ORIGINAL ARTICLE

Body Mass Index among Adult Twins: The Importance of Sex Pairing

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ABSTRACT

Introduction: Opposite-sex (OS) twins provide a unique opportunity to detect sex pairing effects on adult body mass index (BMI) (normal [≤25 kg/m^2] and high [>25 kg/m^2]) while controlling for environmental factors that could have confounding influences in a natural setup. It is hypothesized that male hormones may be accountable for triggering growth both in the male and in his female cotwin. **Objective:** The study objective was to test the hypothesis that twin pairs (female-female, male-male, or male-female) differ with respect to BMI during adulthood adjusted for birth order, birth weight (BW) differences, race, and zygosity. **Design and Method:** This was a cross-sectional study analyzed using generalized estimating equation modeling to examine the association between sex pairing and BMI in a large cohort of twin sample (n = 22810, aged 18–97 years) from the Washington State Twin Registry. **Results:** Considering male-male twin pairs as the reference category, female-female twin pairs were more likely to have higher BMI (odds ratio: 1.64; 95% confidence interval [CI]: 1.44–1.86). Moreover, MF twin pairs had higher odds of high BMI compared with MM twin pairs (1.31; 95% CI: 1.09–1.57) after adjusting for age, race, birth order, BW differences, and zygosity. **Conclusion:** Our study was unique in comparing BMI among adult twins in terms of pair sex. The hormonal imbalance among OS twins relative to same-sex twins, from our hypothesis, with respect to high BMI during adulthood was refuted.

Key words: Body mass index, generalized estimating equation modeling, sex pairing (male-male, male-female, and female-female twin pairs) Washington state twin registry

INTRODUCTION

Globally, the prevalence of obesity has rapidly increased. The obesity epidemic affects all ages, races, and sexes in both developed and developing countries.[1] Childhood obesity is a prominent public health problem in the world, as >30% of children and adolescents were classified as overweight or obese in 2011–2012.[2] There has also been an increase in obesity during childhood continuing into adulthood.[3] Consequently, obesity is considered a major public health threat, as it is associated with adverse health conditions such as Type 2 diabetes, heart disease, stroke, breast cancer in women, and colorectal cancer.[4,5]

Body mass index (BMI) is an indicator that compares weight to body surface, usually calculated as weight (kg)/height (m^2); it is impacted by several environmental and genetic factors.[6,7] BMI is used to define underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obesity (≥30 kg/m^2) in adults.[8,9] The 2011–2012 national surveillance data reported 35% of the U.S. adults 20 years and above as obese. This is a significant increase compared to 31% and 23%, a decade (1999–2000) and two decades ago (1988–1994), respectively.[4,10] As the epidemic in the United States increases, researchers have explored several causes of obesity in their efforts to combat this chronic condition.[4]

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Several twin studies have demonstrated the factors that influence BMI during adulthood. These factors include zygosity, birth order, birth weight (BW) differences, sex, and physical environments.[4,7,11-17] Genetically informed studies predict the heritability of BMI to be on average about 75%.[4,18,19] Twin studies more often provide accurate heritability estimates compared to singleton and family studies for weight, height, and BMI: [3] This is because monozygotic (MZ) twins share 100% of their genetic background, and dizygotic (DZ) twins share on average about 50% of their genetic background. However, behavioral and environmental factors promote the expression of genes that influence BMI levels.[4,20] Twins (MZ or DZ) raised together usually share the same familial environment, thus allowing shared family environment and genetic features to be controlled for when comparing twin characteristics within a pair.[8,11] Furthermore, twin data conveniently control for confounders such as non-shared environment.[8]

Very few studies have examined the impact of sex pairing on BW and BMI among adult twins.[14,21,22] Bogl *et al.* showed that the transfer of testosterone from male-to-female fetus in opposite-sex (OS) twin pairs at birth is associated with higher BMI during adulthood compared to female-female twin pairs. They found BMI to be different between OS female (OS females: 47.6%), same-sex male (SS males: 47.0%), and same-sex female (SS females: 30.2%) twin pairs.[14] Similarly, Haberstick *et al.* found that there is a significant difference between males and females in the distribution of fat and subsequent body weight.[6] Other studies have alluded the relationships between sex pairing and reproductive outcomes in OS females compared to same-sex females.[23,24] Results showed that OS females have higher masculinized behavior; thus, this leads to reduced reproductive success over time. Since the literature lacks data on the effects of sex pairing on adult BMI among twins, the main objective of this study was to test the hypothesis that twin pairs (FF, MM, or MF) differ with respect to adult BMI adjusted for birth order, BW differences, race, and zygosity.

METHODS

Participants

Participants for this research study were recruited from the Washington State Twin Registry (WTR), a community-based registry.[25] The registry collects survey data on physical as well asm mental health and serves as a biorepository that includes DNA of over 8800 individual twins.[25,26] Twins completed surveys that encompassed items, such as zygosity, birth order, sociodemographic (race and gender), weight, height, and self-reported BW to infer BW differences. However, twins were classified into identical (MZ) or fraternal (DZ) using standard questions about childhood similarity that determined zygosity with >90% precision when compared with DNA-based methods.[27-29] The study was approved by the University of Washington's Institutional Review Board, and written informed consent was obtained from participants. Both male and female twins from Washington State have been recruited from driver's license and ID applications since 2002 into the WTR.[11]

Variables

BMI

The primary outcome, BMI (kg/m^2), was calculated from self-reported height and weight. The question asked, "What is your current height (in feet and inches) and weight (in pounds)? For our study, BMI was categorized into two; normal (≤25 kg/m^2) and high (>25 kg/m^2).

Birth order

Information on birth order was collected from all participants. The question asked, "Which twin was born first - you or your twin?

Higher BW

All participants completed a questionnaire asking which twin had a higher BW. The question asked, "Which twin weighed more at birth - you or your twin? In our study, sex pairing was coded as MM (male-male twin pairs; reference category) = 1, FF (female-female twin pairs) = 2, and MF (male-female twin pairs) = 3.

Statistical analyses

Descriptive statistics and bivariate analysis were computed: *t*-test and Mann–Whitney U-tests were used for quantitative variables, and Chi-square test for qualitative data comparisons. $P < 0.05$ was considered statistically significant.

Generalized estimating equation modeling (GEE) was conducted for modeling the best fit for twin data.

Twins provide naturally matched pairs or clusters within-twin-pair and between-pair effects.[30] This type of data requires a specialized standard regression model that reflects the paired structure of the data, which induces correlation between twins. The statistical analysis included estimating several factors influencing BMI using GEE modeling for bivariate and multivariate analysis. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N. Y., USA).

RESULTS

There were 2,2,810 individual twins (MM: 6062, FF: 12,176, and MF: 4572 pairs) included in this analysis. Mean ± SD for age was 41.57 (±18.15), for BMI was 25.86 (±5.57), and for the age twins started living apart was 4.52 (±1.64)

Table 1: Descriptive statistics

Continuous variables		
Variables (*n*=22810)	**Mean±SD**	**Minimum–Maximum**
BMI, kg/m²	25.86±5.57	13–72
Age, years	41.57±18.15	18–97
Age apart, years	4.52±1.64	0–7
Categorical variables	**Frequency (%)**	
Sex		
Male	8348 (36.6)	
Female	14462 (63.4)	
Race		
White	21352 (93.6)	
Hispanic	762 (3.3)	
Native	321 (1.4)	
Black	514 (2.3)	
Asian	814 (3.6)	
Pacific islander	162 (0.7)	
Others	270 (1.2)	
Country born		
USA	8866 (38.9)	
Elsewhere	13945 (61.1)	
Sex concordance		
Sex concordant	18238 (80)	
Sex discordant	4572 (20)	
Pair sex		
MM	6062 (26.6)	
FF	12176 (53.4)	
MF	4572 (20)	
Zygosity		
Dizygotic twins	10288 (45.1)	
Monozygotic twins	12522 (54.9)	
Birth order		
First	4059 (17.8)	
Second	4056 (17.8)	
BWD		
Different birth weight	6412 (28.1)	
Same birth weight	495 (2.2)	

BMI: Body mass index

[Table 1]. Overall, the sample population included 21,352 (93.6%) White, 514 (2.3%) Black, 814 (3.6%) Asian, 321 (1.4%) Native Americans, 162 (0.7%) Pacific Islander, and others 270 (1.2%). There were also 762 (3.3%) Hispanic.. About 80% of the sample population were sex concordant twins (male-male [MM] or female-female [FF] twin pairs). The frequency of MM was about 27%, FF was 54%, and MF was 20%. Majority of the twins were MZ (MZ, 54.9%).

Table 2 shows the bivariate analysis between BMI - categorized into ≤25 kg/m² and >25 kg/m² - and other study variables. A significant association was found between BMI and age, sex, sex concordance, sex pairing, zygosity (all $P = 0.01$), BW differences ($P = 0.03$), and all race ($P = 0.01$), except for the Hispanic ($P = 0.14$).

Table 3 contains the analysis of continuous and categorical variables according to sex pairing. We compared three sex pairing categories of MM: $n = 6062$, FF: $n = 12176$, and MF: $n = 4572$ twin pairs. While the mean age was significantly different between sex pair groups (MM: 41.81 ± 18.90, MF: 43.44 ± 19, and FF twins: 40.75 ± 17.37; $P = 0.01$), there was no significant association between mean age lived apart and sex pairing [Table 3]. Furthermore, our study showed a statistically significant association between sex pairing and BMI ($P = 0.01$), in all three comparisons (MM vs. FF, MM vs. MF, and MF vs. FF). FF twin pairs had higher frequencies of high BMI (47.6%) compared to MM twins (30.9%) and MF twin pairs (21.4%) ($P = 0.01$). There was no significant association between sex pairing and birth order. Of all the sex pair groups, FF pairs had higher (59.7%) different BW and were mostly MZ twins (66.5%).

The association between BMI and other study variables was further investigated using unadjusted and adjusted GEE analysis [Table 4]. Considering MM twin pairs as the reference category, FF twin pairs were more likely to have higher BMI (odds ratio: 1.64; 95% confidence interval [CI]: 1.44–1.86). Moreover, MF twin pairs had higher odds of high BMI compared with MM twin pairs (1.31; 95% CI: 1.09–1.57) after adjusting for age, race, birth order, BW differences, and zygosity.

Adjusted odds for association between BW differences and zygosity were not found to be significant. Although pair sex - the main independent variable in the model- was significantly associated with BMI, the contribution of sociodemographic factors, such as belonging to Asian race; 3.32 (95% CI: 1.99–5.56) and belonging to White; 2.04 (95% CI: 1.24–3.36), were the strongest in the adjusted model. The odds of high BMI among the natives were found to be 1.93 (95% CI: 1.22–3.06) higher compared with the reference category. While natives were less likely to have high BMI after adjustment for possible confounders native Americans were less likely to have high BMI (0.45; 95% CI: 0.27–0.73). Birth order was also found to be associated with BMI after adjustment for confounders. Second-born twins compared to the first-born were found to be more likely to have higher BMI (1.15; 95% CI: 1.04–1.28).

DISCUSSION

This current cross-sectional study examined a large cohort of twin sample ($n = 22,810$) from the WTR. Our study is unique

Table 2: Comparing sociodemographic characteristics, sex pairing, zygosity, birth order, and BWD between twins with BMI ≤ 25 and>25 kg/m^2 (*n*=22810)

Continuous variables	BMI (≤25 kg/m^2)	BMI (>25kg/m^2)	*P* value
	Mean±SD	Mean±SD	
Age	37.46±17.42	47.09±17.43	0.01*
Age apart	4.48±1.70	4.56±1.58	0.29*
Categorical variables	***n* (%)**	***n* (%)**	
Sex			0.01
Male	3445 (44.1)	4362 (55.9)	
Female	7665 (56.9)	5800 (43.1)	
Sex concordance			0.01
Sex concordant	8964 (52.9)	7985 (47.1)	
Sex discordant	2146 (49.6)	2177 (50.4)	
Sex pairing			0.01
MM	2509 (44.4)	3145 (55.6)	
FF	6455 (57.1)	4840 (42.9)	
MF	2146 (49.6)	2177 (50.4)	
Country born			0.21
USA	4306 (51.7)	4024 (48.3)	
Elsewhere	6804 (52.6)	6138 (47.4)	
Race			
White	10375 (52)	9572 (48)	0.01
Hispanic	356 (49.5)	363 (50.5)	0.14
Native	97 (31.6)	210 (68.4)	0.01
Black	210 (45.4)	253 (54.6)	0.01
Asian	555 (77.2)	164 (22.8)	0.01
Pacific islander	95 (62.5)	57 (37.5)	0.01
Others	120 (46.5)	138 (53.5)	0.06
Zygosity			0.01
Dizygotic twins	4878 (50.6)	4760 (49.4)	
Monozygotic twins	6232 (53.6)	5402 (46.4)	
Birth order			0.09
First	1830 (50.3)	1806 (49.7)	
Second	1904 (52.3)	1737 (47.7)	
BWD			0.03
Different BW	3029 (52.5)	2739 (47.5)	
Same BW	211 (47.1)	237 (52.9)	

*Mann–Whitney U-test. BW: Birth weight

in that we explored the relationship between sex pairing and adult BMI among twin pairs. Sex, sex discordance, and sex pairing showed significant relationships with adult BMI among twin pairs. However, for our study, we used sex pairing. We adjusted for birth order, age, race, BW differences, and zygosity. Frequency of high BMI was found to be greater among FF twin pairs, while MF twin pairs had the lowest frequency of high BMI [FF; 47.6% vs. MF; 21.4%; Table 3]. Our findings suggest that FF pairs and MF pairs are more likely to have higher BMI when compared to MM pairs [1.64; 95% CI: 1.44–1.86 vs. 1.31; 95% CI: 1.09–1.57; Table 4]. OS twins provide a unique opportunity to detect sex pairing effects on adult BMI while controlling for environmental factors that could have confounding influences in a natural setup. We observed that females with a female cotwin are more likely to have a higher BMI than females with a male

Table 3: A comparison between MM, FF, and MF

Variables	Total	Mean±SD MM (*n*=6062)	Mean±SD FF (*n*=12176)	Mean±SD MF (*n*=4572)	*P* MM and FF	*P* MM and MF	*P* FF and MF
Age	22810	41.81±18.90	40.75±17.37	43.44±19	0.01	0.01	0.01
Age apart	9726	4.53±1.63	4.54±1.64	4.47±1.66	0.77	0.27	0.13
		n (%)	*n* (%)	*n* (%)	*P* value	*P* value	*P* value
BMI							
Normal	11110	2509 (22.6)	6455 (58.1)	2146 (19.3)			
High	10162	3145 (30.9)	4840 (47.6)	2177 (21.4)	0.01	0.01	0.01
Race							
Hispanic	762	164 (21.5)	488 (64)	110 (14.4)	0.01	0.34	0.01
Native	321	64 (19.9)	203 (63.2)	54 (16.8)	0.01	0.54	0.02
Black	514	124 (24.1)	286 (55.6)	104 (20.2)	0.19	0.42	0.78
Asian	814	224 (27.5)	500 (61.4)	90 (11.1)	0.18	0.01	0.01
Pacific islander	162	42 (25.9)	100 (61.7)	20 (12.3)	0.35	0.09	0.01
White	21352	5699 (26.7)	11281 (52.8)	4372 (20.5)	0.01	0.01	0.01
Others	270	52 (19.3)	192 (71.1)	26 (9.6)	0.01	0.08	0.01
Birth order							
First	4059	1045 (25.7)	2283 (56.2)	731 (18)			
Second	4056	1035 (25.5)	2272 (56)	749 (18.5)	0.93	0.62	0.63
BWD							
Different BW	6412	1421 (22.2)	3829 (59.7)	1162 (18.1)			
Same BW	495	176 (35.6)	234 (47.3)	85 (17.2)	0.01	0.01	0.17
Zygosity							
Dizygotic	10288	1894 (18.4)	3846 (37.4)	4548 (44.2)			
Monozygotic	12522	4168 (33.3)	8330 (66.5)	24 (0.2)	0.64	0.01	0.01

cotwin. Note that living apart was not significantly different between the three sex pair groups; therefore, environmental factors were adjusted for. This observation, however, was contrary to a rather large population-based cohort study (n = 17,575 twins) that is based on a nearly complete registration of all twin births in Sweden between 1886 and 1958, where BMI was found to be moderately, but significantly higher, in MF pairs compared with FF twin pairs.[31]

Alexanderson *et al.* further explored the effects of age on BMI by examining a cohort in which twin subjects were divided into those <60 years of age and those 60 years or older. There was only a significant difference in subjects 60 years or older with respect to BMI (MF: 25.3 ± 4.0 and FF: 24.8 ± 3.9).[31] We excluded women who were of menopausal age (>50 years) to control for the confounding effects of age and menopause on adult BMI when compared to MF and MM twin pairs; the significantly high BMI among FF twin pairs persisted in our study after controlling for menopausal age (data not shown); our results contradicted the findings of Alexanderson *et al.*, which showed a high BMI among MF twins compared to FF twins, after adjusting for age. Therefore, our findings reject the hypothesis that male hormones may be accountable for triggering growth both in the male and in his female cotwin.[21]

The discrepancy between our results and that of others could be due to the impact of shared environment, which our study did not evaluate in depth. Although we did compare the number of years that twins were living apart to control for differences in factors associated with shared environment, we found no statistically significant association. The similarity between BMI groups (≤25 and >25 kg/m^2) for mean age twins started living apart in our study, controlled for shared environmental differences.

In our study, BW discordance did not show statistically significant associations with BMI after adjusting for age, sex pairing, race, birth order, and zygosity [Table 4]. In general, previous twin studies have showed that BW at the individual level is positively associated with later BMI.[15-17] Jelenkovic *et al.* study, using regression coefficients, found that a 1 kg increase in BW was associated with up to 0.9 kg/m^2 higher BMI.[15] The association between BW discordance and BMI during adulthood of 27 twin cohorts (78,642 twin individuals: 20,635 MZ and 18,686 same-sex DZ twin pairs)

Table 4: Adjusted and crude odds ratio for BMI

Variable	OR (95% CI)	AOR (95% CI)
Age	1.03 (1.02–1.03)	0.97 (0.96–0.97)
Sex pairing		
FF	0.63 (0.56–0.71)	1.64 (1.44–1.86)
MF	0.80 (0.68–0.94)	1.31 (1.09–1.57)
MM	1.00	1.00
Hispanic (yes)	0.89 (0.75–1.07)	0.85 (0.61–1.18)
No	1.00	1.00
Native (yes)	1.93 (1.22–3.06)	0.45 (0.27–0.74)
No	1.00	1.00
Black (yes)	1.75 (1.21–2.54)	0.80 (0.48–1.35)
No	1.00	1.00
Asian (yes)	0.35 (0.25–0.48)	3.32 (1.99–5.56)
No	1.00	1.00
Pacific Islander (yes)	0.50 (0.24–1.02)	2.12 (0.94–4.77)
No	1.00	1.00
White (yes)	0.97 (0.78–1.20)	2.04 (1.24–3.36)
No	1.00	1.00
Others (yes)	1.32 (0.86–2.02)	1.27 (0.53–2.57)
No	1.00	1.00
Birth order		
Second	1.08 (0.99–1.19)	1.15 (1.04–1.28)
First	1.00	1.00
BWD		
Same birth weight	1.22 (1.01–1.48)	0.93 (0.76–1.14)
Different birth weight	1.00	1.00
Zygosity		
Monozygotic	1.13 (1.06–1.20)	1.00 (0.88–1.13)
Dizygotic	1.00	1.00

BMI: Body mass index, CI: Confidence interval, OR: Odds ratio

participating in the Collaborative project of Development of Anthropometrical measures in Twins (CODATwins) project showed that greater BW within MZ and DZ twin pairs is associated with higher BMI.[15] The association between BW differences and BMI persisted during childhood but declined during late adolescence (aged 20–29 years; 0.41 and 0.68 kg/m^2/kg in males and females, respectively).[15] Similarly, in the young adult Belgian MZ twins study, the heavier twin at birth had a higher BMI when the BW difference exceeded 5%, 10%, and 15%.[16,17] Twins, aged 18–34 years, were randomly selected from the East Flanders prospective twin survey: Results showed that BW discordance accounted for differences in adult body composition among twins.[17]

We also did not find statistically significant associations between zygosity and BMI [Table 4]. In contrast, our study showed that MZ twins had higher BMI compared to their DZ counterparts. We did not find statistically significant relationships between zygosity and BMI, after adjustment for age, race, pair sex, BW differences, and birth order. Jelenkovic *et al.* studied the zygosity differences in height and BMI of twins from infancy to old age. They retrieved height and BMI measurements from an international database of 54 twin cohorts (aged 1–102 years, *n* = 8,42,951) to analyze zygosity differences in mean values and variances of height and BMI among male and female twins from birth to adult.[13] Contrary to our study, Jelenkovic *et al.* study showed that DZ twins had 1.9% greater BMI than MZ twins, varying across middle and late childhood. The small but significant zygosity differences detected in this study showed the importance of large sample sizes to detect such differences.[13]

Furthermore, our study found that the second-born twins had greater BMI than their first-born counterparts. This is contrary to the findings from a pooled study of 26 twin cohorts that participated in the CODATwins project. Yokoyama *et al.* showed that, in MZ twins, the first-born twins had greater BMI than the second-born twins; similarly, in DZ twins, the first-born twins had greater BMI than the second-born twins.[12] However, it is important to note that the authors only observed statistically significant associations between birth order and BMI before 12 years of age in MZ twins and 5 years of age in DZ twins.[12] Our findings suggest that the second-born twins had greater BMI than the first-born twins. This may be because the age of our study participants had a narrower range (18 and 97 years), and the association between twins' birth order and BMI was not genetically analyzed based on zygosity differences, compared to Yokoyama *et al.* study.[12]

Interestingly, deviating from the research questions, our study found an association between sociodemographic factors (race) and BMI [Table 4]. Asian and White twins had greater odds of having high BMIs (3.32 [95% CI 1.99–5.56] and 2.04 [95% CI 1.24–3.36]), respectively, while native twins were less likely to have high BMIs, after controlling for age, pair sex, birth order, birth weight differences, and zygosity. We did not find any study that directly evaluated the relationship between race and high BMI among adult twins. Nevertheless, several singleton studies show similar racial/ethnic disparities with respect to high BMI among adults in the United States.[32]

Strengths and limitations

Our study has both strengths and limitations: First, we performed the first twin study of the relationship between sex pairing and BMI. Second, we used GEE analysis; using this twin modeling approach, we were able to take the cluster nature of twins into consideration. Our study used cross-sectional data, thus limiting our ability to infer any of our results causal relationship between sex pairing and BMI. Data on BMI and other study variables were derived from self-reports; they are consistent to a large extent; however, self-reported data are potentially subject to incorrect information and thus subject to recall bias. Although our twin sample was representative of Washington State, it is largely white and well-educated, thus limiting generalizability of results to other populations. A note of warning about our findings is that we had no data on chorionicity and placentation of these twins. This may, however, account for some proportion of intrauterine shared environmental influence.

CONCLUSION

FF twin pairs had higher BMI compared to MF and MM twins. Our study was unique in comparing BMI among adult twins in terms of pair sex. The hormonal imbalance among OS twins relative to same-sex twins, from our hypothesis, with respect to high BMI during adulthood was refuted. Further studies can compare differences in adult BMI among pair sex groups using genetic analyses.

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