Using the Edmonton Obesity Staging System to predict mode of delivery after labor induction

by

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ABSTRACT

Objective: To evaluate the use of the Edmonton Obesity Staging System for Obstetrics (EOSSo) in predicting cesarean delivery amongst term, nulliparous, singleton pregnancies in women with overweight or obesity, who are undergoing an induction of labor.

Methods: A prospective-cohort study was performed in Edmonton, Alberta, Canada. Women undergoing an induction of labor at term were recruited to either a sample cohort, including women with a body mass index (BMI) of ≥25.0 kg/m^2 at first antenatal visit, or a control cohort with a BMI of 18.5-24.9 kg/m^2. Participating women provided a self-reported health history and consented to review of their medical records allowing allocation into EOSSo categories. The primary outcome was the rate of cesarean delivery based on EOSSo category. Secondary outcomes consisted of a summary score of adverse maternal, delivery, and neonatal events.

Results: Overall, 345 women were recruited, with a participation rate of 93.7%. The sample cohort consisted of 276 women with overweight or obesity, while the control cohort included 69 normal weight women. Overall rate of cesarean delivery was 30.4% for the control cohort and 35.8%, 29.9%, 43.2%, and 90.5% for women assigned an EOSSo category 0, 1, 2, and 3, respectively ($P < 0.001$). A summary score was not indicative of overall rate of adverse maternal, delivery, and neonatal events ($P = 0.22$).

Conclusion: The EOSSo may help predict the chance of cesarean delivery in a high-risk group of nulliparous women with overweight or obesity, who are undergoing an induction of labor at term.

PREFACE

The research project, of which this thesis is a part, received research ethics approval from the University of Alberta Research Ethics Board: THE USE OF THE EDMONTON OBESITY STAGING SYSTEM TO PREDICT MODE OF DELIVERY IN PARTURIENTS WITH OVERWEIGHT AND OBESITY AND UNDERGOING AN INDUCTION OF LABOR, No. Pro00075527, October 12, 2017.

This thesis is an original work by Ashley Demsky. At the time of this submission, no part of this thesis has been previously published. I was responsible for project development, project management, data collection and analysis as well as the manuscript composition. S. Stafford assisted with the data collection and contributed to manuscript edits. M. Yaskina assisted with data analysis. A. Sharma was a supervisory author and was involved with concept formation and manuscript edits. D. Birch, J. Schulz, and H. Steed were also supervisory authors and were involved with manuscript edits.

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INTRODUCTION

1.1 OBESITY PREVALENCE AND IMPACT

The health of Canadians is increasingly compromised by soaring rates of obesity. Current estimates suggest that one quarter of Canadian women are classified as having obesity and over half as having overweight or obesity.[1] These numbers are on par with other developed nations, such as the United States, where about 23.4% of women will have a pre-pregnancy body mass index (BMI) that classifies them as having obesity.[2]

There is a growing body of literature examining the adverse effects of obesity on health outcomes. A recent article reviewed the major co-morbidities associated with obesity in non-pregnant individuals.[3] It discussed an increased risk in diabetes, cardiovascular disease (CVD), obesity-hypoventilation syndrome, chronic kidney disease, non-alcoholic fatty liver disease, subfertility, gastroesophageal reflux disease (GERD), cancer, depression, limitations in physical functioning, and osteoarthritis. This represents only some of the significant related health outcomes. A crisis is looming and to date there has been an inadequate response and plan to reduce the burden of this disease.

Obesity remains a leading public health concern worldwide, but the health of pregnant women, with obesity, is particularly concerning. Elevated weight in pregnancy can be detrimental to maternal and fetal health and its impact can persist after delivery. Obesity itself is considered a modifiable risk factor. Therefore, strategies to reduce disease in this population could significantly improve maternal and fetal health outcomes.

1.2 OBESITY AND MEDICAL EDUCATION

Recognizing obesity as a pervasive chronic disease is only the initial step in attempting to reduce the burden of disease. A literature search on PubMed using the defining terms "pregnancy and obesity and outcomes" yielded only 5 results year 2000, whereas in 2018 the result count increased to 385. While there has been an increase in research velocity, particularly over the past two decades, and the breadth of knowledge regarding the detrimental effects of obesity is increasing, the rate of knowledge translation to healthcare practitioners may be lagging. There is currently a lack of obesity curriculum and training in medical schools. When the US medical licensing examinations were audited, it was determined that these exams missed key concepts in addressing obesity as there was an overemphasis on the diagnosis and treatment of obesity-related co-morbidities but a failure to directly examine obesity as an individual entity.[4] In particular, of all obesity-related exam items, pregnancy and childbirth represented only 4%.

The failure of medical curricular to require trainees to have specific, in-depth knowledge about obesity is also present in obstetrics and gynecology. The Royal College of Physicians and Surgeons of Canada publishes a list of training objectives that obstetrics and gynecology residents in Canada must meet before graduation.[5] While it does require a working knowledge of "medical diseases in pregnancy", and addresses a need for an extensive knowledge of obesity-related co-morbidities such as hypertensive disorders and diabetes, it does not specifically acknowledge learning objectives in caring for women with obesity. In addition, of those staff physicians who have received specialty certification with the American Board of Obesity Medicine (ABOM), obstetricians and gynecologists represent only 4.9% or 130 out of a total of 2656 diplomates.[6]

Even if health care professionals identify that obesity is an important obstetrical condition, this does not always translate into appropriate care for these women. A study of maternity care providers in Queensland, Australia identified that while the majority (88.1%) understand that this is an important topic, only 50% of practitioners could correctly identify BMI categorization, and less than 8% were able to provide appropriate gestational weight gain targets for patients.[7] In addition, despite being front-line health care workers in obstetrics, only 20.2% said they had received training to care for women with overweight or obesity. Despite an increase in available knowledge on obesity in pregnancy there is still a large gap in knowledge translation to healthcare practitioners. Simply increasing knowledge may not be improving the standard of care for women with obesity.

1.3 CONSEQUENCES OF OBESITY IN PREGNANCY

With the rapid surge in obesity rates, individuals are now developing serious obesity-related health outcomes at younger ages. A significant proportion of those affected are reproductive-aged women. Estimates suggest that 46% of Canadian women of reproductive age are affected by excess adiposity.[8]

The negative influence of maternal obesity on neonatal and maternal outcomes is increasingly described in the literature. In a recent report on maternal mortality rates in the UK, of all reported maternal deaths, one-third (33%) of the women were classed as having obesity and an additional 18% were classed as overweight.[9] Obesity, and its sequelae, were associated with an increased risk in maternal death. While overall maternal mortality remains low in developed countries, the morbidity from excess adiposity in pregnancy is significant.

Excess maternal weight impacts all phases of a pregnancy including the antepartum, intrapartum, and postpartum periods. During the antepartum period, women, with obesity, are at an increased risk of hypertensive disorders,[10-12] preeclampsia (PEC),[12-17] gestational diabetes (GDM),[10-12,15-19] hydraminos,[19] and stillbirth.[10,11,20] These pregnancy complications lead to a higher rate of an induction of labor – an intervention that carries its own independent risk.[12,13,15-17] The risk of induction is further augmented as women, with obesity, have prolonged gestations and increased rates of post-date pregnancies.[21] Currently, post-date pregnancies represent a top indication for an induction of labor.

Abnormalities in fetal growth can yield infants with macrosomia.[11,13,16,18,19] This may explain an increase in the rates of shoulder dystocia.[11,14] In addition, there is also an association between obesity and increased blood loss at the time of delivery.[12,13,18] Also, women with obesity consistently have higher rates of cesarean delivery when compared with normal weight women.[11-16,18,19,22,23] This outcome is likely amplified by the increase in complications that have developed over the course of pregnancy and labor. Emerging evidence suggests that excessive gestational weight gain in pregnancy is also associated with adverse maternal outcomes including an increased rate of cesarean delivery.[23,24] The Society of Obstetricians and Gynecologists of Canada (SOGC) recommends that all classes of obesity should limit weight gain to 7 kg throughout the entire pregnancy.[25] Unfortunately, 60% of pregnant Canadian women with obesity are gaining weight above the current recommended guidelines.[26] Further, recent American evidence has demonstrated that women who gained more than 20 lbs of weight above the current recommended guidelines were at a higher risk of severe maternal morbidity. This included an increased risk of eclampsia, heart failure during a procedure, pulmonary edema or acute heart failure, transfusion, and ventilation.[27] Conversely, women with overweight or obesity

that limited weight gain within the current recommended guidelines had lower rates of adverse outcomes such as gestational hypertension, cesarean delivery, and abnormal fetal birth weights, when compared with those who gained excessive weight.[28] In addition, pregnancy related weight gain within recommendations was not associated with an increase in overall fat mass in women with obesity.[29]

Fetal risks related to maternal obesity are also significant and increasingly appreciated. The related neonatal risks include increased neonatal death,[20] admission to the neonatal intensive care unit (NICU),[11] fetal distress,[14] and meconium aspiration.[14] It is important to recognize that the risks are not limited to the immediate post-partum phase of the infant's life. Children born to mothers with a high pre-pregnancy BMI are also more likely to have overweight or obesity themselves, further propagating the cycle of obesity into the next generation.[30] Mothers with metabolic conditions during pregnancy such as obesity, diabetes, or hypertension are more likely to yield children with autism spectrum disorder and developmental delay.[31] Additionally, the rates of childhood epilepsy were higher amongst women with overweight and obesity.[32]

Given the propensity for fetal and maternal complications, women with obesity place higher demands on healthcare resources. These complications are costly to the health care system. Cost analysis has demonstrated an estimated direct cost increase of 202.46 pounds (~350 CAD) per patient, with obesity, and 350.75 pounds (~610 CAD) for patients with severe obesity in a UK based study.[33] Additional indirect costs, such as absenteeism and loss of productivity, are not easily quantified but are estimated to be more significant than the direct health care costs attributable to obesity.[34] It has been estimated that a 1% decrease in maternal obesity could reduce the number of cesarean sections by 16,000 per year in the United States.[22] This is one example of the benefits of addressing weight reduction with patients in the preconception phase.

By focusing on obesity as a modifiable risk factor, even small reductions in maternal obesity rates would not only benefit fetal and maternal health, but may result in significant direct and indirect cost savings to the health care system.

1.4 MEASURES OF OBESITY IN PREGNANCY

To date there is no clear and concise way to classify obesity in pregnancy and there is a lack of consistent definitions within the current literature.

1.4.1 Body mass index

Worldwide, body mass index (BMI) is the most utilized method to categorize weight both clinically and in research. The World Health Organization guidelines classify BMI as follows: Underweight <18.5 kg/m^2, normal-weight 18.5-24.9 kg/m^2, overweight 25.0-29.9 kg/m^2, obese class I 30.0-34.9 kg/m^2, obese class II 35.0-39.9 kg/m^2, and obese class III ≥40.0 kg/m^2.[35]

As obesity rates increase, this rudimentary classification scheme has been scrutinized. The simplistic measure of BMI alone cannot individualize risk profiles, especially in maternal health. In addition, BMI was developed for use in a non-pregnant population but continues to be applied during obstetrical care. Currently, one of the biggest challenges of obesity research in pregnancy is the lack of a consistent and reliable way to measure obesity. BMI does not differentiate between lean tissue and fat tissue.[36] Furthermore, there are dynamic physiologic and body composition changes that occur throughout pregnancy, such as a change in fat mass and total body water, which is not accounted for by BMI.[29] Lastly, BMI does not account for the mass of the fetus and its supporting tissues from overall maternal weight.

While there is a technical inability to accurately measure body composition and adiposity in pregnancy, there are also logistical concerns. Much research attempts to categorize BMI based on pre-pregnancy weight. However, many women do not present to physicians or researchers in the immediate preconception phase. As such, BMI is often self-reported or taken at the first antenatal visit at varying gestational ages. Self-reporting of weight is subject to recall bias and has been shown to underestimate true body weight while weight at the first antenatal visit may be an overestimate due to pregnancy related weight gain.[37,38]

Lastly, BMI does not assess fat distribution. There is an important distinction between central and peripheral adiposity in obesity-related outcomes. Central adiposity is considered more sinister and has been shown to increase the risks of diabetes, CVD and hypertension in non-pregnant adults.[35,39,40] In addition, assessment of central adiposity may be important for care providers to be aware of as excess abdominal tissue may affect surgical planning.

Despite its limitations, BMI remains a mainstay classification tool. Strength of this scheme includes its simplicity, pervasiveness, and its utility as a common communication tool amongst health care providers and researchers. It has also been validated in numerous population studies as an indicator for adverse outcomes.

1.4.2 Alternative measures of obesity

With controversy surrounding the utility of BMI, researchers have attempted to delineate a more accurate measure of body composition in pregnancy. Other alternatives have been suggested such as computerized tomography (CT), magnetic resonance imaging (MRI), dual-energy x-ray absorptiometry (DXA), bioelectrical impedance analysis (BIA), waist circumference, skin-fold thickness, and subcutaneous fat thickness.

CT, MRI, and DXA have shown some accuracy in the measurement of body composition, but are considered prohibitive due to cost, limited resources, and the need for skilled technicians. In addition, the use of CT and DXA is prohibitive due to non-essential radiation exposure. BIA uses electrical impedance through body tissue to estimate body composition and while it is inexpensive and non-invasive its use is not validated in pregnancy. Further, its assessment of body fat relies on estimating total body water and there may be significant differences in body water composition during pregnancy.[41]

Skin-fold thickness is a promising tool for weight analysis as it is inexpensive and easy to perform with proper training. Unfortunately, it is easily influenced by water retention and peripheral edema, which are common issues during pregnancy, and therefore may not reliably measure maternal adiposity. Even shortly after delivery significant changes in assessments with skin-fold thickness have been identified, which is likely reflective of fluid shift rather than a rapid loss of fat mass.[42]

Waist circumference is another simple, inexpensive way to assess body fat but it too has limitations. There is a lack of normative values in pregnancy and measurements can be affected with increases in the size of the gravid uterus, especially at higher gestational ages. At up to 16 weeks of gestation waist circumference has been found to be predictive of pregnancy-induced hypertension and PEC.[43] In another study, waist circumference between 20-28 weeks gestation was comparable to BMI in predicting obesity-related outcomes such as PEC, GDM, and macrosomia.[44] Since waist circumference has not been determined to be superior to BMI, and its measures are limited by gestational age, the use waist circumference may be used as an adjunct but should not replace the use of BMI to measure adiposity in pregnancy at this time.

Ultrasound is a promising tool for the measurement of abdominal subcutaneous fat thickness. Currently, ultrasound assessment for fetal development is routinely recommended at 18-22 weeks gestation. A measure of the subcutaneous fat thickness could be performed during this scan and used to evaluate the degree of central adiposity. An average of three measurements of subcutaneous fat thickness were taken from a standard cervix-placental view. Limited evidence has demonstrated that this is a better indicator of adverse obesity-related pregnancy outcomes, such as GDM or cesarean delivery, than BMI.[45] This tool could be easily incorporated into prenatal care without significant strain on the health care system in developed countries. However, it still requires further validation before widespread use could be advocated and its use would be restricted in areas with limited imaging services.

With all these tools in development, there is still no clear recommendation on how to accurately assess obesity in pregnancy. The SOGC recommends obtaining a pre-pregnancy BMI when possible, but does not comment on the acceptability of self-reported versus measured weights. If a measured weight is obtained, then the preconception window in which it remains valid is uncertain. The Canadian guideline also recognizes alternative definitions of obesity in pregnancy, such as overall body weight >91kg (200lbs) or if the patients weight during pregnancy is >110-120% over their ideal body weight.[25] The American Congress of Obstetricians and Gynecologists (ACOG) advocates for a measured pre-pregnancy weight and obtains first antenatal visit weight when that is unavailable.[46] While major obstetrical guidelines continues to advocate for these standard definitions based on pre-pregnancy BMI this is impractical given most women are not seen by their physicians in the immediate preconception phase.[47] Regardless, BMI remains a necessity in the antenatal period due to its pervasive use and as current gestational weight gain recommendations are based on their values.

Until other measures of obesity are proven superior, BMI will remain the mainstay classification of adiposity in pregnancy. Therefore its inherent flaws must be recognized and accepted and continued research should attempt to improve its utility. A modified Edmonton Obesity Staging System is proposed here and offers an improvement to the standard BMI measure. This classification scheme provides a BMI-based clinical tool that individualizes risk, is inexpensive, and does not rely on specialized skills or technology.

1.5 THE EDMONTON OBESITY STAGING SYSTEM

Obesity affects people differently and there is significant heterogeneity in the medical co-morbidities experienced within each class of obesity. It is difficult to predict the severity of health concerns, or what treatment interventions to offer a patient, based on BMI alone. As such, efforts have been made to delineate a more useful classification scheme for patients with obesity.

In 2009, Sharma and Kushner proposed the Edmonton Obesity Staging System (EOSS).[48] Patients are assessed in a bimodal fashion. First, height and weight are assessed to calculate BMI and to examine, objectively, the presence of obesity based on current practice and understanding. Second, the patient's medical co-morbidities are assessed through a health history, physical exam, and basic laboratory investigations. The patients risk profile is then stratified to a 5-point Likert scale. Individuals are categorized with increasing severity from an EOSS score of 0 to 4 (Table 1.1).

After describing the EOSS, and its rationale for use in clinical practice, researchers subsequently challenged its use in two studies. First, a retrospective analysis of 29 533 individuals was performed in which 6224 had obesity (BMI $\geq$30.0 kg/m^2) and were assigned an EOSS category.[49] Those classified as EOSS category 2 or 3 were found to be at a greater risk for

all-cause and cardiovascular related mortality than normal-weight individuals. There was no difference between category 0 or 1 and normal-weight individuals suggesting that the EOSS may be a useful predictive tool of mortality. Secondly, another retrospective study made similar conclusions by examining two populations of almost 8000 individuals with overweight and obesity.[50] The EOSS was able to reliably predict mortality risk even after controlling for BMI and metabolic syndrome. Both studies were unable to assess EOSS stage 4.

Since then, the scale has been successfully applied to alternative patient populations. In patients undergoing metabolic surgery it was found that the EOSS was a better predictor of 30-day complication rates than BMI alone.[51] Additionally, when applied to a group of women with a BMI $\geq$ 25.0 kg/m^2, who were undergoing fertility treatments, it was more predictive of pregnancy rates than relying solely on the use of BMI.[52]

As evidence grows in support of the EOSS, its use has been modified and expanded for use in the pediatric population.[53] To date, there has been no adaptation of this scale in an obstetrical population.

1.6 PROPOSED CLINICAL CLASSIFICATION OF OBESITY IN PREGNANCY

In Table 1.2, the EOSS has been modified for use in an obstetrical population and will be referred to as the Edmonton Obesity Staging System for Obstetrics (EOSSo). The original scale was included in its entirety as all medical illnesses related to obesity in the non-pregnant adult may also be present before or during pregnancy. To adapt this scale for use in the obstetrical population the national Canadian guideline from the SOGC on obesity in pregnancy was first reviewed to identify the key medical conditions unique to pregnancy and related to obesity.[25] In addition, the authors have experience working in a high obstetrical volume and tertiary care

centre which provided further knowledge regarding the clinical significance of these conditions. Relevant literature was then reviewed to ensure the strength of these associations and medical comorbidities where incorporated where appropriate based on the original definitions provided by the scale. Expert consultation was also elicited from the original developer (AMS) of the EOSS to provide face validity.

The original EOSS includes hypertension and diabetes as two integral components of the scale. Therefore, the addition of hypertensive disorders in pregnancy and the expansion of the definition to include GDM are essential. GDM has been included alongside type 2 diabetes as both are strongly associated with obesity.[10-12,15,16,18] Those with GDM are at increased risk for the development of Type 2 diabetes postpartum, an established obesity-related chronic disease.[54] In addition, even those women who have not met diagnostic criteria for GDM, but have demonstrated abnormal screening on a 50-g oral glucose challenge test (GCT), have an elevated risk for developing Type 2 diabetes later in life.[55] As such, an abnormal GCT and GDM have been incorporated into the EOSSo.

As mentioned, hypertensive disorders of pregnancy have also been strongly linked with obesity.[10-16] Much like in the non-pregnant population, hypertensive disorders in pregnancy occur on a spectrum, from mild to severe. Mild disease may only show borderline or limited elevations in blood pressure, that do not require medical therapy, while the most severe cases impact end-organ function. The disorders have been categorized by severity as set out by the original scale: mild disease includes borderline or gestational hypertension, while PEC falls near the severe end of the spectrum. End-organ dysfunction is an important component in the diagnosis of preeclampsia and falls within the jurisdiction of an EOSSo category 3. Current SOGC guidelines delineate the various organ systems that may be altered resulting in serious

adverse conditions or complications.[56] This includes effects to the cardiorespiratory, hematologic, renal, hepatic, feto-placental, or central nervous systems. Those patients most affected by severe PEC would be classified as an EOSSo category 4. They may require dialysis, which has already been included in the scale, or may further progress towards fulminate eclampsia. One major difference specific to hypertensive disorders of pregnancy is their potential to progress from mild to severe quickly. Ongoing reclassification of EOSSo category would be required with disease progression.

Another unique addition to the scale includes the use of advanced reproductive technology (ART), such as in-vitro fertilization (IVF), intra-uterine insemination (IUI), or ovulation induction agents. ART may therefore act as a surrogate marker for obesity-related disease and sub-fertility and as such has been included. Women with obesity often have difficulties conceiving due to anovulatory menstrual cycles, or obesity-related hormonal disruptions. A 4% decline in spontaneous conception rate was demonstrated for every 1.0 kg/m^2 increase over a BMI of 29.0 kg/m^2.[57] Polycystic ovary syndrome has previously been included in the scale and may be responsible for reduced fertility due to anovulation. However, even in the presence of ovulatory menstrual cycles, obesity has been associated with reduced fertility.[57,58]

Impaired fertility may be overcome with the use of ovulation induction agents such as clomiphene citrate, letrozole, or gonadotropins possibly in combination with IUI. Women with obesity often require higher doses of these medications for ovulation induction.[59] In addition, IVF in women with obesity may be less likely to result in a clinical pregnancy.[60] Currently, many fertility clinics restrict access to IVF at higher BMIs making their fertility rates harder to examine. Therefore, women who have had IVF may not contribute in a significant way to the scale at present. As ethical discussions about restricted access to IVF in this population progress

and as access to community anesthetic services improves, there may be an increase in women with obesity receiving this service.

1.6.1 Implications of the Edmonton Obesity Staging System in Obstetrics

The EOSSo is a novel clinical tool that has not previously been applied to an obstetrical population and may prove useful to assess patient risk. It is hypothesized that women stratified to a higher EOSSo category will experience a higher number of adverse obstetrical and neonatal outcomes. This classification system will serve as a risk assessment tool to help guide clinical decision making in the ante-, intra-, and immediate postpartum period. If a relationship between EOSSo category and adverse events in pregnancy is determined, allocation of more resources to patients with the higher EOSSo classification may be justified. Higher-risk pregnancies usually warrant closer follow-up by obstetricians including serial imaging, multidisciplinary care, in-depth discussions around timing and mode of delivery, and often delivery at a tertiary referral hospital. Conversely, those with lower classifications could opt for lower-risk care providers. Therefore, the EOSSo may help individualize the most appropriate care for each patient.

For ease of use, the classification scheme needs to be adapted for use when patients present to labor and delivery units for assessment. As such, the variables that have been included in the scale are items attainable from a health history, physical exam and lab investigations that would be performed during pregnancy or easily acquired at the time of patient presentation.

Lastly, the previous applications of the EOSS have included commentary on weight loss interventions. It's use in pregnancy, however, is not to guide weight reduction. Rather, the EOSSo will assist in the maintenance of weight gain within the current recommended guidelines

and it will guide patient management to minimize the effects of obesity related co-morbidities that could detrimentally affect maternal and neonatal health.

1.6.2 Clinical case examples

Case 1

A 28 year-old G1P0 female with a BMI of 32.0 kg/m^2 at first prenatal visit and no obesity-related co-morbidities would have class 1, EOSSo category 0, obesity. Potential management options of this pregnancy would include education surrounding nutrition, exercise in pregnancy, and appropriate gestational weight gain targets. The patient may choose to deliver with the maternity care provider of her choice (Obstetrician, Family Doctor, or Midwife) and at the center of her choice. All patients with obesity should undergo timely screening for diabetes and hypertensive disorders of pregnancy. Clinics should have equipment available for the care of these women such as large blood pressure cuffs.

Case 2

A 34 year-old G2P1 female with a BMI of 34.0 kg/m^2 at first prenatal visit and a history of polycystic ovary syndrome and the use of assisted reproductive technology in this pregnancy would have class 1, EOSSo category 2, obesity. Management considerations beyond basic nutrition, weight, and exercise counseling could include early screening for GDM, referral to an obstetrician for pregnancy care, and delivery at a hospital with an anesthetic team with experience treating patients with obesity.

Case 3

A 32 year-old G1P0 female with a BMI of 41.0 kg/m^2 at first prenatal visit with a history of chronic hypertension, type 2 diabetes on insulin treatment, and evidence of diabetic retinopathy would have class 3, EOSSo category 3, obesity. Special management considerations would involve coordinating multidisciplinary care. This includes care from an obstetrician, obstetrical medicine specialist, and regular monitoring of fetal wellbeing from a high-risk perinatal clinic. Delivery should be planned at a tertiary referral center and early consultation with an anesthesiologist should be arranged. Lastly, additional time in the antenatal period should be dedicated to educating patients on the increased likelihood of potential pregnancy complications including the risk of cesarean delivery.

1.6.3 Limitations of schema in the obstetrics population

The EOSSo, as with any classification scheme, has important limitations that should be discussed. First, significant overlap can occur between transient medical conditions that present during pregnancy and those that are related to obesity. For example, many women will experience a new onset of GERD or urinary incontinence secondary to the hormonal changes of pregnancy or from a mass effect of the gravid uterus. These are also common illnesses that affect women with obesity. As such, distinction should be made between more longstanding conditions that existed prior to pregnancy and those that may dissipate quickly after delivery. Differentiating the onset of these conditions may be associated with recall bias skewing the incidence of these illnesses.

Secondly, the overall rate of obesity related illness in this population might be underreported. Obstetrical patients typically consists of young women and many have had limited interactions with the health care system prior to pregnancy. Pregnancy represents the first

time in their lives with dedicated, frequent, longitudinal health care. Many obesity-related conditions such as dyslipidemia, gallstones, and obstructive sleep apnea are initially asymptomatic or unrecognized and require screening for diagnosis. Screening for obesity related illnesses such as these is currently not part of routine prenatal care and attempting to do so may overburden the system. Therefore, these types of medical conditions would remain undiagnosed and underrepresented in the confines of this scale.

Third, as discussed previously, there is currently no consensus on the definition of obesity in pregnancy. While the use of BMI is almost universally accepted, with the lack of accurate pre-pregnancy weights, this measure remains inherently unreliable. Further, the literature uses a combination of definitions based on various measured and self-reported weights at non-standardized gestational ages throughout pregnancy or at the time of delivery. This results in problematic comparisons in the literature and compounds the inaccuracies of this measure. Therefore, the inherent limitations of BMI are incorporated into this scheme and the rate of true obesity may be over or under represented.

Lastly, the original EOSS was developed in a non-pregnant population and this scale requires validation for use in this population.

1.7 OBJECTIVES

Current methods of assessing risk are inadequate, especially for cesarean delivery. To our knowledge the EOSS has not previously been adapted for use in obstetrics and this is the first attempt to validate this scale in this population. The aim of this study is to validate the use of the EOSSo to predict mode of delivery, in women with overweight or obesity, who are undergoing

and induction of labor. We predict that women staged to a higher EOSSo category will be at a greater risk of cesarean delivery.

This study is important because it attempts to address the needs of patients and care providers in two ways. First, patients present to maternity care units with expectations of how they believe their labor will progress. In reality, labor is a dynamic, often unpredictable process that can vary from routine to a life-threatening emergency. For patients with obesity, labor represents a potential risk to maternal and fetal wellbeing. Most obstetricians recognize that women with obesity, who are undergoing an IOL, generally have a higher risk for a cesarean delivery than women of normal weight. However, since there is no individualized risk assessment tool to help determine the likelihood of cesarean delivery, opportunities to educate patients on risk may be lost. This tool equips obstetricians with an objective assessment of cesarean delivery risk in an unbiased and nonjudgmental manner. This will open a dialogue between care providers and patients to more adequately prepare the patient for the possible outcomes of their birth experience. To date, very little time is spent in the antenatal period discussing the prospects of a cesarean delivery in first time pregnancies. This is important because maternal postnatal wellbeing can be impacted by the mode of birth. Women who have had an emergency or unplanned cesarean delivery score lower on scales of health and psychological wellbeing.[61] Up to 76% of women who have had an emergency cesarean delivery experienced it as a traumatic event and many experience post-traumatic stress reactions.[62,63] There is often no time to discuss even simple questions in these scenarios. Better counseling regarding potential cesarean delivery in the antenatal period may help mitigate this risk.[64] Providing clinicians with a tool to address the risk of cesarean delivery with the patient, should allow for more educational opportunities in the antenatal period.

Secondly, the development of a risk assessment tool has the potential to improve outcomes in patients, with obesity, who are undergoing an induction of labor. Establishing more accurate cutoffs to assess when an IOL may result in a cesarean delivery also allows clinicians to better prepare the necessary healthcare resources for their delivery and may even alter IOL guidelines in the future.

1.8 TABLES

Table 1.1 Original Edmonton Obesity Staging System[48]

Category	Description
0	No apparent obesity-related risk factors (e.g., blood pressure, serum lipids, fasting glucose, etc. within normal range), no physical symptoms, no psychopathology, no functional limitations and/or impairment of well being
1	Presence of obesity-related subclinical risk factors (e.g., borderline hypertension, impaired fasting glucose, elevated liver enzymes, etc.), mild physical symptoms (e.g., dyspnea on moderate exertion, occasional aches and pains, fatigue, etc.), Mild psychopathology, mild functional limitations and/or mild impairment of wellbeing
2	Presence of established obesity-related chronic disease (e.g., hypertension, type 2 diabetes, sleep apnea, osteoarthritis, reflux disease, polycystic ovary syndrome, anxiety disorder, etc.), moderate limitations in activities of daily living and/or of well being
3	Established end-organ damage such as myocardial infarction, heart failure, diabetic complications, incapacitating osteoarthritis, significant psychopathology, significant functional limitations and/or impairment of well being
4	Severe (potentially end-stage) disabilities from obesity-related chronic diseases, severe disabling psychopathology, severe functional limitations and/or severe impairment of well being

Table 1.2 The Edmonton Obesity Staging System for Obstetrics (EOSSo)

Category	Classification	Common Disease Examples
0	No apparent risk factors	-No apparent obesity-related risk factors -No physical symptoms -No psychopathology -No functional limitations -No impairment of wellbeing
1	Subclinical risk factors associated with obesity	-Borderline hypertension not requiring medical therapy -Impaired glucose tolerance, self reported or abnormal gestational diabetes screen -History of irregular menses of unknown cause -Mild physical symptoms related to obesity -Mild psychopathology or impairment in wellbeing
2	Established obesity-related chronic disease	-Essential or gestational hypertension -Gestational diabetes -Type 2 Diabetes -Polycystic Ovarian Syndrome -Use of assisted reproductive technology -Dyslipidemia -Non-alcoholic fatty liver disease -Known gallstones or prior cholecystectomy -Osteoarthritis -Obstructive sleep apnea -Incontinence prior to pregnancy -Moderate psychopathology (depression, anxiety, disordered eating behavior, body image disturbance) -Moderate impairment of wellbeing
3	Established obesity-related chronic disease with end-organ damage	-Preeclampsia -Stroke -Myocardial Infarction -Angina -Heart failure -Diabetic complications -Thromboembolic disease -Hepatic dysfunction or hematoma -Pulmonary edema -Renal insufficiency -Incapacitating osteoarthritis -Significant impairment of wellbeing
4	Severe (potentially end-stage) disabilities from obesity-related chronic diseases	-Eclampsia -Dialysis -Bed ridden or unable to mobilize -Disabling psychopathology or severe impairment of wellbeing

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CHAPTER 2

THE EDMONTON OBESITY STAGING SYSTEM IN OBSTETRICS TO PREDICT MODE OF DELIVERY AFTER LABOR INDUCTION

2. 1 ABSTRACT

Objective: To evaluate the use of the Edmonton Obesity Staging System for Obstetrics (EOSSo) in predicting cesarean delivery amongst term, nulliparous, singleton pregnancies in women with overweight or obesity, who are undergoing an induction of labor.

Methods: A prospective-cohort study was performed in Edmonton, Alberta, Canada. Women undergoing an induction of labor at term were recruited to either a sample cohort, including women with a body mass index (BMI) of ≥25.0 kg/m^2 at first antenatal visit, or a control cohort with a BMI of 18.5-24.9 kg/m^2. Participating women provided a self-reported health history and consented to review of their medical records allowing allocation into EOSSo categories. The primary outcome was the rate of cesarean delivery based on EOSSo category. Secondary outcomes consisted of a summary score of adverse maternal, delivery, and neonatal events.

Results: Overall, 345 women were recruited, with a participation rate of 93.7%. The sample cohort consisted of 276 women with overweight or obesity, while the control cohort included 69 normal weight women. Overall rate of cesarean delivery was 30.4% for the control cohort and 35.8%, 29.9%, 43.2%, and 90.5% for women assigned an EOSSo category 0, 1, 2, and 3, respectively ($P < 0.001$). A summary score was not indicative of overall rate of adverse maternal, delivery, and neonatal events ($P = 0.22$).

Conclusion: The EOSSo may help predict the chance of cesarean delivery in a high-risk group of nulliparous women with overweight or obesity, who are undergoing an induction of labor at term.

Keywords: Obesity, Labor Induction, Body Mass Index (BMI), Edmonton Obesity Staging System (EOSS), Edmonton Obesity Staging System for Obstetrics (EOSSo), Cesarean Delivery

2.2 INTRODUCTION

Obesity is compromising the health of populations worldwide. Current estimates suggest that about one in five Canadian women, aged 18-34 years, are classified as having obesity and almost half as having overweight or obesity.[1] With over 380,000 births in Canada per year, an estimated 190,000 are therefore impacted by excess maternal weight.[2] With rising rates of obesity, this number will continue to grow. Excess maternal weight is associated with adverse events in pregnancy, including increased rates of hypertensive disorders, gestational diabetes, abnormal labor patterns, and obstetrical interventions like cesarean delivery.[3-7] The risk of stillbirth and fetal death are also augmented.[8] Further, high body mass index (BMI) is associated with an increased need for an induction of labor from both complications related to pregnancy and prolonged gestations.[9,10] This intervention compounds delivery related risk for women with obesity, as those who are induced are more likely to undergo an emergency cesarean delivery.[10] An emergency cesarean delivery after a failed induction of labor carries a higher rate of complications than a vaginal or elective cesarean delivery.[11]

Historically, BMI has been used to stratify obesity related risk for women at term. As BMI increases, risk of adverse pregnancy and surgical outcomes also increases. Not all women, however, are equally affected by obesity. BMI alone fails to convey these differences and is therefore insufficient to guide clinical-decision making. A more accurate approach to delineate which women will be at highest risk for cesarean delivery is needed. The Edmonton Obesity Staging System (EOSS) has been proposed as a more accurate measure of determining outcomes in patients with increased weight, than BMI alone.[12] The EOSS is a clinical staging system that individualizes risk profiles by incorporating knowledge of a patient's current health status and weight related co-morbidities. To date, the EOSS has been more successful than BMI at

predicting long-term mortality rates, poor post-operative outcomes in non-obstetrical patients, and pregnancy rates in women undergoing fertility treatments.[13-16]

This study aims to validate the use of a modified version of the Edmonton Obesity Staging System for Obstetrics (EOSSo) to predict mode of delivery amongst women with overweight or obesity, who are undergoing an induction of labor. Women who are more affected by obesity-related co-morbidities may be at higher risk of cesarean delivery. We hypothesize that parturients at higher EOSSo categories will have an increased likelihood of cesarean delivery.

2.3 METHODS

2.3.1 Study design and population

A prospective-cohort study was performed at two high volume obstetrical centers in Edmonton, Alberta. The Lois Hole Hospital for Women is a tertiary referral center and the Grey Nuns Hospital is a community hospital. Both perform over 7000 deliveries per annum. Ethical approval was obtained prior to commencement of the study from the Human Research Ethics Board at the University of Alberta (Pro00075527).

Recruitment was performed simultaneously at each site between January 2018 and August 2018. Two researchers were responsible for all recruitment to ensure consistency. Women scheduled for an induction of labor were screened daily by nursing staff for possible inclusion in the study. Researchers were then contacted for recruitment. All initiated inductions in nulliparous women, ≥37 weeks and 0 day's gestational age, ≥18 years old with singleton, vertex pregnancies and documented prenatal care were included. Nulliparity was defined as no previous deliveries ≥20 weeks gestational age. Exclusion criteria included a previous myomectomy, BMI <18.5 kg/m^2, midwifery care, those presenting for a planned assisted second

stage, the presence of congenital fetal anomalies or predetermined fatal fetal outcomes, no prenatal care and non-English speaking women. To limit bias, researchers were not involved in patient care, and if a researcher provided emergency care, that participant was removed from the study.

At recruitment, participants provided written consent. Participants were asked to complete a personal health history. In addition, they consented for a full review of their medical records including their prenatal, delivery, and current hospital admission records. Research participants were stratified into two groups based on their measured weight at their first antenatal visit. The sample cohort consisted of women with a BMI $\geq$25.0 kg/m^2 and the control cohort consisted of normal weight women with a BMI of 18.5-24.9 kg/m^2. There were no interventions or alterations to patient care.

After enrollment and prior to delivery, two researchers independently assigned women in the sample cohort to an EOSSo category based on their obesity related co-morbidities. The EOSSo used in this study has been modified for use in pregnancy by incorporating pregnancy related complications that have been previously associated with obesity, such as gestational diabetes and hypertensive disorders of pregnancy (Table 1.2). Its creator, AMS, reviewed the modified version of this scale for face validity. In patients with multiple co-morbidities, the most severe comorbidity determined the EOSSo category.

Data was entered into REDCap, a secure platform for data storage supported by the University of Alberta. At the conclusion of the study, all records were reviewed for accuracy.

Maternal demographics (age, smoking status, gestational age at first antenatal visit, gestational age at delivery, self-reported BMI, BMI at first antenatal visit, BMI at delivery, gestational weight gain, cervical dilation at admission, group B streptococcus (GBS) status,

epidural use, indication and mode of induction), maternal co-morbidities (hypertensive disorders, diabetes, dyslipidemia, non-alcoholic fatty liver disease, gallbladder disease, menstrual irregularities, polycystic ovary syndrome, joint pain or osteoarthritis prior to pregnancy, pre-pregnancy incontinence, obstructive sleep apnea, depression, anxiety, disordered eating behavior, thromboembolic disease, heart failure, and stroke) and labor information (mode of delivery, labor augmentation, rupture of membranes, fetal birth weight, and details of cesarean delivery including indication, cervical dilation, incision type, and complications) were evaluated. Variables were recorded from a combination of self-reported data or as documented on hospital records by their care providers.

2.3.2 Study outcomes

The primary outcome was rate of cesarean delivery. The secondary outcome consisted of a summary score of maternal, delivery, and neonatal outcomes. This included the incidence of excessive gestational weight gain, based on the Society of Obstetricians and Gynaecologists of Canada recommended weight gain guidelines (BMI 18.5-24.9 kg/m^2, >16.0 kg; BMI 25.0-29.9 kg/m^2, >11.5 kg; BMI ≥30.0 kg/m^2, >7.0 kg)[17], poly- or oligohydraminos, chorioamnionitis, abruption, shoulder dystocia, severe perineal tear (≥third-degree tear or episiotomy), manual removal of placenta, excessive blood loss (estimated blood loss >500cc in vaginal delivery or >1000 cc in cesarean delivery), blood transfusion, meconium, low Apgar score (≤7 at 1 and 5 minutes), stillbirth after initiation of induction, abnormal birth weight (<2500g or ≥4000g), admission to the NICU, maternal death, thromboembolic disease, and mode of delivery.

2.3.3 Sample size

The sample size calculation is based on predicted proportion of cesarean section rate for each category. After reviewing the literature, we anticipated that the emergency cesarean delivery rate of normal-weight controls, after an induction of labor, would be approximately 20%.[18] With each increase in EOSSo category, there should be an increase in cesarean delivery rate as these patients suffer from obesity related co-morbidities to a greater degree. Calculations were based on the estimate that the cesarean delivery rate in the EOSSo category 0, 1, 2, and 3 category would approach 30%, 35%, 40%, and 45%, respectively. EOSS stage 4 was excluded from our sample size calculation, as the presentation of individuals with this degree of illness was unlikely to be encountered and would be unreliably sampled. This resulted in a sample size calculation of 345 patients, including EOSSo stages 0-3 and a group of normal-weight controls. The control cohort represented one-fifth the overall sample size and was collected continuously until fulfillment. Overall, this sample size of 345 achieves 80% power using 4 degrees of freedom chi-square test with a significance level (alpha) of 0.05.

2.3.4 Statistical analysis

Statistical analysis was performed on the predefined primary and secondary outcomes. For the primary outcome, Pearson chi-square tests were used to detect differences amongst groups with categorical variables and binomial logistic regression was performed to ascertain odds ratios. For the secondary outcome, a one-way ANOVA was conducted to determine if there were differences in mean summary scores. For all analyses, a statistical difference was taken at a $P < 0.05$ level of significance. In instances where pairwise comparisons were performed, the type I error was adjusted for multiplicity using Bonferroni correction and a p-value of 0.05 remained

statistically significant. All statistical analyses were performed using SAS Version 9.4 (SAS Institute Inc., Cary, NC, USA).

2.4 RESULTS

2.4.1 Patient characteristics

Overall, 397 patients were approached for recruitment into the study from January 2018 to August 2018 (Figure 2.1). A total of 25 women declined to participate yielding an overall participation rate of 93.7%. An additional 27 women were excluded from the study after they were consented and their medical records were reviewed (refer to Figure 2.1). A total of 154 (55.8%) women from the sample cohort and 36 (52.2%) women from the control cohort were recruited from the tertiary care center, with the remainder derived from the community hospital. The incidence of medical comorbidities in the control and sample cohorts is presented in Table 2.1.

Maternal demographics and EOSSo group characteristic information is presented in Table 2.2. The control cohort consisted of a total of 69 (20%) women. The sample cohort consisted of 53 (15.4%), 77 (22.3%), 125 (36.2%), and 21 (6.1%) women distributed by EOSSo category 0, 1, 2, and 3, respectively. Distribution of the sample cohort by BMI class at first antenatal visit resulted in 129 (39.5%) classed as having overweight (BMI 25.0-29.9 kg/m^2) and 147 (42.6%) classed as having obesity (BMI ≥30.0 kg/m^2). If further divided by obesity class there were 74 (50.3%), 39 (26.5%), and 34 (23.1%) in class I (BMI 30.0-34.9 kg/m^2), II (BMI 35.0-39.9 kg/m^2) and III (BMI ≥40.0 kg/m^2), respectively. The proportion of weight class amongst each EOSSo category has been presented and demonstrates representation from each

BMI class within each EOSSo category (Figure 2.2). The indication for IOL is presented in Table 2.3.

2.4.2 Rates of cesarean delivery

The rate of cesarean delivery by EOSSo category is presented in Figure 2.3. Baseline rate of cesarean delivery for the control cohort was 30.4%. When stratified by EOSSo category 35.8%, 29.9%, 43.2%, and 90.5% of women underwent cesarean delivery in EOSSo category 0, 1, 2, and 3, respectively ($P < 0.001$). Pairwise comparisons evaluated the difference in rate of cesarean delivery between the control cohort and each EOSSo category. Compared with the control cohort, EOSSo category 0 ($P = 0.53$) and EOSSo category 1 ($P = 0.94$) were not statistically significant. Compared with the control cohort, EOSSo category 2 approached, but did not research statistical significance ($P = 0.08$). Lastly, compared with the control cohort, EOSSo category 3 reached statistical significance ($P < 0.001$). A binomial logistic regression was performed to ascertain the effect of EOSSo category on cesarean delivery. In unadjusted analysis there was no difference in EOSSo category 0 (OR, 1.3; 95% CI, 0.6-2.7), EOSS Category 1 (OR, 0.97; 95% CI, 0.5-2.0), and EOSSo category 2 (OR, 1.7; 95% CI, 0.9-3.2) but there was for EOSSo category 3 (OR, 21.7; 95% CI, 4.6-101.8). There was no statistically significant difference when the model was adjusted by age ($P = 0.07$) or mode of induction ($P = 0.44$). Artificial rupture of membrane as a primary mode of induction was not included in the analysis due to the low frequency of occurrence.

The rate of cesarean delivery was also reviewed after excluding all women with a self-reported BMI <25.0 kg/m^2 to assess whether any significant misclassification may have altered the described outcomes. This yielded 210 patients and overall cesarean delivery rates showed a

similar trend with the highest rate of cesarean delivery in EOSSo category 3 (EOSSo 0, n=14 (40.0%); EOSSo 1, n=13 (25.0%); EOSSo 2, n=46 (44.2%); EOSSo 3, n=17 (89.5%); P < 0.001). The most common indication for cesarean delivery was fetal heart rate abnormalities and was the same for each patient category (Control = 42.9%; EOSSo 0 = 47.3%; EOSSo 1 = 60.9%; EOSSo 2 = 57.4%; EOSSo 3 = 47.4%). Failure to progress in the first stage of labor was the second most common indication (Control = 38.1%; EOSSo 0 = 31.6%; EOSSo 1 = 39.1%; EOSSo 2 = 38.9%; EOSSo 3 =31.6%). Multiple indications for cesarean delivery were sometimes provided (Table 2.4).

Rates of cesarean delivery were then compared by BMI (Figure 2.4). Overall rate of cesarean delivery was 39.5%, 40.5%, 43.6%, and 50.0% for overweight, obesity class I, II, and III, respectively. The difference in proportion of cesarean delivery between weight classes did not reach statistical significance (P = 0.37).

2.4.3 Secondary outcome

Lastly, secondary outcomes were analyzed using a summary score of adverse maternal, delivery, and neonatal events (Table 2.5). While there was a slight trend of increasing mean summary score with increasing EOSSo category, overall this was not statistically significant between EOSSo categories (P = 0.22). There was one perinatal death in this study in an EOSSo category 2 participant. The patient was known to have poorly controlled gestational diabetes. She received an induction of labor with prostaglandins that was subsequently complicated by uterine tachysystole. After removal of the prostaglandin and resolution of the tachysystole, she refused further intervention and left against medical advice. After one week she re-presented for induction with an unexplained fetal death.

2.5 DISCUSSION

Obesity during pregnancy, and its related complications, presents an ongoing challenge for maternity care providers. Our study is consistent with previous reports that determined higher rates of cesarean delivery in women with overweight and obesity, when compared with normal weight women.[18,19] Despite this, there was no statistically significant impact of BMI class on mode or delivery and therefore, BMI stratification provides no significant predictive utility. Thus, BMI alone is not clinically powerful enough to guide recommendations for mode of delivery. In contrast, the EOSSo more clearly delineates a subpopulation of women who are at a high risk of cesarean delivery. When the EOSSo is applied, the rate of cesarean delivery in the high-risk subpopulation (EOSSo category 3) is over 90%. Moreover, cesarean delivery rates in the EOSSo 0 and 1 categories were no higher than in the control populations despite a markedly higher BMI than in controls. Given that emergency cesarean delivery carries the highest complication rate, and that women classed as an EOSSo category 3 are at over a 90% risk of this outcome, interventions for risk reduction should be focused on these women. If these results persist, patients may be offered an elective cesarean delivery instead of an induction of labor. This may help reduce the risk of complications associated with emergency cesarean delivery, allow for more adequate resource planning, and spare women from an induction process with a high chance of failure.

The EOSSo may be better able to predict cesarean delivery at the higher EOSSo category, than BMI alone, because it identifies those women who have been most affected by excess adiposity. Some hypotheses attempt to explain the altered physiology of women with obesity, which may account for some of the differences in cesarean delivery rates. At a cellular level, decreased contractility in the myometrium may be responsible.[7,20-22] The force and rate of

myometrial contractions relies on the influx of calcium into the myocyte. Cholesterol and leptin, which are shown to be increased in women with obesity, reduce the influx of calcium and antagonize the actions of oxytocin.[7,22] Thus, reduced myometrial contractility may explain prolonged labour, increased oxytocin demands, and higher rates of postdate pregnancies.[7,9,21,23] It is unknown at this time, but would be of interest, to determine if women with more obesity related co-morbidities experience these phenomena to a higher degree than those without co-morbidities.

Contrasting outcomes between normal weight women and women with obesity may not be solely explained by intrinsic patient factors. Consideration should also be given to factors associated with care providers that may affect clinical decision-making. Healthcare providers have been shown to respond differently to patients based on their size.[24,25] This weight bias can be explicit – conscious and intentional, or implicit – unconscious and unintentional.[26] For example, there may be an implicit tendency to offer a controlled cesarean delivery rather than pursuing a vaginal delivery, given the unpredictability of labor and inherent risk of emergency cesarean delivery. This bias may partly explain the lower rates of operative vaginal delivery in women with obesity.[3,5,19] Our study also demonstrated a decreasing trend towards operative vaginal delivery with increasing EOSSo category. Physicians may inherently view these patients as at a higher risk for complications such as macrosomia and shoulder dystocia, and therefore be hesitant to offer instrumentation, resulting in higher rates of cesarean delivery.

Strengths of this study include the use of multiple centers, a high participation rate, and a comprehensive data set due to the prospective nature of the study. Some limitations, however, should be noted. First, as overall rates of EOSSo category 3 participants were low in this study, attempts should be made to replicate this finding on a larger scale before altering care patterns.

Secondly, there continues to be varying definitions of overweight and obesity applied to pregnancy in the literature making it difficult to interpret and compare previous results. At our centers, a maternal weight is rarely documented in the preconception phase and as such accurate pre-pregnancy weights are unavailable. Self-reported weights have often been used but underestimate weights, and the degree of obesity, particularly in patients at higher BMIs.[27-29] As such, we used a measured weight at first antenatal visit. This is the earliest and most readily available assessment of measured weight that can be used in clinical decision-making at point of care. As patients may have gained some weight in early pregnancy, there may be an overestimation of overweight in this study. This should have only diminished results by theoretically including more normal weight, and therefore a lower risk population of women, into the sample group. Despite this, after removing all women with a self-reported BMI <25.0 kg/m^2, we still observed a high rate of cesarean delivery in our EOSSo category 3.

Thirdly, obesity-related co-morbidities were documented based on a combination of self-reported medical history and medical records. Therefore, there may be an underreporting of medical co-morbidities. Due to the young nature of obstetrics patients, many have had limited interactions with the health care system prior to their pregnancy. Many obesity-related conditions such as non-alcoholic fatty liver disease, dyslipidemia, and obstructive sleep apnea are initially asymptomatic or unrecognized and require screening for diagnosis. Therefore, these conditions may have not yet been recognized and would be underestimated in the confines of this study.

Lastly, in examining secondary outcomes based on a summary score, all outcomes were weighted equally. Outcomes with more significant clinical impact, such as stillbirth or maternal death, should potentially be weighted more heavily. In addition, a summary score does not

provide insight into individual adverse outcomes that would need to be studied separately in order to ensure adequate power and to draw appropriate conclusions.

2.6 CONCLUSION

Given the significant morbidity associated with cesarean delivery, particularly after a failed induction, ascertaining guidance in managing these patients would be helpful to mitigate risk. To date, the use of BMI has inadequately assessed the risk of cesarean delivery in women, with overweight and obesity, who are undergoing an induction of labor. The EOSSo, however, provides a superior method of determining women at high risk for this outcome. Future research examining ways to minimize risk in this population is warranted.

2.7 TABLES

Table 2.1 Overall incidence of medical comorbidities

Medical Condition	Control Cohort (N=69)	Sample Cohort (N=276)
Borderline Gestational Hypertension	4 (5.8)	20 (7.2)
Chronic Hypertension	1 (1.4)	14 (5.1)
Gestational Hypertension	3 (4.3)	38 (13.8)
HELLP Syndrome	0 (0)	2 (0.7)
Preeclampsia	1 (1.4)	16 (5.8)
Eclampsia	0 (0)	0 (0)
Impaired Glucose Tolerance or self-reported "prediabetes"	3 (4.3)	32 (11.6)
Gestational Diabetes	11 (15.9)	65 (23.6)
Diet Controlled	7 (63.6)	18 (27.7)
Insulin Controlled	4 (36.4)	45 (69.2)
Metformin Controlled	0 (0)	2 (3.1)
Type 2 Diabetes	0 (0)	5 (1.8)
Dyslipidemia	1 (1.4)	9 (3.3)
Non-alcoholic Fatty Liver Disease	0 (0)	5 (1.8)
Gallbladder Disease	0 (0)	17 (6.2)
Menstrual Irregularities	9 (13.0)	71 (25.7)
Polycystic Ovary Syndrome	1 (1.4)	30 (10.9)
Mild Joint Pain prior to pregnancy	7 (10.1)	48 (17.4)
Osteoarthritis	1 (1.4)	3 (1.1)
Sleep Apnea	1 (1.4)	15 (5.4)
Incontinence prior to pregnancy	0 (0)	12 (4.3)
Depression	7 (10.1)	54 (19.6)
Anxiety	8 (11.6)	63 (22.8)
Disordered Eating Behavior	2 (2.9)	10 (3.6)
Thromboembolic Disease	0 (0)	1 (0.4)
Heart Failure	0 (0)	1 (0.4)
Stroke	0 (0)	0 (0)

Data are presented as n (%)

Table 2.2 Maternal characteristics by EOSSo category

Demographic	Control N=69	EOSSo 0 N=53	EOSSo 1 N=77	EOSSo 2 N=125	EOSSo 3 N=21
Age (years), median (IQR)	30.0 (27.0-32.0)	29.0 (26.0-31.0)	29.0 (25.0-31.0)	30.0 (28.0-33.0)	31.0 (27.0-34.0)
Smoker, n (%)	3 (4.3)	0 (0)	7 (9.1)	11 (8.8)	3 (14.3)
GA (weeks and days), median (IQR)					
Delivery	41.0 (39.6-41.1)	41.1 (40.1-41.3)	41.0 (39.6-41.3)	39.3 (39.1-40.3)	38.3 (37.6-39.3)
First Antenatal Visit	17.0 (14.4-19.6)	21.6 (16.6-27.0)	21.0 (16.1-24.6)	18.9 (13.0-23.6)	18.1 (13.7-24.7)
BMI, median (IQR)					
Delivery	27.0 (25.9-28.4)	32.7 (30.6-37.2)	33.4 (30.9-37.6)	35.2 (32.0-41.1)	37.5 (32.8-45.1)
First Antenatal Visit	22.4 (21.3-23.4)	28.5 (26.6-31.9)	29.1 (26.8-33.2)	31.7 (28.4-38.4)	33.5 (30.4-41.1)
GWG (kg), median (IQR)	13.5 (9.9-16.7)	9.0 (5.7-13.6)	9.7 (6.9-12.8)	10.7 (6.3-12.0)	11.6 (6.8-14.5)
Primary mode of induction, n (%)					
-Prostaglandin only	47 (68.1)	35 (66.0)	51 (66.2)	90 (72.0)	9 (42.9)
-Oxytocin	15 (21.7)	8 (15.1)	17 (22.1)	14 (11.2)	3 (14.3)
-Foley catheter only	2 (2.9)	3 (5.7)	5 (6.5)	4 (3.2)	3 (14.3)
-Combined*	3 (4.3)	3 (5.7)	2 (2.6)	8 (6.4)	2 (9.5)
-Sequential†	2 (2.9)	3 (5.7)	2 (2.6)	2 (9.5)	4 (19.0)
-ARM	0 (0)	1 (1.9)	0 (0)	0 (0)	0 (0)
Cervical dilation at admission (cm), median (IQR)	2.5 (1.5-3.0)	2.0 (1.0-3.0)	3.0 (1.5-3.0)	3.0 (1.5-3.0)	1.0 (0.0-2.0)
GBS Positive, n (%)	11 (15.9)	9 (17.0)	11 (14.3)	27 (21.6)	5 (23.8)
Epidural Use, n (%)	59 (85.5)	42 (79.2)	68 (88.3)	108 (86.4)	14 (66.7)
Received ARM, n (%)	46 (66.7)	25 (47.2)	51 (66.2)	81 (64.8)	14 (66.7)
Received Oxytocin, n (%)	53 (76.8)	44 (83.0)	66 (85.7)	108 (86.4)	20 (95.2)
Duration of Labor (minutes), median (IQR)					
Stage 1	422 (227-558)	515 (317-768)	327 (213-542)	400 (240-696)	715 (214-1215)
Stage 2	89 (38-136)	89.0 (50-122)	64 (38-137)	90 (46-170)	71 (24-118)
Stage 3	5 (3-8)	4 (3-6)	4 (3-6)	4 (3-7)	6 (5-6)
Birth weight (grams), median (IQR)	3370 (3110-3550)	3590 (3280-3880)	3580 (3230-3910)	3450 (3140-3710)	3300 (2830-3570)

ARM, artificial rupture of membranes; BMI, body mass index; GA, gestational age; GBS, group B streptococcus; GWG, gestational weight gain;
*Combined, Foley catheter induction with simultaneous prostaglandin insertion
†Sequential, Foley catheter induction after a trial of prostaglandin induction

Table 2.3 Indication for induction of labor by EOSSo category

Patient Group	Indication for Induction of Labor
Control (n=69)	-Postdates, 37 (53.6) -Gestational Diabetes, 9 (13.0) -Intrauterine Growth Restriction, 5 (7.2) -Gestational Hypertension, 3 (4.3) -Advanced Maternal Age, 2 (2.9) -Other Maternal Health Issue, 2 (2.9) -Cholestasis of Pregnancy, 2 (2.9) -Other, 1 (1.4) each (Preeclampsia, Oligohydraminos, Polyhydraminos, PROM, Chronic Kidney Disease, Suspected LGA, PUPPS, Marginal Cord Insertion, Gestational Thrombocytopenia)
EOSSo Category 0 (n=53)	-Postdates, 35 (66.0) -Advanced Maternal Age, 4 (7.5) -Other Maternal Health Issue, 4 (7.5) -Suspected LGA, 3 (5.7) -PROM, 2 (3.8) -Obesity, 2 (3.8) -Other, 1 (1.9) each (Cholestasis of Pregnancy, Gestational Thrombocytopenia, Umbilical Vein Varix)
EOSSo Category 1 (n=77)	-Postdates, 45 (58.4) -Borderline Gestational Hypertension, 10 (13.0) -Suspected LGA, 5 (6.5) -Other Maternal Health Issue, 3 (3.9) -Advanced Maternal Age, 2 (2.6) -Intrauterine Growth Restriction, 2 (2.6) -Oligohydraminos, 2 (2.6) -Other, 1 (1.3) each (Polyhydraminos, PROM, Obesity, Decreased Growth Velocity, PUPPS, Unstable Lie, Two-vessel Cord, Decreased Fetal Movements)
EOSSo Category 2 (n=125)	-Gestational Diabetes, 48 (38.4) -Postdates, 24 (19.2) -Gestational Hypertension, 16 (12.8) -Chronic Hypertension, 7 (5.6) -Advanced Maternal Age, 7 (5.6) -PROM, 4 (3.2) -Decreased Growth Velocity, 4 (3.2) -Decreasing Insulin Requirements, 3 (2.4) -Other Maternal Health Issue, 3 (2.4) -Cholestasis of Pregnancy, 2 (1.6)

	-Other, 1 (0.8) each (Suspected LGA, Obesity, Type 2 Diabetes, Oligohydraminos, Unstable Lie, Decreased Fetal Movements, Fetal Heart Rate Abnormality)
EOSSo Category 3 (n=21)	-Preeclampsia, 13 (61.9) -Maternal Mental Health Issue, 2 (9.5) -Other, 1 (4.8) each (Abnormal Fetal Doppler, Obesity, Suspected LGA, Gestational Diabetes, Type 2 Diabetes, HELLP Syndrome)

PROM, prelabour rupture of membranes; LGA, large for gestational age; PUPPS, pruritic urticarial papules and plaques of pregnancy
Data are presented as n (%)

Table 2.4 Indication for cesarean delivery by EOSSo category

Patient Group	Indication for Cesarean Delivery
Control (n=21)	-Fetal Heart Rate Abnormality, 9 (42.9) -Failure to Progress Stage 1, 8 (38.1) -Failure to Progress Stage 2, 7 (33.3) -Failed Induction of Labor, 1 (4.8) -Failed Instrumental Delivery, 1 (4.8)
EOSSo Category 0 (n=19)	-Fetal Heart Rate Abnormality, 9 (47.3) -Failure to Progress Stage 1, 6 (31.6) -Failure to Progress Stage 2, 3 (15.8) -Choriamnionitis, 2 (10.5) -Failed Induction of Labor, 2 (10.5) -Undiagnosed Breech, 1 (5.3) -Cephalopelvic Disproportion, 1 (5.3) -Fetal Malposition, 1 (5.3)
EOSSo Category 1 (n=23)	-Fetal Heart Rate Abnormality, 14 (60.9) -Failure to Progress Stage 1, 9 (39.1) -Failed Induction of Labor, 3 (13.0) -Chorioamnionitis, 3 (13.0) -Failure to Progress Stage 2, 2 (8.7) -Abruption, 1 (4.3)
EOSSo Category 2 (n=54)	-Fetal Heart Rate Abnormality, 31 (57.4) -Failure to Progress Stage 1, 21 (38.9) -Failed Induction of Labor, 6 (11.1) -Failure to Progress Stage 2, 4 (7.4) -Chorioamnionitis, 4 (7.4) -Undiagnosed Breech, 1 (1.9)
EOSSo Category 3 (n=19)	-Fetal Heart Rate Abnormality, 9 (47.4) -Failure to Progress Stage 1, 6 (31.6) -Failed Induction of Labor, 5 (26.3) -Chorioamnionitis, 1 (5.3) -Failed Instrumental Delivery, 1 (5.3) -Cephalopelvic Disproportion, 1 (5.3) -Fetal Malposition, 1 (5.3)

Data are presented as n (%)
Multiple indications may be provided

Table 2.5 Summary score and secondary outcomes by EOSSo category

Outcome	Control N=69	EOSSo 0 N=53	EOSSo 1 N=77	EOSSo 2 N=125	EOSSo 3 N=21
Summary Score P = 0.22	1.83±1.26	2.02±1.28	2.06± 1.37	2.13± 1.36	2.62± 1.66
Excessive GWG	21 (30.4)	26 (49.1)	41 (53.2)	63 (50.4)	14 (66.7)
Abnormal fluid level	2 (2.9)	1 (1.9)	3 (3.9)	4 (3.2)	1 (4.8)
Chorioamnionitis	1 (1.4)	4 (7.5)	6 (7.8)	11 (8.8)	1 (4.8)
Abruption	1 (1.4)	0 (0)	2 (2.6)	3 (2.4)	0 (0)
Shoulder dystocia	0 (0)	2 (3.8)	6 (7.8)	6 (4.8)	0 (0)
Severe perineal tear	19 (27.5)	14 (25.4)	12 (15.6)	22 (17.6)	0 (0)
Manual removal of placenta	7 (10.1)	1 (1.9)	2 (2.6)	6 (4.8)	0 (0)
Excessive blood loss	5 (7.2)	10 (18.9)	12 (15.6)	21 (16.8)	5 (23.8)
Blood transfusion	1 (1.4)	0 (0)	0 (0)	0 (0)	1 (4.8)
Meconium	15 (21.7)	11 (20.8)	18 (23.4)	22 (17.6)	4 (19.0)
Low Apgars	8 (11.6)	2 (3.8)	4 (5.2)	9 (7.2)	3 (14.3)
Stillbirth	0 (0)	0 (0)	0 (0)	1 (0.8)	0 (0)
Abnormal birth weight	6 (8.7)	7 (13.2)	17 (22.1)	18 (14.4)	3 (14.3)
Admission to NICU	1 (1.4)	1 (1.9)	2 (2.6)	7 (5.6)	2 (9.5)
Maternal death	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Thromboembolic disease	0 (0)	0 (0)	0 (0)	0 (0)	1 (4.8)
Instrumental delivery	18 (26.1)* -Forcep, 13 (72.2) -Vacuum, 6 (33.3)	9 (17.0) -Forcep, 8 (88.9) -Vacuum, 1 (11.1)	11 (14.3) -Forcep, 11 (100) -Vacuum, 0 (0)	18 (14.4) -Forcep, 16 (88.9) -Vacuum, (11.1)	1 (4.8)† -Forcep, 0 -Vacuum, 1 (100)
Cesarean delivery	21 (30.4)	19 (35.8)	23 (29.9)	54 (43.2)	19 (90.5)

NICU, neonatal intensive care unit; GWG, gestational weight gain
Data are presented as mean ± SD or n (%)
*Includes one combined vacuum + forceps
†Includes a failed instrumental delivery resulting in a cesarean delivery

2.8 FIGURES

Figure 2.1 Cohort flow diagram

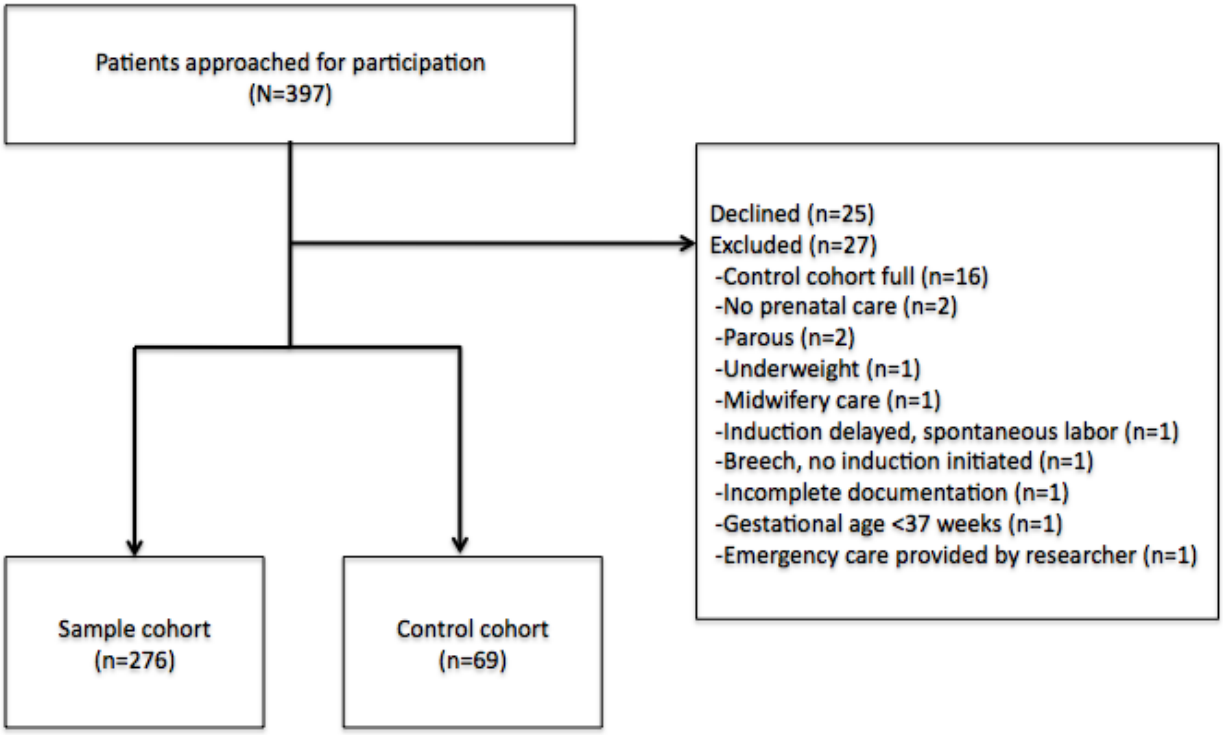


Figure 2.2 Composition of BMI within each EOSSo category

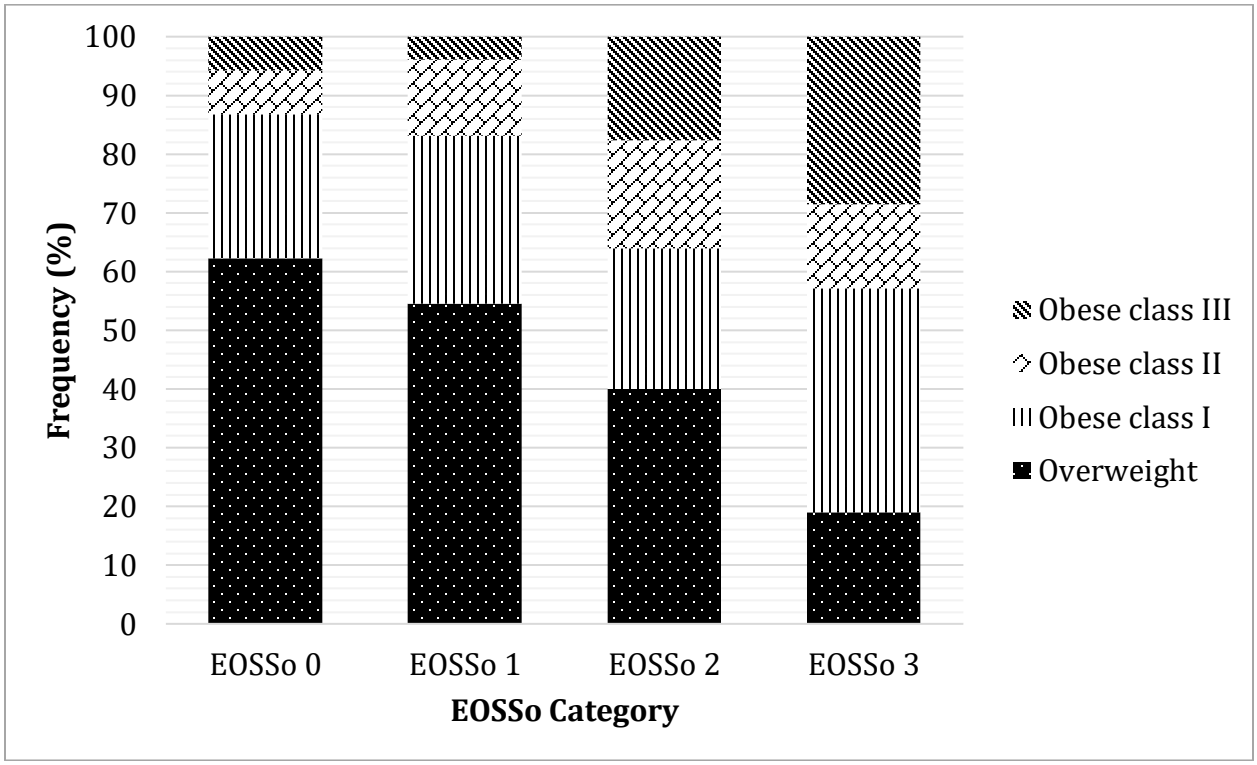


Figure 2.3 Rate of cesarean delivery by EOSSo category (P < 0.001)

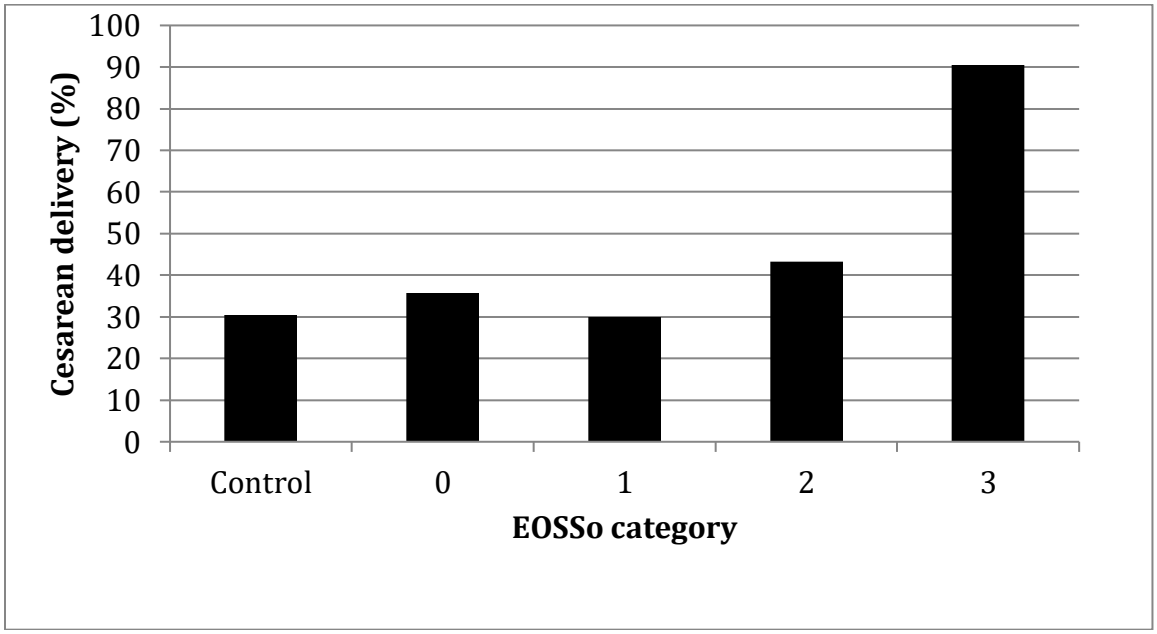
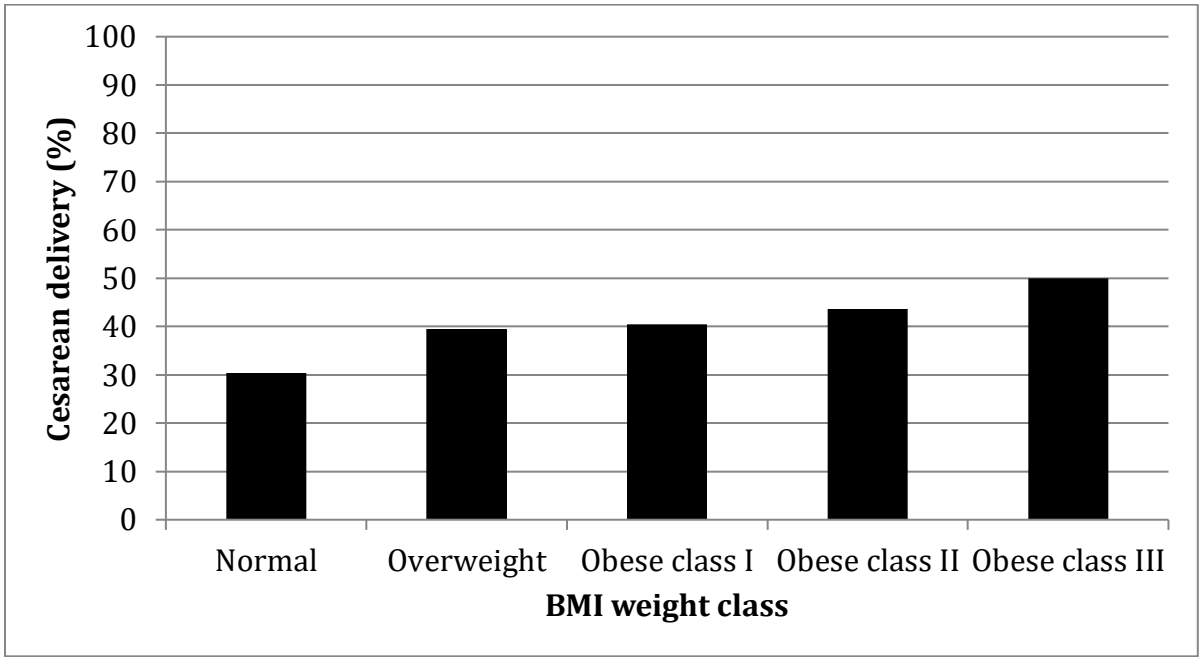


Figure 2.4 Rate of cesarean delivery by BMI class (P = 0.37)



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CHAPTER 3

SUMMARY & CONCLUSION

3.1 SUMMARY OF RESULTS

The main objective of this study was to determine if the EOSSo could be used as an individualized risk assessment tool to predict the risk of cesarean delivery, after an induction of labor, in women with excess weight. Thus, a prospective cohort study attempted to validate the use of the EOSSo for this purpose.

The rate of cesarean delivery was 30.4% for the control cohort and 35.8%, 29.9%, 43.2%, and 90.5% for women assigned an EOSSo category 0, 1, 2, and 3, respectively ($P < 0.001$). Overall, the EOSSo was able to identity a subpopulation of women (EOSSo category 3) who were at a high risk of cesarean delivery. Current practice suggests that BMI alone may be a good indicator of cesarean delivery risk and suggests that those with the greatest BMI are at the highest risk. In our study, rates of cesarean delivery were also compared by BMI. Overall rates of cesarean delivery were 39.5%, 40.5%, 43.6%, and 50.0% for overweight, obesity class I, II, and III, respectively ($P = 0.37$). In our study, BMI was not predictive of cesarean delivery and therefore should not be the foremost principal guiding clinical decision-making around delivery outcomes. The EOSSo however, does offer superior predictive utility.

3.2 FUTURE DIRECTIONS

The extent to which obesity plagues current first world nations is still a relatively new phenomena and the incidence of obesity is continuing to rise. With such a high proportion of patients suffering from this condition, significant resources need to be devoted to research in this

area. Building on this current study, there are a few suggestions for future research. First, the most impactful outcome of this study was the identification of a subpopulation of women (EOSSo category 3) who are at an over 90% risk of cesarean delivery. The overall number of participants in this group, however, was low and attempts should be made to replicate this finding on a larger scale. As discussed earlier, if this outcome persists, it may be more appropriate to offer women in this subpopulation an elective cesarean delivery instead of an induction of labor. Research should then examine the differences in maternal and neonatal outcomes between women who receive an elective cesarean delivery and those that receive an IOL. In addition, and perhaps more importantly, these two delivery management strategies should be examined from the patient's perspective to ensure acceptability and satisfaction, especially as it pertains to maternal mental health status. Lastly, larger scale studies dedicated to the secondary outcomes defined in this study should be examined separately. This will allow adequate power and appropriate conclusions with regard to individual maternal and fetal outcomes.

3.3 FURTHER CONSIDERATIONS FOR THE EDMONTON OBESITY STAGING SYSTEM IN OBSTETRICS

The nature of working in a scientific field like medicine is that care providers are constantly confronted with a rapidly changing and evolving profession. Ongoing research and innovation propel patient care forward and continually works to improve outcomes. The EOSS was originally described in 2009 and since that time there have been advances in medicine that were not accounted for in the original scale or this study.[1] In 2013, the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) was updated to recognize the new medical classification

of binge eating disorder (BED).[2] While psychological impairment is included in the previous iteration of this scale, BED, in particular, was not accounted for and BED behaviors were not specifically probed. As this is a relatively new diagnosis, it may therefore have been underreported and underrecognized.[3] In practice, knowledge about BED is important in the event that a patient requires additional psychological supports and to ensure healthy GWG. Women with BED were found to have negative feelings with a diagnosis of pregnancy and were more likely to have higher rates of excessive GWG.[4] This translated into poorer maternal and fetal outcomes including an increased rate of hypertensive disorders and macrosomia. Pregnancy also reflects a period of vulnerability for women with BED where they may be prone to relapse or propagation of this disorder. Ensuring specific knowledge about this relevant comorbidity is therefore imperative to provide appropriate care.

The EOSSo described in this study was not a comprehensive examination of obesity-related comorbidities in pregnancy. This study was limited to an investigation of women at term and conditions affecting preterm gestations were not included. Obesity has been related to other adverse outcomes in pregnancy including increased rates of spontaneous abortion and preterm birth.[5-7] Further review and adaptation of the scale is therefore necessary should this scale be applied more broadly in pregnancy.

Importantly, while the results of this study are striking, it needs to be stressed that further validation of this scale needs to be performed. This study serves as a proof of concept to use the EOSSo as a clinical staging tool to assess obesity-related risk in pregnancy. The current study draws its patient cohort from a single city and with care providers of which many were trained locally. This scale needs to be applied on a broader scope and its inter-rated reliability needs to be tested. Assessing the scale on a national level will improve generalizability by ensuring

heterogeneity of both patient and care provider populations. By expanding its use, and proving its utility in a variety of settings, care providers will then feel confident applying this scale in untested populations as you would in a clinical setting for risk prediction.

3.4 CONCLUSION

A significant proportion of patients presenting for maternity care are now afflicted with obesity and rates are continuing to rise. Obesity associated risks are innumerable and represent significant detriments to both women and their offspring. To date, BMI has been the most widely accepted measure for obesity in both non-pregnant and pregnant populations. Despite its use in pregnancy, there is no consensus that BMI is the most accurate measure of adiposity and risk. In the present study, the Edmonton Obesity Staging System for Obstetrics yields a better assessment of individualized risk for cesarean delivery in women with excess weight who are undergoing an IOL.

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