The Impact of Prenatal Diagnosis of an Upper Extremity Anomaly on Pregnancy Outcome

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Abstract

Objective: Upper extremity anomalies (UEA) occur when there is an interruption in the normal process of embryonic limb development. The prenatal diagnosis of an UEA may impact the decision to deliver or terminate the pregnancy. We sought to elucidate factors associated with pregnancy outcome in the setting of a known UEA.

Methods: We reviewed electronic medical records at three affiliated hospitals to identify mothers with an UEA diagnosed by prenatal ultrasound. Maternal demographics, anomaly type, and clinical management variables were collected. Patients were stratified by primary outcome of either delivery or elective termination. Multivariate analysis was performed to identify factors associated with pregnancy termination.

Results: Thirty mother/child dyads were confirmed to have an UEA by prenatal ultrasound. Fourteen pregnancies resulted in live birth of the fetus (47%) and 16 pregnancies were terminated (53%). Pregnancies with multiple anomalies (P<0.05) and/or bilateral UEAs (P<0.05) were more likely to undergo termination. Consultation with an upper extremity surgeon was associated with delivery (P<0.05). Maternal demographics were not associated with pregnancy outcome.

Conclusions: Fetal anomaly characteristics are associated with pregnancy outcome. Although prenatal consultation with an upper extremity surgeon was associated with delivery, this subset of patients were more likely to have isolated, unilateral anomalies.

Keywords: Upper extremity anomaly; Congenital hand differences; Abortion; Pregnancy termination; Prenatal ultrasound; Prenatal diagnosis

Introduction

An upper extremity anomaly (UEA) occurs when the natural development of the embryonic limb is altered due to environmental factors or genetic mutations [1]. While the prevalence of UEAs in the United States has yet to be thoroughly investigated, prevalence in other countries is estimated to occur in 3.4-21.5 per 10,000 live births [2-5].

Larger studies have found most UEAs to be isolated cases [3,4]. However, children with radial longitudinal deficiency, humeral defects, or bilateral reductions have a higher risk for associated anomalies and neonatal mortality [4,5]. Those with syndromic manifestations have higher rates of both neonatal mortality and spontaneous pregnancy termination [6].

The decision-making process related to pregnancy termination is extremely complex. The socioeconomic status, race, religion, age of the mother, as well as physician 'certainty' or 'recommendations', have been shown to significantly influence a mother's decision after discovering a congenital anomaly [7-14]. These decisions are further complicated in cases of UEAs, where underlying diagnoses and syndromic risks may be uncertain, and the perceived impact on quality of life is variable and multifactorial. Our goals are to provide clarity with regard to determinants of pregnancy termination after a prenatal diagnosis of an UEA and to determine whether there are variations in the rate of pregnancy termination based on type of UEA. For upper extremity surgeons, who rarely see mothers for prenatal counseling regarding a child with an UEA, this information will help facilitate a well-informed discussion.

Materials and Methods

After institutional review board approval, we performed a longitudinal analysis of medical records at three affiliated medical centers (Northwestern Memorial Hospital, Ann and Robert H. Lurie Children's Hospital of Chicago, and Prentice Women's Hospital) for the years 2002 to 2015. We queried the prenatal ultrasound report database at Prentice Women's Hospital and Northwestern Memorial Hospital to identify mothers given a prenatal diagnosis of an UEA. The search parameters were developed by a Reproductive Geneticist with a thorough knowledge of the database. We reviewed the Northwestern Memorial Hospital Electronic Data Warehouse (EDW) to capture patients not included in the prenatal ultrasound database. As there are no discrete ICD-9 codes attributed to structural fetal anomalies of the limbs, we developed a hierarchical text search (Table 1) based on keywords as well as a query for all patients who underwent an elective pregnancy termination (ICD-9 codes: 635.xx, 636.xx, 637.xx, 638.xx) in combination with the search term "prenatal". Consultation notes in the electronic medical record (EMR) at Ann and Robert H. Lurie Children's Hospital were also included using the search parameters outlined in Table 1.

Mother/child dyads were included in the cohort when an UEA diagnosed via prenatal ultrasound was confirmed by review of the medical record. Mother/child dyads were excluded when further chart review revealed a false positive diagnosis, no definitive diagnosis, or skeletal dysplasia. For patients meeting inclusion criteria, we collected maternal demographics (age, race/ethnicity, gravida/para, marriage or equivalent status, socioeconomic status, characteristics of the UEA

Item 1	"prenatal ultrasound"
Item 2	"upper limb" or "upper extremity" or "forearm" or "arm" or "hand"
Item 3	"reduction deformity" or "longitudinal deficiency" or "transverse deficiency" or "syndactyly" or "polydactyly" or "congenital abnormality" or "congenital malformation"

Table 1: 'Electronic Data Warehouse' (EDW) text search.

(type, unilateral vs. bilateral, date of detection, concomitant extremity anomalies), and maternal care clinical encounters (consultation with maternal fetal medicine [MFM], upper extremity surgeon, and/or other medical services). Socioeconomic status was extrapolated from the median household income by zip code, as reported by US Census Bureau data from the 2014 American Community Survey. Fetal UEA types observed in the present study were categorized into three main groups: hand anomalies (polydactyly, clinodactyly, cleft hand), limb deficiency (transverse, longitudinal), and other/complex anomalies (congenital contracture, micromelia, and limb body-wall complex (LBWC)).

Pregnancies were classified by the primary outcome of either delivery or elective termination. Statistical analysis was conducted to compare categorical data and to analyze demographics and clinical variables for our primary outcomes (delivery and termination) (SAS Software). Variables were dichotomized or reclassified into categories, when possible, to standardize the analysis and to achieve statistical power. P-values were calculated by chi-squared analysis and Fisher's exact test. Statistically significant differences in demographic and clinical data were calculated via Wilcoxon-Mann-Whitney analyses. Statistical significance was set at $P<0.05$.

Results

We identified 981 mother/child dyads who met initial search criteria; 30 of which were confirmed to have an UEA by prenatal ultrasound (Figure 1). Fourteen pregnancies resulted in live birth of the fetus (47%) and 16 pregnancies were terminated (53%). Maternal demographics for each cohort are shown in Table 2. In univariate analysis, there were no statistically significant differences in maternal demographics between cohorts (Table 3). No significant differences in termination rates were found between the three categories of UEAs (hand anomalies (polydactyly, clinodactyly, cleft hand; N=11), limb deficiencies (transverse, longitudinal; N=11), and other/complex (constriction band, micromelia, LBWC; N=8) (Table 4).

Those with multiple anomalies were more likely to undergo termination as compared to those with isolated anomalies ($P<0.05$). Bilateral UEAs were associated with a statistically significantly higher rate of termination as compared to isolated anomalies ($P<0.05$). Surgeon consultation was obtained in 55% (6/11 patients) of isolated UEA cases versus 21% (4/19 patients) when associated with other anomalies. Consultation with an upper extremity surgeon was more likely to be obtained in the setting of an isolated UEA, but this did not reach statistical significance ($P=0.06$).

Consultation with an upper extremity surgeon was statistically significantly associated with delivery ($P<0.05$) (Table 5). Significant differences were also found when comparing median MFM encounters ($P<0.05$) and duration of care ($P<0.05$).

Discussion

The prenatal diagnosis of an UEA sets in motion a complex sequence of doctor-patient interactions and maternal decision-making

Figure 1: Cohort identification flowchart.
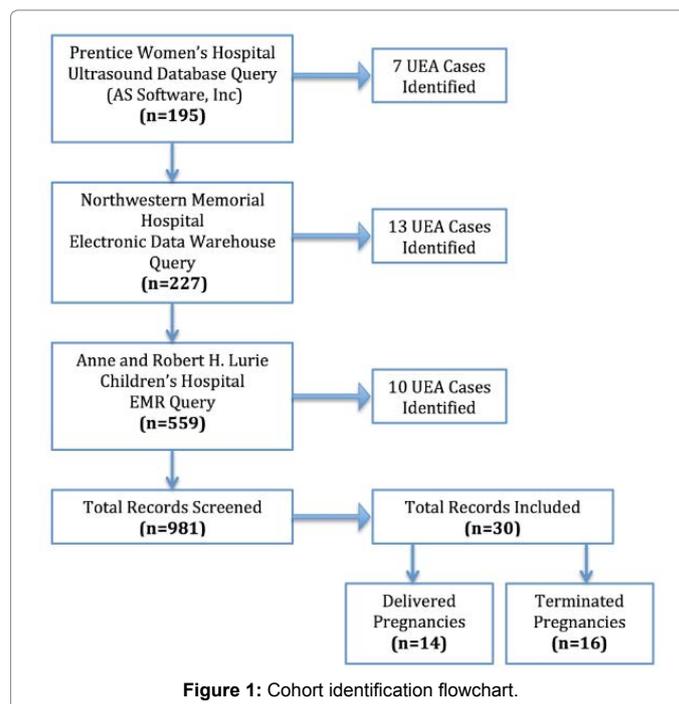
processes. We found several factors that are associated with pregnancy outcome. Mothers were significantly more likely to undergo elective pregnancy termination after diagnosis of bilateral UEAs. This decision may be influenced by the known association of bilateral UEAs with genetic trisomy or other syndromes linked to poor fetal outcomes [15]. Similarly, when the UEA was found in the setting of other non-upper extremity anomalies, pregnancy termination was more common. This aligns with previous studies showing that mothers are more likely to terminate a pregnancy in the setting of severe systemic anomalies [16-19].

Our data indicate that prenatal consultation with an upper extremity surgeon is significantly associated with delivery. This is confounded, however, by the fact that surgeons evaluated a disproportionate number of patients with unilateral, isolated anomalies. Of the mothers that underwent prenatal surgical consultation (n =10), the diagnosed fetal anomaly was more often unilateral (80%, 8 of 10) and isolated (60%, 6 of 10). These findings reflect the logical notion that referring obstetricians determine which children with prenatally diagnosed UEAs may theoretically benefit from future upper extremity reconstruction; patients with more complex or systemic anomalies are rarely, if ever, referred for evaluation. Many surgical options exist to improve both hand function and aesthetics in the setting of a variety of different congenital hand anomalies, though the impact on these outcomes depends heavily on the clinical phenotype and severity of the defect. We believe that greater access and referral to surgical counsel may improve outcomes for infants with remedial defects by allowing for surgical planning in the antepartum period or immediately after birth.

There were no significant associations between maternal sociodemographic variables and the ultimate decision to pursue pregnancy termination. This implies that the decision-making process is predominantly influenced by the UEA characteristics and associated anomalies, as well as MFM physician input. Other studies have shown that physician recommendations have a significant influence on maternal decisions regarding pregnancy termination [20]. Several other factors that may impact maternal decision-making were considered for

	Delivered Pregnancies	Terminated Pregnancies
N	14	16
Age (yrs)		
Mean	31.85	34.125
Range	25-38	24-40
Race/Ethnicity		
White	4	11
Asian	0	2
Black	0	1
Hispanic	3	0
Declined	3	2
Unknown	4	0
Marital Status		
Married	11	12
Single	2	2
Divorced	1	0
Unknown	0	2
Insurance		
Medicaid	1	2
Private	12	13
Self-Pay	0	1
Unknown	1	0
Household Income		
$0-$25k	0	0
$25-$50k	5	3
$50-$75k	1	5
$75-$100k	7	6
$100k+	1	2
Gravida		
0	6	4
1	3	5
≥ 2	5	7
Para (>37 wks)		
0	7	5
1	4	5
≥ 2	3	6
Prior Preterm Births (<37 wks)		
0	12	14
≥ 1	0	2
Prior Abortions (<20 wks)		
0	10	12
≥ 1	2	4
Living Children		
0	7	5
1	4	6
≥ 2	1	5

Table 2: Maternal demographics.

	Delivered Pregnancies (N=14)a	Terminated Pregnancies (N=16)a	P-value
Maternal Age			
Median	30.5	33.5	0.168
Range	25-38	24-40	
Maternal Race/ Ethnicity			
White	4/7 (57.1%)	11/14 (78.6%)	0.306
Black, Hispanic, Asian, Declined, Unknown	3/7 (42.9%)	3/14 (21.4%)	
Marital Status			
Married	11/14 (78.6%)	12/16 (75.0%)	0.564
Single, Divorced, or Unknown	3/14 (21.4%)	4/16 (25.0%)	
Insurance			
Private	12/13 (92.3%)	13/16 (81.3%)	0.39
Medicaid, Self-Pay	1/13 (7.7%)	3/16 (18.8%)	
Household Income ($)			0.589
Median	77,248	76,491	
Gravida			
0	6/14 (42.9%)	4/16 (25.0%)	0.576
1	3/14 (21.4%)	5/16 (31.3%)	
≥ 2	5/14 (35.7%)	7/16 (43.8%)	
Para			
(term births >37 wks)			
0	7/14 (50.0%)	5/16 (31.3%)	0.518
1	4/14 (28.6%)	5/16 (31.3%)	
≥ 2	3/14 (21.4%)	6/16 (37.5%)	
Prior Preterm Births (<37 wks)			
0	12/12 (100.0%)	14/16 (87.5%)	0.204
≥ 1	0/12 (0.0%)	2/16 (12.5%)	
Prior Abortions (<20 wks)			
0	10/12 (83.3%)	12/16 (75.0%)	0.595
≥ 1	2/12 (16.7%)	4/16 (25.0%)	
Living Children			
0	7/12 (58.3%)	5/16 (31.3%)	0.236
1	4/12 (33.3%)	6/16 (37.5%)	
≥ 2	1/12 (8.3%)	5/16 (31.3%)	

a some N values lowered by exclusion of declined or unknown demographic information

Table 3: Univariate analysis of patient cohorts: delivery vs. termination.

on detection of UEAs by ultrasound as well as the heterogeneous documentation of prenatally diagnosed fetal anomalies. Although recognition of structural anomalies has increased in recent years with advancements in sonography and diagnostic protocols [21,22] detection rates in the United States are confounded by disparities in ultrasonographer expertise and the lack of national guidelines requiring documentation of anomalies in the distal extremities in low-risk pregnancies [23]. Because the management of complicated pregnancies may be distributed across different adult and pediatric health care systems, we may have lost patients to attrition. Further, the patients seen in our health care system may not be representative of those in other parts of the country; this is significant because of geographical variation in physician practice patterns as well as maternal beliefs regarding pregnancy termination. Lastly, our study cohort was small and this important factor limited the power of our statistical analysis.

Pregnancy termination due to a fetal anomaly has been associated with significant maternal emotional distress, perinatal grief, depression and post-traumatic stress disorder [24,25]. Asplin et al. found that such

inclusion in this study (i.e., social history, family history, environmental exposures, severe pregnancy complications), though this data was very rarely noted in the chart and was not sufficient for further analysis.

This study has several notable limitations. Our patient identification protocol was rigorous, but still limited by the lack of medical record integration between affiliated institutions. Without discrete ICD-9 codes for prenatally diagnosed structural fetal anomalies of the upper limbs, identification of our target population was imperfect. Despite efforts to maximize study inclusion, we were necessarily limited by dependence

	Delivered Pregnancies	Terminated Pregnancies	P-value
Gestational Age at Dx	145.43	133.67	0.498
Hand Anomalies			
Polydactyly	4/14 (28.6%)	4/16 (25.0%)	0.759
Clinodactyly	0/14 (0%)	1/16 (6.3%)	
Cleft Hand	1/14 (7.1%)	1/16 (6.3%)	
Deficiency Anomalies			
Transverse Deficiency	5/14 (35.7%)	5/16 (31.3%)	
Longitudinal Deficiency	1/14 (7.1%)	0/16 (0%)	
Other/Complex Anomalies	t		
Congenital Contracture	1/14 (7.1%)	0/16 (0%)	
Micromelia	1/14 (7.1%)	5/16 (31.3%)	
Limb Body Wall	1/14 (7.1%)	0/16 (0%)	
Complex			
Laterality			0.030*
Unilateral	9/14 (64.3%)	4/16 (25.0%)	
Bilateral	5/14 (35.7%)	12/16 (75.0%)	
Other Anomalies on Prenatal Ultrasound			0.030*
0	8/14 (57.1%)	3/16 (18.8%)	
≥ 1 (Non-UEAs)	6/14 (42.9%)	13/16 (81.3%)	

*statistically significant value (P-value <0.05)

Table 4: Comparison of fetal anomalies by outcome.

	Delivered Pregnancies (N=14)	Terminated Pregnancies (N=16)	P-value
Upper Extremity Surgeon Consult			0.001*
Obtained	9/14 (64.3%)	1/16 (6.3%)	
Not obtained	5/14 (35.7%)	15/16 (93.8%)	
Total MFM Encounters	12.5	3.5	0.0033*
Median Duration of Care (days from diagnosis to delivery/termination)	125.5	3.5	<0.0001*

*statistically significant value (P-value <0.05)

Table 5: Categorical comparisons of maternal clinical data.

mothers most often asked for changes in care related to "provision of adequate support through state-dependent communication, in-depth understanding and compassion…and increased resources". As such, it is essential that the mother is well-informed regarding any realistic options for reconstruction and possible implications of the UEA on quality of life. This emotionally charged consultation should be driven by an understanding of the best available evidence with an appreciation for systemic conditions beyond the scope of care of the upper extremity surgeon [13,14]. Understanding the variables associated with pregnancy outcome in the setting of an UEA can lead to a more informed and useful prenatal consultation.

This study sought to identify differences between mothers who chose to deliver or to abort a complicated pregnancy to better understand factors that affects the decision making process. It must be clear that in all such cases, there is no preferred decision other than that chosen by the mother. The findings of this paper are intended to clinically facilitate an unbiased decision on behalf of the mother who is thoroughly informed on all possible treatments, therapies, and outcomes that exist after an upper extremity anomaly is diagnosed.

Conclusion

The arrangement of surgical treatment may be obtained when it can provide improved quality of life for those with less severe upper extremity anomalies. By contrast, termination may be selected when the prognosis is perceived as poor. Appropriate consultation with obstetricians, genetic counselors, and upper extremity surgeons can all play a critical role in the mother's decision-making process. Understanding these factors and the influence they have on the mother will facilitate better-coordinated care and more informed decision-making for parents facing this choice. Of the variables assessed in this study, severity of the upper extremity anomaly was the factor most predictive of the pregnancy outcome. Surgical consult should be considered in all cases of upper extremity anomaly diagnoses for a more completely informed decision-making process.

Acknowledgements

Statement of Ethics

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5).

The Ann and Robert H Lurie Children's Hospital of Chicago Institutional Review Board Panel #2 (Lurie Children's IRB) reviewed and approved this study (Reference Number: IRB 2015-378) under risk/benefit determination as described in the Code of Federal Regulations (CFR) 45 Part 46, Subpart D: 45 CFR 46.404 Research not involving greater than minimal risk. This protocol was authorized by 45 Code of Federal Regulations (CFR) 46.111 and via expedited review as authorized by 45 CFR 46.110 the above-named protocol.

Statement of Informed Consent

The Lurie Children's IRB waives the requirement of obtaining informed consent

for this study in accordance with 45 CFR 46.116(d): (1) the research involves no more than minimal risk to subjects; (2) the waiver or alteration will not adversely affect the rights and welfare of the subjects; (3) the research could not practicably be carried out without the waiver or alteration; (4) whenever appropriate, the subjects will be provided with additional pertinent information after participation.

The Lurie Children's IRB granted a complete (full) waiver of HIPAA authorization requirement under 45 CFR 164.512 (i) as the following criteria were satisfied: (1) The research could not be feasibly conducted without the waiver; (2) The research could not feasibly be conducted without access to the PHI; (3) The use or disclosure of PHI involves no more than minimal risk to the subject's privacy and includes a plan to protect identifiers, a plan to destroy the identifiers at the earliest opportunity, and written assurances that the PHI will not be reused for purposes beyond what is described in the current study protocol.

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