn survival (88% vs. 47%) in patients with cerclage placement in 86 pregnancies with anomalous uteri (excluding arcuate and septate uteri) compared to 106 controls [26]. Another small study reported favorable results in patients with uterine anomalies and cerclage placement, but was confounded by small sample size and concomitant progesterone supplementation [27]. A case series of 275 patients with spontaneous pregnancy loss and uterine malformations also noted improved outcomes with use of cerclage [28]. Most recently, an Iranian study of 40 women (32 with bicornuate uteri) reported a 76.2% term delivery rate in patients with cerclage placement at 15 to 16 weeks' gestation compared to a 27.3% term delivery rate in patients without cerclage placement [29].

Congenital Uterine Anomalies and Data Limitations

Many factors confound the data surrounding congenital uterine anomalies. In addition to small sample size, poor study design, publication bias and lack of randomized clinical trials many other factors create difficulties understanding the benefit of cervical cerclage placement in patients with uterine anomalies. Among these are lack of definitional uniformity [30-35] differences in timing of cerclage technique, a lack universal screening process to identify uterine anomalies, wide variations of obstetrical complications associated with each specific uterine anomaly [26,36]. Further confounding variables arise when women with infertility or subfertility thought to be due to a structurally abnormal uterus undergo assisted reproductive technology to achieve pregnancy. These challenging clinical scenarios make it difficult to discern if subfertility, a structurally abnormal uterus or assisted reproductive technology are the main cause of adverse pregnancy outcomes [37]. Lastly, some uterine anomalies remain unclassifiable and management is based on case reports and expert opinion [38].

Future Questions: Where do we go from here?

Despite nearly 40 years of data seeking to understand the relationship between congenital uterine anomalies, cervical insufficiency and utilization of cerclage, many basic questions remain unanswered. Currently, the majority of consists of case-control studies, case reports, and small cohort studies. Future studies need to better characterize the obstetrical outcomes associated with each uterine anomaly, including: the risk of preterm birth for each anomaly, the cause of preterm birth (e.g. cervical incompetence), the role of serial cervical screening [23], benefit from prophylactic vs. exam or ultrasound indicated cerclage, and the role of other therapeutics like progesterone supplementation or pessary. Based on the limited data, a risk-benefit discussion should occur with patients who have known congenital uterine anomalies regarding the potential options to reduce the risk of preterm birth. It seems reasonable to offer a history indicated cerclage to women with a history of late first trimester loss or mid-trimester loss in the setting of uterine anomaly related to a fusion defect (e.g. arcuate, bicornuate, unicornuate or didelphys). Discussion of prophylactic cerclage placement should be considered in patients with bicornuate uterus given some data suggesting benefit in this patient population [25].

Conclusion

Cervical length screening remains controversial given the conflicting data and the lack of improved outcomes in patients with congenital uterine anomalies. Future research should seek to create well designed prospective studies that minimize heterogeneity, confounding factors, and bias to assess which uterine anomaly confers the highest risk of preterm birth as a result of cervical insufficiency. Randomized clinical trials are needed to assess if cervical cerclage reduces the risk of preterm birth and neonatal morbidity and mortality in patients with uterine anomalies. Serial cervical lengths and other interventions such as progesterone supplementation and pessary should also be assessed in this population.

References

1. Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB (2012). National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: A systematic analysis and implications. Lancet 379: 2162-2172.
2. Martin JA, Hamilton BE, Ventura SJ, Osterman MJK, Wilson EC, et al. (2012) Births: Final Data for 2010. National Vital Statistics Reports 61: 72.
3. Martin JA, Hamilton BE, Ventura SJ, Osterman MJK (2016) Births in the United States, 2015. 258.
4. Martin JA, Hamilton BE, Ventura SJ, Osterman MJK (2020) Births in the United States, 2015. 387.
5. Ananth CV, Vintzileos AM (2006) Maternal-fetal conditions necessitating a medical intervention resulting in preterm birth. Am J Obstet Gynecol 195:1557-1563.
6. Danforth DN (1947) The fibrous nature of the human cervix and its relation to the isthmic segment in gravid and nongravid uteri. Proc Inst Med Chic 16:295.
7. Danforth DN (1959) Cervical incompetency as a cause of spontaneous abortion. Clin Obstet Gynecol 2: 45-56.
8. Roddick JWJ, Buckingham JC, Danforth DN (1961) The Muscular Cervix-A Cause of Incompetency in Pregnancy. Obstetrics & Gynecology 17: 562-565.
9. Myers KM, Feltovich H, Mazza E, Vink J, Bajka M, et al. (2015) The mechanical role of the cervix in pregnancy. J Biomech 7:1388-90.
10. Chan YY, Jayaprakasan K, Tan A, Thornton JG, Coomarasamy A, et al. (2011) Reproductive outcomes in women with congenital uterine anomalies: A systematic review. Ultrasound Obstet Gynecol 38:371-382.
11. Reichman D, Laufer MR, Robinson BK (2009) Pregnancy outcomes in unicornuate uteri: A review. Fertility and Sterility 91:1886-1894.
12. Acién P, Acién M, Mazaira N, Quesada-Rico JA (2014) Reproductive outcome in uterine malformations with or without an associated unilateral renal agenesis. J Reprod Med 59(1-2):69-75.
13. Raga F, Bauset C, Remohi J, Bonilla-Musoles F, Simón C, et al. (1997) Reproductive impact of congenital Müllerian anomalies. Hum Reprod 12:2277-2281.
14. Xia EL, Li TC, Choi SNS, Zhou QY (2017) Reproductive outcome of transcervical uterine Incision in unicornuate uterus. Chin Med J (Engl). 130:256-261.
15. Venetis CA, Papadopoulos SP, Campo R, Gordts S, Tarlatzis BC, et al. (2014) Clinical implications of congenital uterine anomalies: a meta-analysis of comparative studies. Reproductive BioMedicine Online 29:665-683.
16. Mastrolia SA, Baumfeld Y, Hershkovitz R, Loverro G, Di Naro E, et al. (2017) Bicornuate uterus is an independent risk factor for cervical os insufficiency: A retrospective population based cohort study. J Matern Fetal Neonatal Med. 2017; 30:2705-2710.
17. Mastrolia SA, Baumfeld Y, Hershkovitz R, Yohay D, Trojano G, et al. (2018) Independent association between uterine malformations and cervical insufficiency: a retrospective population-based cohort study. Arch Gynecol Obstet 297:919-926.
18. Grimbizis GF, Camus M, Tarlatzis BC, Bontis JN, Devroey P (2001) Clinical implications of uterine malformations and hysteroscopic treatment results. Hum Reprod Update 7:161-174.
19. Grobman WA, Lai Y, Iams JD, Reddy UM, Mercer BM, et al. (2016) Prediction of spontaneous preterm birth among nulliparous women with a short cervix. J Ultrasound Med 35:1293-1297.
20. Goldenberg RL, Culhane JF, Iams JD, Romero R (2008) Epidemiology and causes of preterm birth. Lancet 371:75-84.

21. Esplin MS, Elovitz MA, Iams JD, Parker CB, Wapner RJ, et al. (2017) Predictive accuracy of serial transvaginal cervical lengths and quantitative vaginal fetal fibronectin levels for spontaneous preterm birth among nulliparous women. JAMA 317:1047-1056.

22. Airoldi J, Berghella V, Sehdev H, Ludmir J (2005) Transvaginal ultrasonography of the cervix to predict preterm birth in women with uterine anomalies. Obstetrics & Gynecology 106:553-556.

23. Hughes KM, Kane SC, Haines TP, Sheehan PM (2020) Cervical length surveillance for predicting spontaneous preterm birth in women with uterine anomalies: A cohort study. Acta Obstet Gynecol Scand 99:1519-1526.

24. Abramovici H, Faktor JH, Pascal B (1983) Congenital uterine malformations as indication for cervical suture (cerclage) in habitual abortion and premature delivery. Int J Fertil 28:161-164.

25. Golan A, Langer R, Wexler S, Segev E, Niv D, et al. (1990) Cervical cerclage-its role in the pregnant anomalous uterus. Int J Fertil 35:164-170.

26. Seidman DS, Ben-Rafael Z, Bider D, Recabi K, Mashiach S (1991) The role of cervical cerclage in the management of uterine anomalies. Surg Gynecol Obstet 173:384-386.

27. Leo L, Arduino S, Febo G, Tessarolo M, Lauricella A, et al. (1997) Cervical cerclage for malformed uterus. Clin Exp Obstet Gynecol. 24:104-106.

28. Surico N, Ribaldone R, Arnulfo A, Baj G (2000) Uterine malformations and pregnancy losses: is cervical cerclage effective? Clin Exp Obstet Gynecol 27:147-149

29. Yassaee F, Mostafaee L (2011) The Role of Cervical Cerclage in Pregnancy Outcome in Women with Uterine Anomaly. J Reprod Infertil. 12:277-279.

30. Buttram VC, Gibbons WE (1979) Müllerian anomalies: A proposed classification. (An analysis of 144 cases). Fertil Steril 32:40-46.

31. Acién P, Acién M, Sánchez-Ferrer M (2004) Complex malformations of the female genital tract. New types and revision of classification. Hum Reprod 19:2377-2384.

32. Acién P, Acién M (2016) Diagnostic imaging and cataloguing of female genital malformations. Insights Imaging 7:713-726..

33. Oppelt P, Renner SP, Brucker S, Hucke J, Wallwiener D, et al. (2005) The VCUAM (Vagina Cervix Uterus Adnex-associated Malformation) classification: a new classification for genital malformations. Fertil Steril 84:1493-1497.

34. Grimbizis GF, Gordts S, Di Spiezio Sardo A (2013) The ESHRE/ESGE consensus on the classification of female genital tract congenital anomalies. Hum Reprod 28:2032-2044.

35. Ludwin A, Ludwin I (2015) Comparison of the ESHRE-ESGE and ASRM classifications of Müllerian duct anomalies in everyday practice. Hum Reprod 30:569-580.

36. Bermejo C, Martínez Ten P, Cantarero R, Diaz D, Pedregosa JP, et al. (2010) Three-dimensional ultrasound in the diagnosis of Müllerian duct anomalies and concordance with magnetic resonance imaging. Ultrasound Obstet Gynecol 35:593-601.

37. Lin PC (2004) Reproductive outcomes in women with uterine anomalies. J Women's Health 13:33-39.

38. Schaible B, Haught E, Vozar A, Riggs K, Calhoun B, et al. (2021) Abdominal cerclage in a patient with a neocervix with planned cesarean hysterectomy at delivery. J Obstetrics and Gynaecology Research 47:416-419.