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Female Infertility and Obesity across the United States—A Geographic Cross-Sectional Analysis

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Abstract

This cross-sectional study investigates a connection between female infertility and obesity across various regions of the United States, utilizing data from the NIH's "All of Us" Researcher Workbench. Analysis suggested that the Southern region exhibited the highest percentage of concurrently infertile and obese females at 32.3%, in contrast to the lowest in the Western region at 28.7%. The findings underscore the significant regional disparities in obesity-related infertility, particularly in medically underserved areas where healthcare access is limited. The study highlights the urgent need for targeted public health interventions, particularly in the Southern United States, to address the rising prevalence of obesity and its impact on infertility. Further, these results advocate for enhanced public health education and policies aimed at improving healthcare accessibility, with the goal of mitigating the adverse effects of obesity on reproductive health.

Keywords

Female, Infertility, Medical Deserts, Obesity, South

1. Introduction

Female infertility is a significant health concern in modern America, with notable physical and emotional implications, including stress and grief to both the affected individual and her partner [1]. The Centers for Disease Control (CDC) reports that in the United States, approximately 1 in 5 nulliparous women aged 15 to 49 are unable to conceive after one year [2]. It is recommended that a woman undergo an infertility evaluation if she has not been able to conceive a successful pregnancy within 12 months of unprotected intercourse if younger

than 35 or after 6 months of unprotected intercourse if she is older than 35 years of age [3]. An assessment for infertility can include body mass index and vital signs, thyroid evaluation, breast exam, signs of excessive androgens, inspecting cervical anatomy, presence of pelvic masses or tenderness, uterine and tubal evaluation, and a transvaginal ultrasound [3]. It is also recommended to assess the patient's ovarian function and reserve in addition to specific endocrine serum levels, such as cycle day 3 Follicle Stimulating Hormone (FSH), estradiol, and Anti-Mullerian hormone levels must be obtained. Insufficient production of hormones and reduced follicle count can lead to an elevated FSH and result in a poor ovarian reserve.

Obesity rates have increased in developed countries, and obesity has overtaken smoking as a leading cause of premature death in these countries [4]. With the rates continuously increasing, it has been estimated that the newest generation will have a shorter life expectancy [4]. Studies have shown that 23% of women aged 20 to 44 years old are obese, and that the percentage of obesity increases with increasing age [5]. Obesity can be categorized based on an individual's body mass index (BMI), taking into consideration both their height and weight. Obesity class I is defined as a BMI of 30.0 kg/m^2 to 34.9 kg/m^2. Obesity class II is defined as a BMI of 35.0 kg/m^2 to 39.9 kg/m^2, and obesity class III is a BMI over 40.0 kg/m^2. Obesity has many factors that play into the severity of the disease. To some extent, obesity is an inherited disease, but it is also influenced heavily by environmental factors. With obesity comes substantial social, occupational, and economic burdens for patients. Obesity has also been shown to be associated with higher prevalence in individuals with bipolar disorder and schizophrenia. Being obese carries many burdens on a woman whether that be physically, mentally, or socially, and is influenced by biological, environmental, and culture factors [6].

The health implications of obesity are numerous, with some affecting reproductive ability in both genders. With infertility on the rise, studies have examined the numerous possibilities that implicate obesity in female infertility. One such route associates the increased adipose tissue with reduced oocyte maturation by promoting functional hyperandrogenism and hyperestrogenism, which causes an imbalance of the Hypothalamic Pituitary Axis, which triggers anovulation [7]. Overall, obesity affects sex hormone secretion and metabolism which will ultimately result in differences in the availability of estrogens and androgens, disrupting the menstrual and ovulation cycles, which are both very sensitive to change and important in pregnancy and ovulation. With increased adipose tissue in obese patients, there is an increase in peripheral aromatization of androgens to estrogens. Body fat affects the HPO axis—a main regulator of LH, FSH, Estrogen, and Progesterone, which are all important components of female fertility, ovulation, and pregnancy [7]. This also causes a decrease in sex hormone binding globulin which will result in increased free estradiol and testosterone. Obesity can also cause hyperinsulinemia which further decreases sex

hormone binding globulin and stimulates ovarian androgen production. Hypersecretion of luteinizing hormone occurs leading to increased androgen to estrogen ratio which can impair folliculogenesis and result in follicular atresia. Increased adipose tissue also leads to changes within the body associated with inflammation, coagulation, and fibrinolysis. Additionally, many forms of obesity are characterized by a condition of leptin resistance. This, in turn, impacts GNRH pulsatility which affects fertility. Furthermore, leptin inhibits granulosa and thecal cell steroidogenesis in the ovary impacting ovulation and infertility [7].

It has been shown that with weight reduction, one can significantly alter fertility and pregnancy outcomes. It has also been found that women with a body mass index above 27 kg/m^2 had increased ovulation with weight loss [3]. They found that a loss of 10% of the patient's body weight can restore ovulation in 50 to 100% of patients in less than one year [3].

This study was designed to assess correlations between reported female infertility, obesity, and geography in the United States of America.

2. Methods

This cross-sectional study used the National Institute of Health's (NIH) "All of Us" Researcher Workbench to first create a workspace titled "Incidence of female infertility due to obesity in US regions." The NIH "All of Us" works to get individual data by first getting a consent form after watching videos giving detailed information about the program. Then, a person can consent to have their electronic health record shared with the website, but if not, participants can still participate by answering health surveys. Next, you can consent to sharing your DNA results. You then can answer health surveys. From there, you can visit a partner center to have physical measurements taken and provide biosamples. Our study observed rates of Female Infertility and Obesity via surveys taken from November 2019 to February 2021. The data was extracted, while excluding "sex assigned at birth—male" participants (**Figure 1**). The US was divided into four regions based on zip code. The first three digits of each participant's zip code were logged and localized to the Midwest, Northeast, South, or West. The Midwest had participants from Wisconsin, Michigan, Iowa, Illinois, Indiana, and Ohio. The Northeast region had participants from Pennsylvania, New York, and the District of Columbia. The South had participants from Louisiana, Texas, Mississippi, Alabama, Georgia, Tennessee, South Carolina, Virginia, Florida, and Arkansas. The West region had participants from California, Washington, Colorado, Arizona, Utah, and New Mexico (**Figure 2**). The participant's data was coded into the Python analysis software and then into Microsoft Excel. The number of participants with both female infertility and obesity was then compared to the number of females with infertility only and compared against each region to establish a correlation percentage (**Table 1**). Statistical analysis used Chi-Square and focused on identifying degrees of freedom to determine if there was a real difference in rates among regions.

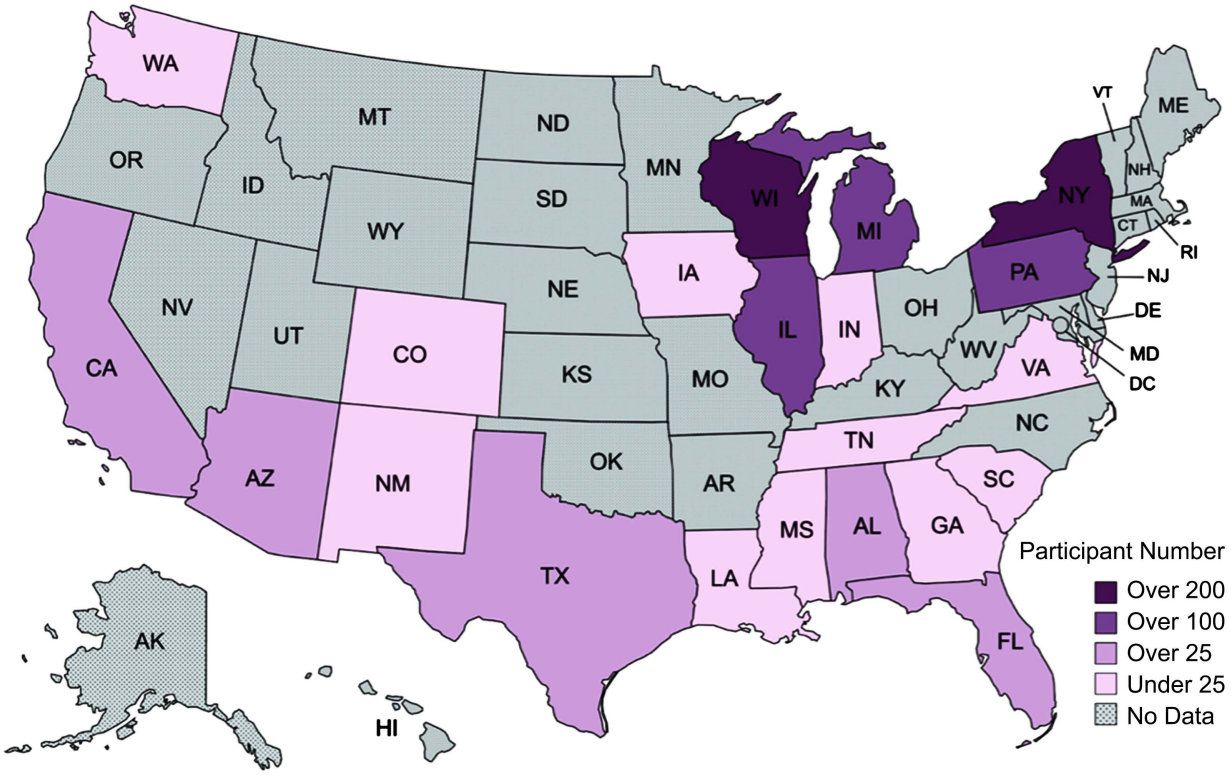

Figure 1. Number of all U.S. participants in each state with female infertility and obesity. States that are grey have no participants. Hyperdensity is relative to the number of participants that are part of all U.S. programs with female infertility and obesity.

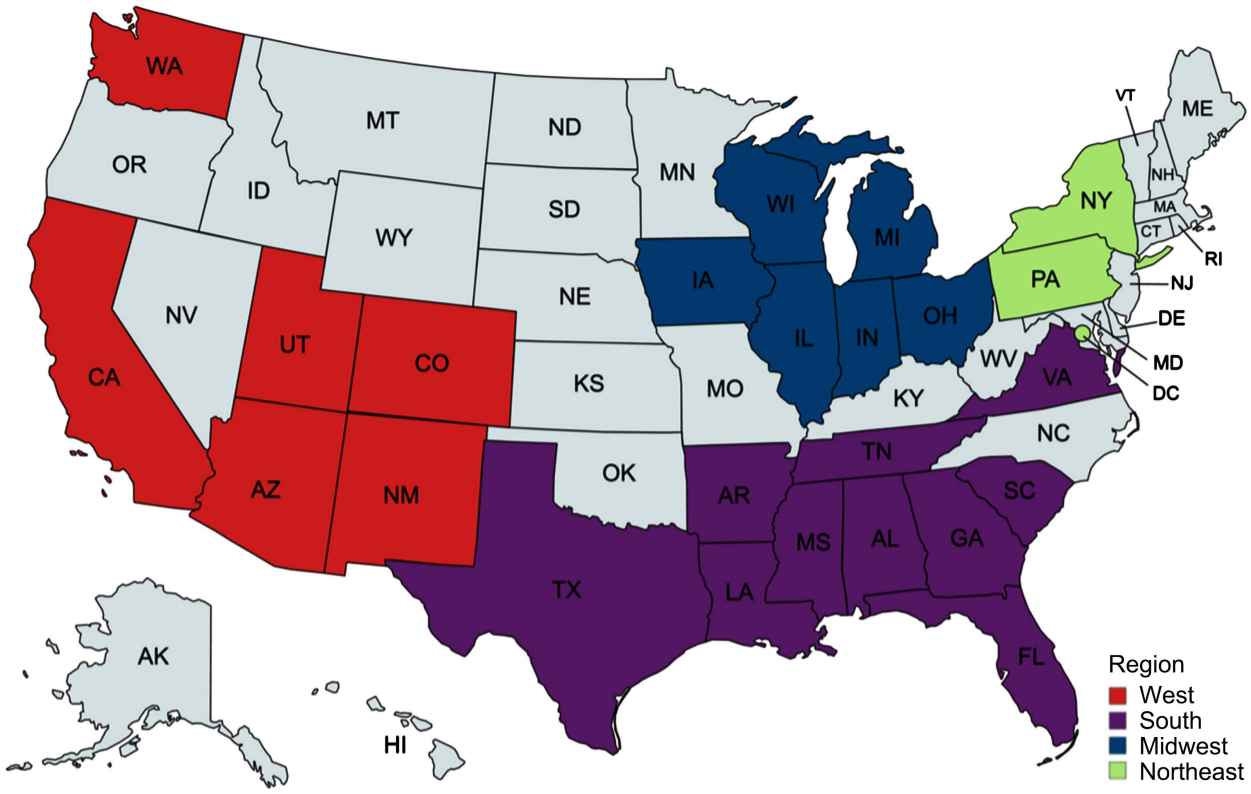

Figure 2. States with participants in the NIH all U.S. database divided into their respective regions.

Table 1. Control vs participant number of infertile + obese females across geographic regions. The number of females with infertility and obesity was compared to number of infertile females (control) in their corresponding regions and expressed as a percentage (females infertile + obese female infertile only).

Region	Females Infertile Only	Female Infertile + Obesity	Region	% Females Infertile + Obese compared to Infertile only
West	231	93	**West**	28.7
Midwest	1182	481	**Midwest**	28.9
Northeast	1062	491	**Northeast**	31.6
South	279	133	**South**	32.3

3. Results

The number of participants who were infertile females was 2754, with 1182 participants from the Midwest, 1062 from the Northeast, 279 from the South, and 231 from the West. Those who were concurrently infertile and obese were 1,198 participants (Midwest = 481, Northeast = 491, South = 133, West = 93). The percentage for each region were: Midwest (28.9%), Northeast (31.6%), South (32.3%), and West (28.7%).

The results suggest that the Southern US region has the highest percentage of concurrently infertile and obese females compared to the rest of the country, whereas the region with the lowest percentage was the West (**Figure 3**). The Southern region was shown to have a significant degree of female infertility and obesity when compared to the other United States regions, via a Chi-squared study with results yielding 467.376 with 3 degrees of freedom. This suggests that there is a statistically significant relationship between the variables in the study being tested. These findings were statistically significant (two-tailed P value < 0.0001). From this research, we can suggest that the Southern region has the highest rates of concurrent female infertility and obesity.

4. Discussion

4.1. Overall Study

This study examined the associations between female infertility and obesity among the different United States regions with the southern region having the highest percentage (32.3%). This study serves as a platform to emphasize the need for increased awareness of the implications of obesity with increased access to health education and medical care, particularly in the southern states, which may help improve infertility. Women of childbearing age (20 - 44) who are obese women have been reported to be 62% more likely than non-obese women to suffer from infertility [8]. The risk of infertility has been shown to be threefold higher in obese than in non-obese women, with the probability of spontaneous conception declining linearly once BMI is above 29 kg/m^2 [9]. Weight loss equal to 5% - 10% of the body weight has been suggested to improve fertility rate, with

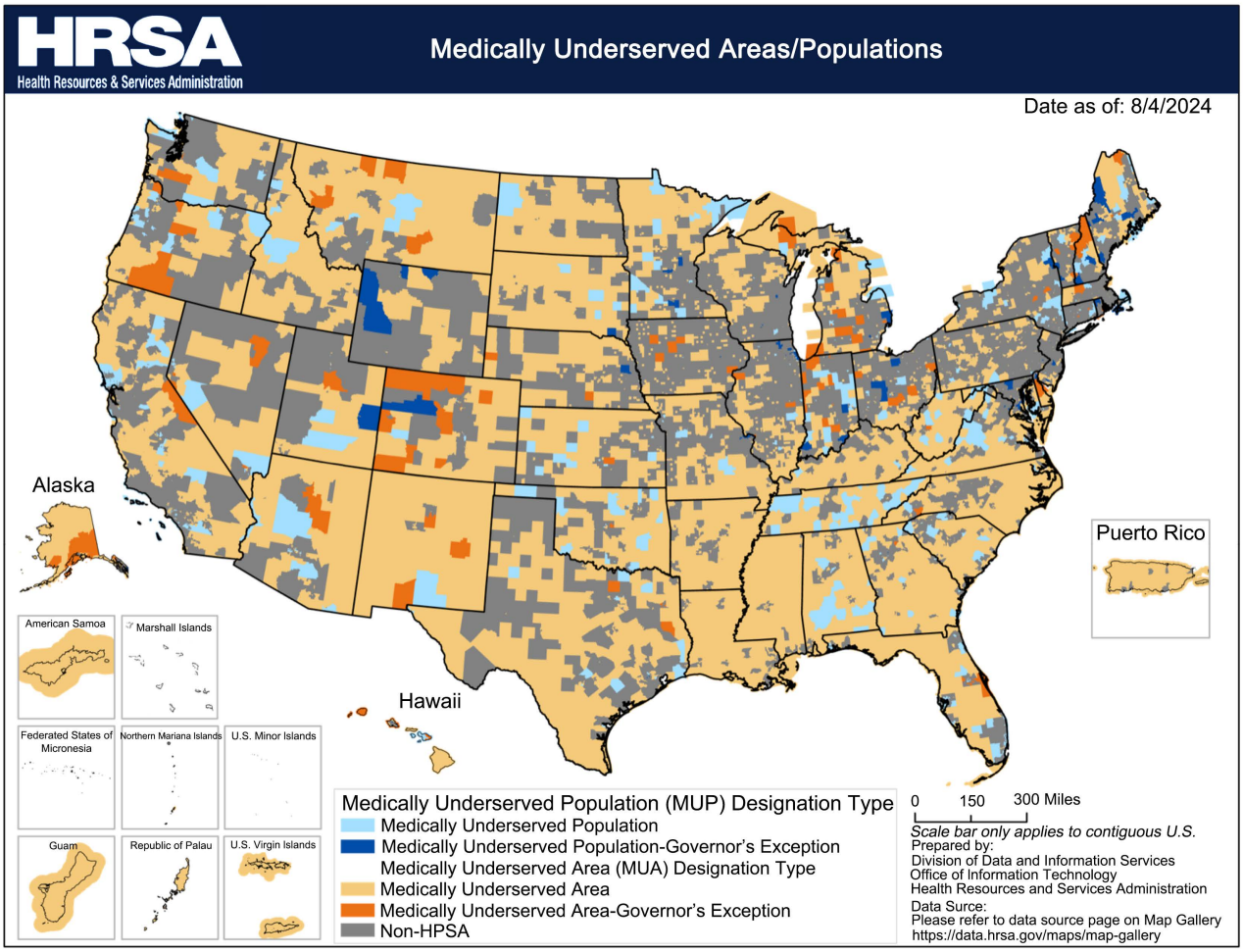

Figure 3. Health resource & services administration medically underserved areas/population USA map.

a loss of just 5% body weight improving the overall endocrine hormone parameters in women [9].

In addition to the southern United States having the highest percentage of both obese and infertile women, the area is also relatively deficient in healthcare with a prevalence of rural and medically underserved areas, suggesting a lack of sufficient access to care. Thus, areas with limited accessibility may have a higher incidence of medical problems such as obesity and the complications that result from it, such as infertility. According to Reference [10], the Health Resources and Services Administration (HRSA), Medically Underserved Areas are areas within the United States that have "too few primary care providers, high infant mortality, high poverty or a high elderly population" [10]. As of January 2024, the HRSA ranks Texas, Georgia, Virginia, and Florida in the top ten states with the most medically underserved areas, all of which are in the southern region of the United States (**Figure 3**). Additionally, a study completed in 2020 on the physician workforce projected that by the year 2030, the southern region of the United States will have the largest physician shortage of any of the four regions, and Louisiana and Mississippi will be two of the top three states with the most

severe physician shortages per capita [11].

According to a study that assessed the enactment rate and efficacy of various state-level policies to combat obesity, "state-level policies can be tailored to address the unique needs in the state, by focusing on specific societal challenges such as inadequate access to healthy foods, barriers to physical activity, and obesogenic food environments" [12]. A targeted approach to obesity prevention and reduction should be taken on a state-by-state basis according to the relative rates of obesity and infertility stratified on the obesity map. If access to care is increased in medically underserved and at-risk populations, obesity rates may decline possibly improving rates of infertility.

One potential confounding variable is the high rate of occurrence of sexually transmitted diseases in the southern United States. According to Reference [13], the Center for Disease Control's most recent Sexually Transmitted Disease (STD) Surveillance Report, seven out of the ten states with the highest rates of sexually transmitted diseases are states in the southern United States, including Mississippi, Florida, Georgia, Louisiana, South Carolina, North Carolina, and Alabama [13]. Notably, these southern states are in the region with the highest rates of both infertility and obesity, as discussed previously in this study. With this in mind, it is important to consider the long-term effects of sexually transmitted diseases on fertility. In one retrospective cohort study investigating the long-term sequelae of Pelvic Inflammatory Disease and its ramifications on reproduction, 25% of participants were shown to meet the criteria for infertility at 69 months (approximately 6 years) post-hospitalization for PID [14].

Many of the states in the southern United States with the highest rates of concurrent obesity and infertility also rank low in education on a national scale [15]. Higher quality, more in-depth health education in these areas has the potential to mitigate some of these factors contributing to both obesity and infertility, both of which can have detrimental effects on one's quality of life. One way to increase public health education in this region could be through enacting new public policies guiding educational requirements tailored for each age level. In some circumstances, in terms of giving students an appropriate knowledge base about reproductive health as well as dietary education, and this lapse in understanding could be a major factor in the high rates of obesity and other morbidities in the United States. Educational programs within schools designed to revolutionize the way children in America learn about diet, exercise, and reproductive health have the potential to mitigate many of these detrimental health concerns. Additionally, more policies and initiatives to then build on this education base as those students become adults would be instrumental in making a true difference in these poor health statistics. Aside from educational initiatives in schools, physicians can make a large impact in the effort to increase awareness by informing patients individually about the modifiable risk factors affecting fertility, such as obesity, and what can be done to intervene and improve fertility and overall health.

4.2. Limitations

A strength of the study includes the use of the NIH All of Us Researcher Workbench, which offers diversity and representation by accessing many areas and populations across the United States. Although the database is large, the data contained is dependent on personal contributions, resulting in both limited input across some states and triggering a reporting bias. Another limitation of the study includes the presence of confounding factors such as STDs may play a role in the findings reported.

5. Conclusions

Our study suggests that southern states are associated with disproportionately high rates of obesity, infertility, and limited access to healthcare resulting in a vicious cycle of medical concerns for the region's inhabitants. Similarly, patients in these areas are affected by the higher sexually transmitted disease rates which can have short and long-term medical implications. Addressing medical access may improve obesity which can ultimately help reduce infertility.

The results of this cross-sectional study have many significant implications for reproductive healthcare. Firstly, the findings necessitate increased awareness about infertility and its correlation with obesity and insufficient healthcare, specifically in the southern region of the United States. Many laypersons without extensive healthcare knowledge—and potentially even many professionals within the healthcare field—may be unaware of the impact that obesity can have on one's ability to conceive. While many factors contribute to infertility, this study has reaffirmed the importance of the correlation between obesity and infertility and has brought attention to the degree to which the prevalence of these healthcare issues differs between regions within the United States. One of the most important conclusions that must be drawn from this study is the need for increased awareness about the relationship between obesity and infertility and more public health education about the prevalence of obesity and infertility, particularly in at-risk populations and regions in which the incidence is high for both conditions. One pivotal step towards increased awareness is improved public health education, specifically with regard to reproductive health. Physicians and other healthcare professionals are often trusted by their patients, affording them a unique position to be able to discuss sensitive issues with their patients such as weight loss and infertility. When patients feel comfortable with their healthcare provider and a trusting relationship has been established, it opens the door for these conversations to take place in a humanistic, caring way, allowing for increased awareness and education about potential avenues of medical management for these comorbidities that are often reversible. Many factors affecting fertility and leading to the rise in infertility nationwide can be mitigated if the public is aware of them. Studies such as this only help to further inform medical professionals and the public alike on how to manage these risk factors to decrease the rising infertility rates.

In addition to increasing awareness nationwide about the implications of obesity on infertility, more effort must be focused on managing obesity to hopefully help improve fertility, and this study highlights the true importance of this. As previously discussed, the prevalence of obesity has increased at such a rate that it has surpassed smoking as a leading cause of premature death in developed countries. As mentioned previously in this study, it has been predicted in the New England Journal of Medicine that approximately half of the American population will be considered obese by 2023. If the United States continues this trajectory, countless other comorbidities and effects of obesity will become extremely prevalent, claiming even more lives prematurely and decreasing the quality of life of many individuals who are members of the American population. The results of this cohort study provide promising insight, however, into the potential for reversal of one of the most devastating effects of obesity—infertility—with proper weight management and dietary control. Considering that one in five women of childbearing age are unable to conceive within one year of trying to conceive according to the Centers for Disease Control, infertility must be discussed openly and studied further if society is to see true improvement of these statistics. Additionally, results of studies such as this should be used to guide current clinical practices and information given to patients in an effort to help combat infertility with tangible, realistic interventions.

The region-based approach of this study is also useful in guiding educational efforts to increase awareness in the most at-risk regions of the United States. If a region-based approach is taken perhaps by federally funded programs to decrease obesity rates in at-risk populations, the southern region of the United States would be of the utmost priority and should be the first region targeted with initiatives. The combination of efforts by physicians and other medical professionals, educators, and federal and state governments, increased awareness about the unfortunate effects of obesity—namely, infertility—and ways to combat these effects is not only attainable but more necessary than ever for the health of the American population.

One extremely important factor to consider is that the lack of access to medical deserts and medically underserved areas plays a significant role in the higher rates of infertility and obesity in many areas of the United States. Therefore, this necessitates increased access to health education and medical care across the country, particularly in these medically underserved populations, if any true decrease in obesity and infertility rates is to be seen. The results of this study showed, unsurprisingly, that many of the areas that are considered medically underserved populations are also in the southern region of the United States, which is the region with the highest rates of concurrent obesity and infertility. It is entirely reasonable to deduce that a large factor in the high prevalence of these medical conditions is the lack of access to healthcare education and timely, high quality medical care. With access to the proper tools and information, many patients who are considered to be members of a medically underserved population

who also have concurrent obesity and infertility could likely have an excellent chance of drastically improving both conditions.

This cross-sectional study aimed to show just how prevalent the correlation between obesity and infertility is in today's modern society and how concentrated in certain regions of the United States these problems can be; this necessitates further research into all the factors that are potentially contributing to this high concentration of concurrent obesity and infertility in the southern region of the United States specifically. While we postulate that this could be due to the high concentration of medically underserved communities in the south as well as cultural aspects such as cuisine and potentially sedentary lifestyles in many cases, there are other factors that must be considered and researched as well in future studies. With the extremely impressive developments in modern medicine that have changed millions of lives and improved the quality of life of countless patients, we as a society often forget that sometimes the simplest interventions can make the largest difference. For conditions as prevalent and detrimental as both obesity and infertility, the quality of life of millions could be drastically improved by the findings and interventions suggested in this study.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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