

A Cross-Sectional Study of Obstetrical and Gynecological Parameters in Twins – A Potential Increase in Prelabor Rupture of Membranes and Pre-eclampsia in Twin Women

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Abstract

Objective: This cross-sectional study of 192 twin women across a wide geographical area compared obstetrical and gynecological parameters between twins and the general population.

Materials & Methods: The study is a cross-sectional study involving surveys. Gynecological variables included age of menarche, abnormal pap smears, birth control usage, endometriosis, fibroids, infertility, gynecological cancer, and osteoporosis. Obstetrical variables studied included gravida and para, ectopic pregnancies, hypertension of pregnancy, pre-eclampsia, gestational diabetes, and prelabor rupture of membranes (PROM). Chi Square and Fisher's Exact tests were utilized to compare these binary variables between identical and fraternal twins. Finally, odds ratios were used to compare the rates of PROM, pre-eclampsia, hypertension, ectopic pregnancy, and gestational diabetes among twins compared to the general population using reputable literature sources.

Results: Identical twins reported the same age of menarche more frequently than their fraternal counterparts ($p=0.0021$) with an odds ratio of 4.56 (95% CI=1.62,12.83). There was also an increase in the odds of PROM 1.37 to 5.42 (95% CI=0.95,1.96 and 4.21,6.98) and pre-eclampsia 1.17 to 3.16 (95% CI=0.66,2.09 and 2.16,4.62) in our twin sample verse the general population. Finally, only 9.9% (18/184) reported knowledge of amnionicity and chorionicity.

Conclusion: Our findings suggest that further large scale research concerning PROM and pre-eclampsia in twin women may be warranted.

Keywords: Prelabor Rupture of Membranes; Pre-eclampsia; Amnion; Chorion; Twins

Abbreviations: PROM: Prelabor Rupture of Membranes

Introduction

Twin pregnancies have long been a topic of investigation. One has little difficulty finding an abundance of information on the diagnosis, management, complications and delivery recommendations for twin gestations. There have been tremendous advances in monochorionic twin pregnancy management and therapy including the role of fetoscopic laser coagulation of placental anastomoses for Twin-Twin Transfusion Syndrome management. What happens when these very twins become of childbearing age however? It is possible that these twin women could be more likely to develop pre-eclampsia or experience premature rupture of membranes. Additionally, they may be more likely to develop gestational diabetes than those born of singleton pregnancies. If twins would be more likely to develop pre-eclampsia

or gestational diabetes then perhaps they should routinely be offered aspirin for pre-eclampsia prophylaxis or early glucose tolerance testing when they become pregnant. These questions remain unanswered. Interestingly, data to answer such questions is nonexistent. Given the increased incidence of prelabor rupture of membranes, pre-eclampsia, and gestational diabetes in twin gestations and the increased acceptance of the concept of perinatal programming of the fetus it seems feasible that these twin women could be at increased risk of these conditions when they themselves become pregnant.

The gynecological questions surrounding twins are equally unknown. Identical twins may be more likely than fraternal twins to both have the same age of menarche, abnormal pap smears, use birth control, develop endometriosis or fibroids, experience infertility, or develop gynecological cancer or osteoporosis. The goals of this study were to investigate some of these questions. More specifically, social, obstetrical, and gynecological relationships between female identical and fraternal twins were investigated. Additionally, obstetrical frequencies among twins were compared to those in the general population.

Materials and Methods

This study was fully approved by the Institutional Review Board of Albany Medical Center/Albany Medical College before its commencement. The study was a cross sectional study involving the distribution of surveys to female twins. The surveys were developed specifically for this study and were printed in English language. In order to be eligible to participate in the study twins needed to be female and be at least 18 years of age. Triplets were not included in this study. Surveys were given in registration packets to all twins who attended the *Twins Days Festival* in Twinsburg, Ohio, in August of 2014. Additionally, surveys were electronically mailed to all twins on the *Twins Days Festival* mailing list which included twins from the festival's inception in 1976. Of note, the *Twins Days Festival* is the largest annual gathering of twins and multiples in the world. Twins were instructed to complete the surveys independently of their twin counterpart and not to collaborate with their twin in any way. Participation in this survey was completely optional and twins could readily opt out of participating. Once a survey was completed it was mailed back to the Department of Obstetrics and Gynecology at Albany Medical Center in Albany, New York. Each survey couplet had a unique tracking number on it so the surveys could be matched back together upon receipt.

The contents of the individual surveys contained demographic, social, gynecological, and obstetrical questions. Questions were constructed in a binary manner to elicit a yes/no response. Results were tabulated and coded as binary variables either yes (1) or no (0). SAS University Edition was then utilized to perform all statistical analyses. Specifically, Chi Square and Fisher's Exact Tests were used to compare all binary variables. To compare obstetrical ratios in our twin sample to the general population a literature review was performed and odds ratios were calculated. The incidence of prelabor rupture of membranes in the general population was estimated to be 10% of all pregnancies [1], the incidence of pre-eclampsia was estimated to be 4% of all pregnancies [2], the incidence of hypertension was estimated to be 10% of all pregnancies [3], the incidence of ectopic pregnancies was estimated to be 2% of all pregnancies [4], and the incidence of gestational diabetes was estimated to be 6% of all pregnancies [5]. Using these population estimates, it was determined that an adequate sample size was obtained for all the above variables in this survey to have a confidence level of 95% that the real value is within $\pm 5\%$ of the surveyed value with each individual population proportion.

(Needed sample size of 139 for PROM, 60 for Pre-eclampsia, 139 for hypertension, 31 for ectopic, 87 for gestational diabetes: all of which were obtained). Finally, in order to calculate odds ratios to the general

population the number of pregnancies and births in the United States both had to be estimated. Recent CDC data was utilized to estimate the annual number of births in the United States as 3,791,712 [6] and the annual number of pregnancies as 6,155,000 [7].

Results

In total 192 surveys were received representing 96 sets of twins. Using the attendance at the festival alone, in which there is estimated to be 2,000 female twins annually, the response rate was estimated to be 9.6%. When factoring in the large number of surveys that were sent electronically, the response rate was likely much smaller than this. In total, surveys were received from 23 states, Canada, and Great Britain. 41.7% were from Eastern States, 40.6% were from the Midwest, 9.4% were from Southern States, 6.3% were from Western States, and 1% were from Canada and Great Britain respectively¹ (Figure 1). 172 of the twins identified as identical twins and 20 identified as fraternal twins. The average age of respondents was 43.3 years with a standard deviation of 17.0 years (Figure 2). Of the respondents, 87.5% identified as White/Hispanic, 8.3% identified as Black, 2.1% identified as Asian, and 2.1% identified as other. This racial breakdown is similar to the United States general population in which it is estimated that 78% are White/Hispanic, 12% are Black, 6% are Asian, and 4% identify as other [8]. Social factor results are identified in Table 1. Overall, the socio-economic factors that make up this twin cohort are similar to the general United States population.

Gynecological factors are identified in Table 2. A statistically significant greater number of identical twins reported having the same age of menarche than did fraternal twins (69.51% verse 33.33%, p-value: 0.0021). Other gynecological parameters did not have a statistically significant difference between identical and fraternal twins (Table 2).

Obstetrical factors are identified in Table 3. There was a total of 258 reported pregnancies. There were no statistically significant differences detected among the obstetrical parameters tested between identical and fraternal twins (Table 3). Only 9.8% of respondents reported knowing the number of amnions and chorions in their pregnancy. 11% (18/164) of identical twins reported knowing amnions and chorions in their pregnancy compared to 0% (0/18) of fraternal twins (p-value: 0.22). In the twin sample 9.1% of pregnant women reported smoking

¹ Eastern States: ME, NH, VT, MA, RI, CT, NY, NJ, PA, MD, DE.
Midwest States: OH, IN, MI, IL, WI, MN, IA, MO, AR, ND, SD, NE, KS, OK, TX
Southern States: WV, VA, KY, NC, SC, TN, GA, AL, MS, LA, FL
Western States: WA, OR, CA, NV, AZ, NM, CO, UT, WY, ID, MT, AK, HI



Figure 1: Respondent location by geographical area

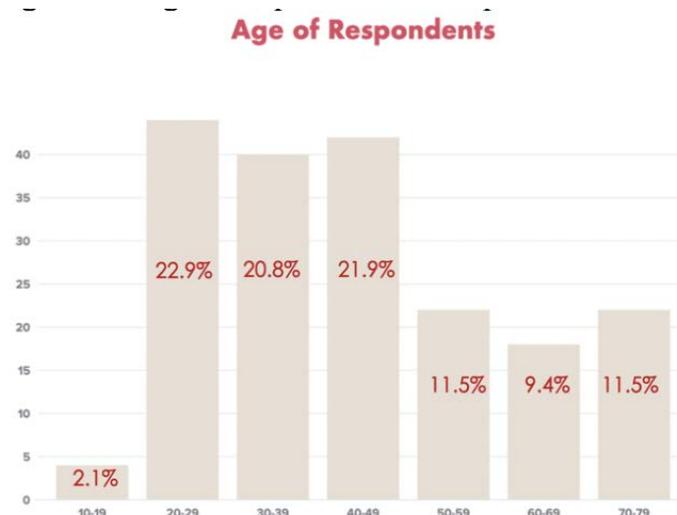


Figure 2: Age of respondents in sample

Tables 1: Social parameters in identical and fraternal twins.

Condition	Identical Percentage	Fraternal Percentage	P-Value (Chi Square or Fisher's Exact Test)	Total Percentage
Live in Same State	134/166 = 80.72%	16/20 = 80.0%	1.00*	150/186 = 80.65%
Same Occupation	82/159 = 51.57%	8/16 = 50.0%	0.9	90/175 = 51.43%
Smoker	13/166 = 7.83%	0/19 = 0%	0.37*	13/185 = 7.03%
Diabetes	9/167 = 5.39%	0/19 = 0%	0.60*	9/186 = 4.84%

Fisher's Exact Test represented by asterisk ()

Table 2: Gynecological parameters in identical and fraternal twins.

Condition	Identical Percentage	Fraternal Percentage	P-Value (Chi Square or Fisher's Exact Test)	Total Percentage
Same Age of Menarche	114/164 = 69.51%	6/18 = 33.33%	0.0021	120/182 = 65.93%
Abnormal PAP Smear	42/167 = 25.15%	2/15 = 13.33%	0.53*	44/182 = 24.18%
Birth Control	31/158 = 19.62%	3/19 = 15.79%	1.00*	34/177 = 19.21%
Endometriosis	8/167 = 4.80%	3/19 = 15.79%	0.089*	11/186 = 5.91%
Fibroid	37/167 = 22.16%	5/19 = 26.31%	0.77*	42/186 = 22.58%
Infertility	18/167 = 10.78%	3/19 = 15.79%	0.46*	21/186 = 11.29%
Gynecological Cancer	15/144 = 10.42%	1/19 = 5.26%	0.70*	16/163 = 9.82%
Osteoporosis	18/167 = 10.78%	2/19 = 10.53%	1.00*	20/186 = 10.76%

Table 3: Obstetrical parameters in identical and fraternal twins.

Condition	Identical Percentage	Fraternal Percentage	P-Value (Chi Square or Fisher's Exact Test)	Total Percentage
Pregnancy	96/167 = 57.5%	7/18 = 38.89%	0.14	103/185 = 55.68%
Ectopic	1/165 = 0.61%	0/19 = 0%	1.00*	1/184 = 0.54%
Pre-Eclampsia	9/131 = 6.87%	3/12 = 25.0%	0.065*	12/143 = 8.39%
Hypertension	12/132 = 9.09%	3/12 = 25.0%	0.11*	15/144 = 10.41%
Gestational Diabetes	11/130 = 8.46%	0/12 = 0%	0.60*	11/142 = 7.75%
PROM	32/128 = 25%	2/12 = 16.67%	0.73*	34/140 = 24.29%
Know Amnion and Chorion	18/164 = 10.98%	0/18 = 0%	0.22*	18/182 = 9.9%

Table 4: Percentage of women reporting obstetrical outcomes verse known population percentages.

Obstetrical Condition	Identical Percentage	Total Percentage	Reference Population Approximations
PROM	32/128 = 25%	34/140 = 24.29%	10% of all pregnancies
Pre-Eclampsia	9/131 = 6.87%	12/143 = 8.39%	4% of all pregnancies
Hypertension	12/132 = 9.09%	15/144 = 10.41%	10% of all pregnancies
Ectopic	1/165 = 0.61%	1/184 = 0.54%	2% of all pregnancies
Gestational Diabetes	11/130 = 8.46%	11/142 = 7.75%	6% of all pregnancies

Table 5: Obstetrical odds ratios in twin sample verse general population.

Condition	Reference Percentage	Minimum Percentage	Maximum Percentage	Minimum Odds Ratio	Maximum Odds Ratio
PROM	0.1	0.13	0.38	1.37 (0.95,1.96)	5.42 (4.21,6.98)
Pre-Eclampsia	0.04	0.047	0.12	1.17 (0.66,2.09)	3.16 (2.16,4.62)
Hypertension	0.1	0.058	0.15	0.56 (0.33,0.94)	1.6 (1.14,2.25)
Gestational Diabetes	0.06	0.043	0.13	0.7 (0.38,1.28)	2.38 (1.66,3.41)
Ectopic Pregnancy	0.02	0.0039	0.0039	0.19 (0.03,1.36)	0.19 (0.03,1.36)

at some point during their life. The percentage of women reporting given obstetrical outcomes verse the known reference population pregnancy percentages are represented in Table 4. Since pregnant women reported their total number of pregnancies and if they ever had a given obstetrical complication but did not report in how many of their pregnancies a complication occurred, two separate odds ratios were calculated. The first odds ratio was calculated assuming that only one of their pregnancies was affected (Minimum Odds Ratio) and the second odds ratio was calculated assuming all of their pregnancies were affected (Maximum Odds Ratio). The true odds ratio undoubtedly lies between these two calculations. The minimum and maximum odds ratios are shown in Table 5. Using these calculations, there was an increase between 37% and 442% in the odds of PROM and 17% to 216% in the odds of pre-eclampsia.

Discussion

There was an increased incidence of PROM and pre-eclampsia in our twin sample verse the general population. A literature review identified the incidence of PROM in the general population to be approximately 10% [1], whereas 24.3% of our pregnant women reported undergoing PROM in at least one of their pregnancies. Likewise, the incidence of pre-eclampsia in the general population is estimated to be about 4% [2], whereas 8.4% of our pregnant women reported having pre-eclampsia in at least one of their pregnancies. Since the number of pregnancies effected for each twin who had the condition was not known however, minimum and maximum odds ratios were calculated. Using this technique, the minimum odds ratio for PROM was 1.37 (95% CI=0.95,1.96) and the maximum odds ratio was 5.42 (95% CI=4.21,6.98).

Using the same technique the minimum odds ratio for pre-eclampsia was 1.17 (95% CI=0.66,2.09) and the maximum odds ratio was 3.16 (95% CI=2.16,4.62) in our twin sample verse the general population.

Since both PROM and pre-eclampsia are more likely in subsequent pregnancies when one pregnancy has been affected, it is likely that at least some of the women in our sample were affected in more than one pregnancy. Twin gestations themselves are associated with an increased risk of both PROM and pre-eclampsia. Whether there is a causative role behind the increased risk of PROM and pre-eclampsia during the antecedent twin gestation and subsequent pregnancies of these twin women remains unclear but is a potential area of further research. For instance, if twin women are more likely to develop pre-eclampsia than singleton women, aspirin prophylaxis for twin women may be routinely offered. Although there is wide variation on the usage of aspirin for pre-eclampsia prophylaxis, The American College of Obstetricians and Gynecologists (ACOG) does not currently list being a twin as an indication for prescribing aspirin for pre-eclampsia prophylaxis. Further, since the incidence of PROM and pre-eclampsia is known to vary across race, the racial breakdown in our sample needed to be similar to the general United States population for meaningful comparisons to be made. Overall, the socio-economic factors that make up this twin cohort are similar to the general United States population. The racial distribution of our twin sample was similar to the general population with 87.5% verse 78% identifying as White/Hispanic, 8.3% verse 12% identifying as Black, 2.1% verse 6% identifying as Asian, and 2.1% verse 4% identifying as other in our sample verse the general population respectively [8].

Another important consideration was the impact of smoking and PROM in our sample. Since smoking is a known cause of PROM it was very important to consider the potential role of tobacco use in our twin sample verse the general population. It has been estimated that in 2005, 13.8% of women reported smoking during pregnancy [9]. In our twin sample 9.1% of pregnant women reported smoking at some point during their life. Whether the tobacco use in the twin women occurred during pregnancy or not was not specified so the actual percentage

using tobacco during pregnancy was likely lower than 9.1%. Certainly, while smoking is often under-reported the smaller percentage in our twin sample verse the general population makes it unlikely that tobacco use played a significant role in our PROM findings.

The scant knowledge of amnionicity and chorionicity among twins was also striking. Although this is one of the most critical factors in the management and prognosis of twin gestations, less than 1 in 10 (9.9%) of twins sampled had this knowledge about their pregnancy. Interestingly, no fraternal twins (0/18) reported having this knowledge. However, every single twin who responded to this survey identified as either an identical or fraternal twin. Since 80 percent of all twins are dichorionic [2], and could thus be either identical or fraternal, the fact that 100% of the sample reportedly knew they were either identical or fraternal was curious. There appears to be a general lack of knowledge about the embryology of twin pregnancies among twins themselves.

There were both strengths and limitations to this study. Strengths included a diverse group of female twins in terms of both age and demographics and completely voluntary participation in the study. The cross sectional study design allowed multiple obstetrical and gynecological parameters to be analyzed at the same time. Finally, the medical literature was useful in providing comparisons to our study sample. A significant limitation of the study was that there was no way to definitively corroborate that the twins took the surveys independently despite instructions to not collaborate. Unfortunately, this resulted in the possibility of twin collaboration and respondent bias with a possible increased concordance in responses. Additionally, national population data was used as the population comparison group rather than matching to singleton women during the same time period. There was also a significant possibility of recall bias especially among older twins recounting obstetrical issues. The response rate was also lower than desired. Additionally, there were many non-statistically significant results and more identical twins than fraternal twins responded to the survey.

Conclusion

This study suggests a potential increase in PROM and pre-eclampsia in twin women, although further large scale research is necessary to further investigate if such a relationship exists. Further areas of research could include large scale analysis of PROM and pre-eclampsia in twin women and potential alterations in counseling and management of these pregnancies.

Author Contributions

NAK: Project development, Data collection, Data analysis, Manuscript writing

KCK: Project development, Data collection, Data analysis, Manuscript writing

All authors read and approved the final manuscript.

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Ethics Approval and Consent to Participate

This study was fully Institutional Review Board approved at Albany Medical College and written consent was obtained.

References

1. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics. Prelabor Rupture of Membranes: ACOG Practice Bulletin, Number 217. *Obstet Gynecol.* 2020; 135:e80-e97.
2. Creasy RK, Resnik R, Iams JD, Lockwood CJ, Moore TR, Greene MF. *Creasy & Resnik's Maternal Fetal Medicine, Principles and Practice.* 7th Edition, 2014; 756-781.
3. American College of Obstetricians and Gynecologists; Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstet Gynecol.* 2013; 122:1122-31.
4. American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin Number 193: Tubal Ectopic Pregnancy, 2018.
5. American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin Number 190: Gestational Diabetes Mellitus. 2018.
6. CDC National Vital Statistics Report, 2019. Births: Final Data for 2018. Centers for Disease Control and Prevention.
7. CDC National Center for Health Statistics, 2015. 2010 Pregnancy Rates Among US Women. Centers for Disease Control and Prevention.
8. Kaiser Family Foundation. 2020. Population Distribution by Race/Ethnicity.
9. CDC Morbidity and Mortality Weekly Report Surveillance Summary. Trends in smoking before, during, and after pregnancy – Pregnancy Risk Assessment Monitoring System (PRAMS), United States, 31 sites, 2000-2005. 2009; 58:1-29.