Kofinas Perinatal

Providing Care to the Unborn ®

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Significant improvement in perinatal outcomes and savings in high risk patients managed according to Kofinas Perinatal protocols

Introduction

Kofinas Perinatal provides high risk services to patients in the New York City major metropolitan area with significant concentration in the borough of Brooklyn. We provide all of our services on an outpatient setting in our Brooklyn (Park Slope) and Garden City locations. Our offices are designed to provide comfort, easy access and a calm environment in order to help highly stressed high risk mothers to relax and feel at ease. Our office is equipped with imaging systems that provide the latest and highest quality of imaging helping us achieve the maximum diagnostic capabilities in dealing with unborn patients. All our imaging systems provide high resolution (almost microscopic) imaging of the placenta and its vascular structure and they are equipped with the latest power color Doppler and Pulsed wave Doppler capabilities. These capabilities are of paramount importance in our ability to better diagnose fetal and placental problems. These same systems are fully networked and can be managed remotely over secure networks giving us the ability to evaluate patients (the unborn) anytime and from everywhere.
The imaging systems are also connected to our sophisticated large capacity computer system. All images and all reports are managed online and stored in highly reliable and redundant storage systems as well as permanent tape drive backups. Our computer systems are designed to be fail-safe, and to be able to store reports and images for at least 18 years (statue of limitations for neonates). Back up UPS power supplies as well power generators assure uninterrupted availability of reports and images 24/7 and from everywhere there is an internet access. Sophisticated and dedicated security hardware provides security and protection from intrusion and limit access to unauthorized individuals (fire wall systems).

Services

As a high risk management practice we see patients with the following high risk conditions:

1. Prenatal diagnosis
    a. Fetal anatomical assessment
        i. Level II ultrasound
        ii. Fetal echocardiography
    b. First trimester genetic ultrasound
        i. Nuchal Translucency and nasal bone assessment as a screening tool for fetuses with chromosomal defects
        ii. Ductus venosus PW Doppler assessment for Down syndrome and cardiovascular defects

   c. Chorionic Villous sampling (chromosomal defects)
   d. Amniocentesis (chromosomal defects)
   e. Fetal Blood sampling for diagnostic purposes
2. Selective reduction of higher-order multiple gestations to twins or triplets (these are women that conceived with the latest reproductive technologies (IVF, IUI, etc.) and who have more than 3 fetuses (from 3 to 9 fetuses).
3. Genetic consultation
4. High risk consultation and high risk pregnancy management
   a. History of fetal loss
   b. History of growth retarded neonate
   c. History of preterm birth
   d. Patients in active preterm labor
   e. Incompetent cervix
   f. Oligohydramnios
   g. Polyhydramnios
   h. Gestational and pre-gestational diabetes
   i. Chronic hypertension
   j. Pre-eclampsia
   k. Maternal cardiac disease
   l. Maternal lupus disease
   m. Maternal renal disease
   n. Any other maternal condition that might affect the pregnancy
5. Fetal therapy
   a. Fetal transfusion with percutaneous umbilical cord access under real time ultrasound guidance
   b. Fetal injection
   c. Amniotic fluid reduction in patients with Polyhydramnios and in cases with sever twin-to-twin transfusion syndrome with stuck twin
6. Management of patients with recurrent pregnancy loss and inability to conceive
7. Management of patients that conceived with ART reproductive assistance
8. Management of patients with twins and higher-order multiples (3-9 fetuses)
9. Management of pregnancies complicated by thrombophilia (genetic, acquired and multifactorial)
10. Management of pregnancies complicated by paternal and fetal thrombophilia

Although we are providing all of the above services as needed, due to an unprecedented success and improved outcomes in patients with specific high risk conditions, we are heavily concentrating our efforts in the management of the following specific groups of patients:

1. Recurrent miscarriage (65% are caused by thrombotic conditions, ***{Clin Appl Thrombosis/Hemostasis 2005;11(1) T1-T2},{Journal Reproductive Immunology 2002;55:163-180}).***
2. Fetal loss after 12 weeks (risk for loss in the next pregnancy is up to 75%). ***{Obstet Gynecol 2004;104:521-6}***
3. Preterm birth (recurrence risk is up to 50%)***{N Engl J Med 2003;348:2379-85}***

4. Known maternal thrombophilia and history of thrombosis (Any fetal loss:29% and stillbirth rate of 44/1000), ***{Lancet 1996;348:913-16}***
5. Hypertensive disorders (Recurrence of 30%)
6. Incompetent cervix (prematurity in more than 50% of cases)
7. Singleton pregnancies conceived with assisted reproductive technologies (ART) are at increased risk (25-40%) for prematurity, Very low birth weight, perinatal mortality, growth restriction, pregnancy induced hypertension and placenta previa; these risks are on average 2-4 times the average national risk for such complications) ***{J Obstet Gynaecol Can 2005 May;27(5):449-59},{BMJ 2004 Jan 31;328(7434):261},{Obstet Gynecol 2004 Mar; 103(3):551-63},{Obstet Gynecol 1995 Aug;86(2):188-92}***
8. Multiple gestations (the risk of prematurity and related complications is 8-10 times larger than singleton gestations ***{Twin Res. 2000 Mar;3(1):2-6.}***

Such patients have unique problems that require unique solutions. Dr. Kofinas has devoted the first twenty years of his academic and clinical career in the study of placental vasculature and placental related conditions (see CV for original research publications). Prenatal diagnosis and fetal therapy has been the staple of his clinical practice over the last 25 years. During those years, his clinical exposure to an infinite variety of medical and obstetrical complications, his personal research (published in the most authoritative national and international journals), his unpublished work and the research work of others in the field of Maternal Fetal Medicine guided Dr. Kofinas in the development of unique protocols for the diagnosis and management of the specific conditions mentioned above. The success of the practice has created the need for us to focus further and to devote most of our resources in the treatment of such patients. Kofinas Perinatal is the only practice in the major metropolitan area devoted to such patients almost exclusively. The average practice in Maternal Fetal Medicine devotes most of their resources in the care of patients seeking genetic diagnostic services, in-hospital consultation and management of hospitalized patients, general obstetric care (antepartum and delivery care), and fetal monitoring for high-risk patients and postdate pregnancies. There is no effort whatsoever in such practices to prevent the major complications of pregnancy such as intrauterine growth restriction, pre-eclampsia, PROM, preterm delivery, fetal death in utero and many others. The proof of this statement can be found in the national perinatal statistics of the Center for Disease Control (CDC) as well as other national and private databases. What these statistics show is that despite the billions spent by most of the perinatal services, the outcomes of complicated pregnancies have remained unchanged or are deteriorating. For example, despite universal fetal monitoring by means of electronic fetal monitoring and biophysical profile, fetal death from explainable and unexplainable conditions has remained stubbornly steady at 8-16 per thousand. To this, one must add the 7-10 neonatal deaths that are usually the result of poor perinatal care prior to delivery. Likewise, the incidence of cerebral palsy has remained stubbornly steady at a rate of 1 in 400 live born. Isn't it true that high risk obstetrical (perinatal) management supposed to eliminate or at least reduce these adverse effects? What about preterm birth? For years now March or

Dimes and a plethora of similar organizations have been setting targets for reducing prematurity to less than 7%; every year these targets are moved further and instead are replaced by a new record of prematurity. According to national statistics, approximately 8% of all neonates were born prematurely (<37 weeks) in 1990; in 2005 this number stands at 13.5%. ***{National Center for Health Statistics, final natality data. Retrieved February 05, 2006, from www.marchofdimes.com/peristats}.*** Prematurity is the number one cause of neonatal death and the most dominant cause of neonatal, childhood, and adult morbidity. Likewise, intrauterine growth restriction has been increasing despite our efforts to reduce it and it is now 8-9% of all pregnancies. Intrauterine growth failure has been clearly proven to be the main and only cause of many of the adulthood diseases. ***{Lancet 2002; 360: 1489-97, Obstet Gynecol Survey 2002;57:S9-S34}***
Elaborate research in the last 10 years ***{ Early Human Development 2005;81:721-722}*** has clearly and indisputably shown that obesity, diabetes, cardiovascular disease (heart attacks and heart failure) ***{(Early Human Development 2005;81:745-751), (Early Human Development 2005;81:123-129),(Early Human Development 2005;81:735-741),, cerebrovascular events (strokes) {BMJ 2001;323:1033-4},*** aortic aneurysm ***{Lancet 2005;365:1484-86},*** premature organ (liver, lungs, kidney) failures ***{Early Human Development 2005;81:763-771}*** and altered brain development ***{Early Human Development 2005;81:753-761}*** have their origin in fetal life. Fetuses that develop in a hostile intrauterine environment develop adaptive mechanisms that become a health liability after birth. These fetal adaptive mechanisms lead to the above mentioned adulthood diseases.

A deficient placenta is the main cause of the poor fetal health and growth restriction in the vast majority of pregnancies.

The placental problems in most of these pregnancies are associated with variable degrees of thrombosis secondary to maternal, fetal, and paternal thrombophilia ***[{Obstet Gynecol Surv 1999;54:754, Obstet Gynecol Surv 2002;57:703, Am J Obstet Gynecol 2004;191:412, Eu J Obstet Gynecol Reprod Biol 2004;117:45},{Hum Pathol2004;35:1494-1498}].*** The link between placental thrombosis, thrombophilia and adult diseases is a strong one. In addition, women whose pregnancies were complicated by the 'placental syndrome' were more likely to develop cardiovascular and other thromboembolic condition later on their lives as well as women who experienced miscarriages during their reproductive years and other pregnancy complications were more likely to die from cardiovascular diseases in midlife and beyond; this clearly shows the link between pregnancy loss and cardiovascular pathology relating to thrombophilia. ***{Lancet 2001;357:2002-06}{Lancet 2005;366:1797-803}***
It is known that most of the preterm infants are also growth restricted due to poor placentation ***{ Seminars in Thrombosis and Hemostasis 2001;27:107-113}.*** This is the result of the relationship between poor placental development and preterm delivery. Without extending the discussion further, it is evident that placental thrombosis is caused by various thrombophilic conditions and leads to the most dangerous complications of the pregnancy (growth restriction, PROM, preterm birth, fetal death, preeclampsia, neonatal death, and cerebral palsy) ***{Eur J Obtet Gynecol Reprod Biol 2004;117:144-***

147},{Seminars in Thrombosis and Hemostasis 2005;31:97-103},{Journal of Thrombosis Thrombolysis 2002;14(2);163-169}. Most researchers agree that these conditions are caused by placental pathology associated with vascular thrombosis ***{Placenta 1995;16:165-170},{Placenta 2004;25;s102-s105}*** and degeneration but do not agree as to whether such placental pathologies can be prevented ***{ Seminars in Thrombosis and Hemostasis 2004;29:213- 217}.***

At Kofinas Perinatal we believe that such conditions can be prevented or even be completely eliminated. Placental damage can be prevented and healthy placental development can be assured for most pregnant women. In patients with previous poor outcomes, we plan the pregnancy and treat the patient from the time of conception or sooner. This assures a normal undisturbed placental development which in turn secures a healthy fetal development. We have managed to change poor perinatal outcomes to normal and substantially reduce all serious perinatal adverse outcomes.
In patients with no prior history, careful assessment of the placenta during the first ultrasound assessment may help identify patients at risk for their first poor outcome. Aggressive anti-thrombotic treatment may reverse the condition and lead to a healthy pregnancy. Unfortunately, many of the "low risk pregnancies' do not have an expert ultrasound until 18-22 weeks. By this time, most of the placental development is complete and any damage that has happened is irreparable. Even at the end of the first trimester, half of the placenta is complete and any damage done by then cannot be recovered. In such patients, intense anti-thrombotic treatment for the rest of the pregnancy may salvage enough placental functionality to help the fetus develop in a healthy manner.
Over the last 25 years, our research and clinical expertise helped us develop the various protocols for the management of such patients. The result has been an unprecedented reduction of premature births, growth restriction, preeclampsia, hospitalization, and the elimination of fetal death. Our experience and expertise allows us to manage our patients with almost proprietary means and in stark contrast to other perinatal services. In the tables and notes below we will present the outcomes we have achieved by the use of our distinct management schemes. These outcomes speak for themselves and are the ultimate justification of our unique protocols.

Quality care and preservation of the unborn's genetic potential (health) is our number one priority.

However, in our effort to prevent fetal adverse outcomes, we have achieved enormous cost savings in comparison to patients managed according to conventional approaches. For us, this is the "icing on the cake."

Exhibit 1: Comparison of Kofinas Perinatal outcomes (100% high risk patients) against the average national statistics reported by CDC (70% normal pregnancies and 30% high risk patients). Our outcomes are superior despite the higher risk population.

Complications	Kofinas Perinatal Incidence %	Expected Normal Incidence%	Change in Incidence %
Chronic Hypertension	3%	3%	0%
Chronic Hypertension w/ PE	<0.6%	1.50%	-50%
Pregnancy Induced Hypertension (PIH)	0.30%	10-15%	-97%
Abruptio Placentae	1%	1%	0%
Oligohydramnios	3.7%	8%	-50%
Preterm PROM	0.6%	8%	-87%
Preterm Delivery	5.90%	13.50%	-56%
Total Pregnancy loss	4%	25%	-84%
Fetal death > 20 weeks	0%	1.70%	-100%
Antepartum Admissions	2%	10%	-80%

Exhibit 1 demonstrates the incidence of the listed complications in the patients managed by Kofinas Perinatal according to our protocols, the expected incidence in the obstetrical patients at large **(including all low risk patients)** and the difference between the two. Negative numbers indicate reduction from the expected and positive numbers indicate increase. The incidence of complications is from the total number of the first 893 patients for whom complete outcomes data are available.
The expected incidence reflects the average national incidence of complications as reported in the literature, Natality statistics from the CDC databases, the March of Dimes databases and various state perinatal statistical reports. The most recent data are from 2003 with the exception of preterm delivery which is from 2004 data.

It is important to note that our patients are high-risk patients and the incidence of complications in this group is anywhere from 2-5 times higher than the general population. Of significance also is the fact that the vast majority of complications, if not all of them, occur in the 30 percent of the high-risk pregnancies. Therefore, it is obvious that high-risk patients are on average 3 times more likely to experience any of the listed complications than the entire pool of pregnant women.
Comparisons in Exhibit 2 are more appropriate since we are managing exclusively high risk patients and the magnitude of improvement is more evident in these patients.

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Exhibit 2. Comparison of Kofinas Perinatal outcomes in our high risk patients against expected national outcomes based on published reports in patients with similar risk profiles. Our outcomes are again superior with significant reductions in maternal and neonatal complications.

Complications	Kofinas Perinatal Incidence	Expected in High Risk Patients	Reduction from High risk level
Chronic Hypertension	3%	3%	0%
Chronic Hypertension w/ PE	0.6%	1.50%	-30%
Pregnancy Induced Hypertension. (PIH)	0.30%	10-15%	-98%
Abruptio Placentae	1%	3%	-66%
Oligohydramnios	3.7%	10-15%	-74%
Preterm PROM	0.60%	10%	-94%
Preterm Delivery	5.90%	30%	-80%
Total Pregnancy loss	4%	29%	-86%
Fetal death > 20 weeks	0%	4.40%	-100%
Low birth weight (<2500)	5.30%	30%	-82%
Antepartum Admissions	2%	30%	-94%

Exhibit 2 above depicts the incidence of complications in our patients in comparison to expected incidence in patients with similar risk profiles. It is clear from exhibits 1 and 2 that outcomes at Kofinas Perinatal are substantially better than the American averages at large and even more impressive, when compared with outcomes in patients with similar risk profiles.
Exhibit 3 below demonstrates savings realized based on prevention and reduction of the incidence of the above complications.

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Exhibit 3. All pregnancy outcomes are per 1000 births after 20 weeks.

Complications	Cases Prevented	Cost Savings per case prevented	Total savings per complication
Pre-eclampsia	132	$20,000.00	$2,640,000.00
Abruptio Placentae	18	$20,000.00	$360,000.00
Preterm PROM	82	$30,000.00	$2,460,000.00
Preterm Delivery	215	$100,000.00	$21,500,000.00
Antepartum Admissions	71	$20,000.00	$1,420,000.00
Total Pregnancy loss	250	Inestimable	Inestimable
Fetal death > 20 weeks	44	Inestimable	Inestimable

TOTAL SAVINGS in 893 patients **$28,380,000.00**

We see approximately 1000 patients a year

TOTAL SAVINGS per 1000 patients **$31,780,515.00**

The above statistics are from actual patients managed by Kofinas Perinatal. Outcomes are collected prospectively and kept in our outcomes database for periodic analysis. This is one part of our ongoing quality assessment and performance monitoring that guides our efforts to provide excellent quality of care to our high risk patients. Based on such outcomes-analysis along with continued medical education by means of research and literature reviews, we constantly adjust our management protocols to reflect the ever changing medical knowledge. The formulation of our protocols is based on 20 years or research, clinical experience, continuous quality assessment and improvement techniques and on the scientific developments over the last 20 years.

Unprecedented advancements in computer technologies have given us the ability to look into the womb and assess the condition of our unborn patients in ways not possible just 10 short years ago. Armed with such capabilities we have been able to literally change the destinies of our unborn by been able to reduce the incidence of intrauterine growth restriction, fetal death, and preterm birth, premature rupture of fetal membranes, abruptio placentae and pre-eclampsia. The short list of the above complications constitutes the main cause of fetal and infant morbidity and mortality. *However, let us not forget that healthy development in the womb (prenatal development) reduces substantially the risks for adulthood diseases such as cardiovascular (heart attacks) and cerebrovascular (strokes) diseases, premature organ failure, diabetes, renal disease etc*. ***{(Early Human Development 2005;81:745-751), (Early Human Development 2005;81:123-129),(Early Human Development 2005;81:735-741),, cerebrovascular events (strokes) {BMJ 2001;323:1033-4},*** *aortic aneurysm* ***{Lancet 2005;365:1484-86}***

Financial Implications/Benefits

The financial benefits are calculated based on estimates published in the perinatal literature. The majority of cost analyses that have at times been published are based on administrative sources. These sources are flawed because they are inherently incapable of distinguishing the various sources of morbidity and the level of intensity.
Managed care organizations use similar systems whose primary purpose is to account for crude costs and resource allocation. Such systems are unable to identify types and severity of diseases. Disparity of diagnostic coding complicates things further and ads to the confusion. Managed care systems are even unable to distinguish among the different types of practitioners and when such systems are used to compare cost of various practitioners the result is a meaningless tabulation of codes and $$ with no relationship to reality.

The cost figures we used in exhibit 3 are very conservative because they are based on available statistics that were produced in other states with lower cost of living (Alabama and Vermont) due to lack of such data in New York state. These numbers also suffer from the fact that they have been produced from administrative and financial sources that in many institutions are disparate and have the tendency not to capture the total cost of a patient hospitalized for a number of days. In addition, significant costs that are incurred on an outpatient basis as a result of the hospitalization are never captured. ***{Pediatrics 1999;103:329-335}***

This is extremely important in the calculation of costs of prematurity. For example, a premature neonate may be in the Neonatal Intensive Care Unit (NICU) for 20 days but the money spent are distributed in a variety of cost centers and outsourced services that could never be captured in their entirety. As an example, a premature neonate that remained in the NICU of New York Hospital (Cornell University) for 41 days received a bill for the total amount of $1,200,000.00 for an average daily cost of $27,000.00. This amount was spent and the neonate was deprived of his future suffering from profound mental retardation. This was a preventable complication. {This patient under my expert care in two subsequent pregnancies despite similar complications was able to achieve two healthy term pregnancies with two healthy children.}This of course is an extreme case but for the New York City reality, this cannot be too far from the median regarding the financial cost. In addition, the total cost of such complicated care that involved transfers to special centers for special care could never be captured by the usual administrative sources that provide most of the data that we have at our disposal to evaluate costs of various aspects of health care. The reason for such disparity is the presence of various departments and cost centers within the hospitals as well as outsourced diagnostic services and the resultant fragmentation of the medical charges. Insurance computer systems are likely unable to capture the total cost of pregnancy for similar reasons in addition to the fact some families may be covered by more than one plans with unevenly shared financial responsibilities.

The cost figures we utilized regarding the cost of prematurity (neonatal care cost) are from a recent publication analyzing the cost of neonatal care across the state of California ***{Early Human Development 2006;82:85-95}.*** New York City is far more expensive in all aspects of life in comparison to the average cost of living in the state of California. A publication reporting on costs in the state of Vermont in the period between 1993 and 1994 found the total cost per premature neonate at the day of discharge to be $76,000.00. Factoring in the inflation adjustment brings the figure to more than $100.000.00 ***{Pediatrics 1999;103:329-335}.*** Delaying a delivery from 26 weeks to 37 weeks gestation saves $206,000.00 in year 2000 dollars ***{Early Human Development 2006;82:85-95}.*** If we factor in the health care industry's compound inflation rate (>10% per year) for the last 6 years the cost in today's dollars would be in excess of $400,000.00. This is an enormous amount of money that can be realized by delaying the delivery for only 11 weeks. *There are very few jobs that can produce (save) so much capital in such a short period of time.*

Hospitalization costs are estimates based on a publication from a national managed care organization on data collected from pregnant women that gave birth or lost a pregnancy in 1997 ***{Obstet Gynecol 2002;100:94-100}.*** This is the only and most recent published material. It is well known that the health care costs are rising with double digit percentages in the last 10 years (4 to 5 times the rate of CPI). At such inflation rates health care costs have more than doubled since 1997. Even though we utilized extremely conservative figures for our estimates, the realized savings are enormous and only a "willfully blind" individual or institution would attempt to ignore.

The insurance industry and the health care professionals look at health care delivery from a totally different perspective. As a physician I am responsible medically, ethically and emotionally to the patient who trusts her life and the life of her unborn to me. The majority of my patients have experienced pregnancy loss or pregnancy related complications in previous pregnancies under "expert perinatal care". I have cared for patients that were failed by previous "experts" in all major academic institutions in the tri-state area. Such patients were treated according to the usual and customary perinatal care with devastating outcomes that were attributed to the patient's peculiar "genetic idiosyncrasies". All these patients suffered from placental related complications that lead to their unfortunate outcomes. Such conditions are diagnosable and treatable. Kofinas Perinatal management protocols provide such treatments and achieve the above presented exceptional outcomes. When we evaluate such patients and promise them a healthy and fully developed neonate we sign a moral contract that binds us and obliges us to do everything in our power to help such patients achieve their life-long goal; the goal of heaving a healthy baby which comes to this world not deprived of his genetic potential due to deficient physical and mental development in his mother's womb. This commitment to our patients and the intensive outpatient care provided in our offices is at times construed as "unnecessary and experimental" management. *At Kofinas Perinatal we consider it as the gold standard of excellent outcomes-driven care of the highest quality; our long suffering patients deserve nothing less.*