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Monochorionic twin pregnancy from the perspective of the theory of complexity

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ABSTRACT

In practice, it is very common to associate monochorionic (MC) twin pregnancies with complex or complicated pregnancies, using both terms interchangeably. However, these are not synonyms; dynamism is the protagonist in complex systems, but not in complicated ones. In order to understand a MC pregnancy as a complex system, it is necessary to first look into its main characteristics. The placenta is one of the main sources of problems. Then, the MC pregnancy has to be analyzed from the perspective of complexity, identifying the system characteristics and its complications as emergent properties.

Keywords: *twin pregnancy; placenta; pathophysiology; complexity theory.*

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INTRODUCTION

It is very common to associate monochorionic (MC) twin pregnancies with complex or complicated pregnancies, using both terms interchangeably. However, these are not synonyms.[1] To analyze a MC pregnancy from the perspective of the complexity theory, it is first necessary to understand the difference between a complex and a complicated system.

A system is a set of interconnected elements that make up a totality that performs a function or causes some effect. However, while in a complicated system, such as an ultrasound scanner or an airplane, it is possible to predict what is going to happen and the sum of the parts has a unique and specific purpose, in a complex system, behavior depends on infinite interactions and is unpredictable; the whole is greater than the sum of its parts.[1,2] Indeed, despite countless efforts to predict the course of MC pregnancies, the more experience is gained in their follow-up, the more difficulties and limitations are recognized in identifying complications before they occur.

PREGNANCY FROM THE PERSPECTIVE OF THE COMPLEXITY THEORY

Perinatal care (obstetrics, neonatology) was among the first areas in medicine to include systematic reviews of randomized clinical trials as a guide to develop evidence to define behaviors and treatments.[3] So much so that the Cochrane Library logo depicts the results of an iconic systematic review on the benefits of corticosteroids in women at risk of preterm birth.[4] But it was also one of the first fields to criticize such reductionist approach as an absolute truth, warning against the use and abuse of meta-analyses.[3,5] Indeed, pregnancies involve different spheres that are deeply related. Obstetric outcomes depend not only on the personal and obstetric history of the pregnant woman, but may also be influenced by socioeconomic factors (dangerous neighborhood, precarious work, unemployment), psychosocial factors (unwanted or unplanned pregnancy, discrimination), or family problems (violence, lack of support), among others. Therefore, analyzing pregnant women from the perspective of the complexity theory may improve the understanding and prediction of their perinatal outcomes.

A MONOCHORIONIC PREGNANCY

Compared to singleton pregnancies, twin pregnancies have a higher rate of complications, such as prematurity, malformations, growth alterations, and perinatal death.[6] Such increase is more marked in MC than in dichorionic (DC) pregnancies because of the risks associated with MC placental angioarchitecture, such as twin-to-twin transfusion syndrome (TTTS), selective fetal growth restriction (sFGR), twin anemia polycythemia sequence (TAPS), and twin death, among others.[6] To understand the analysis of a MC pregnancy from the perspective of the complexity theory, basic concepts regarding the placenta must first be analyzed.

A MONOCHORIONIC PLACENTA

A MC pregnancy is characterized by both twins sharing the same placenta, which contains vascular anastomoses between fetal circulations. The vascular equator is an imaginary line along the placental surface at which such anastomoses connect (*Figure 1*). These may be arterioarterial (AA), venovenous (VV), or arteriovenous (AV) anastomoses. AA and VV anastomoses are superficial and allow bidirectional blood flow, while AV anastomoses are deep and unidirectional (*Figure 2*).[7]

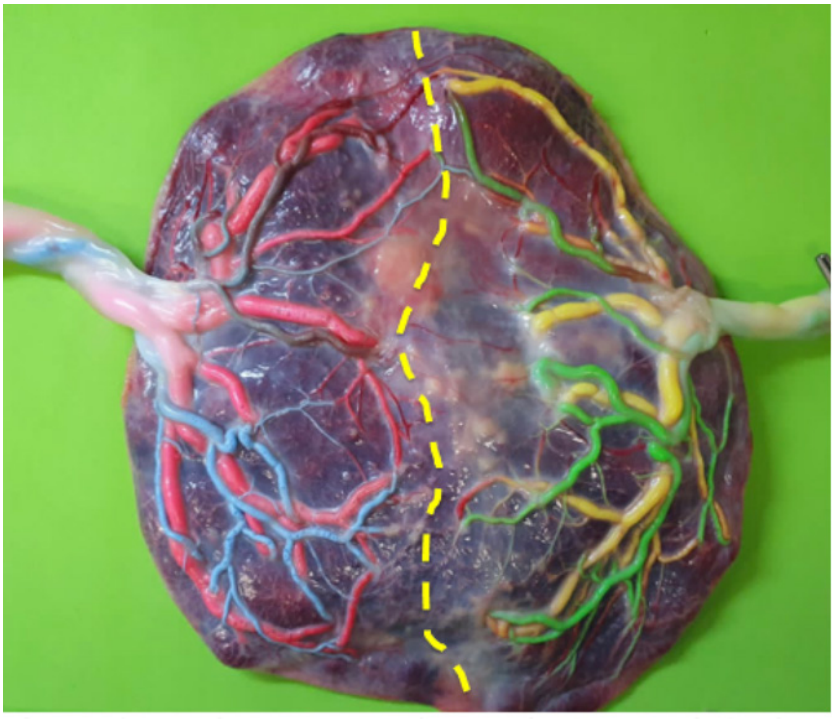
The size of the placental portion corresponding to each fetus and the angioarchitecture of the placenta are determining factors in the course of pregnancy.[7]

When the placental territory corresponding to each twin is similar and there is a hemodynamic balance between both fetuses, the pregnancy is usually "uncomplicated" (*Figure 3a*). If the placental territory corresponding to each twin is disproportionate, sFGR usually occurs (*Figure 3b*). When the main problem lies in the alteration of the hemodynamic balance between both fetuses (*Figure 3c*), with a greater blood flow to one of the twins through the deep anastomoses, TTTS will develop. If hemodynamic instability occurs chronically through filiform AV anastomoses (< 1 mm), TAPS may develop (*Figure 3c*). A protective factor against this hemodynamic instability is the presence of AA anastomoses (*Figure 2*), which, by allowing a bidirectional blood flow, may compensate for potential flow instability caused by AV anastomoses and reduce, although not eliminate, the risk for TTTS.[7]

WHY ANALYZE MONOCHORIONIC PREGNANCY FROM THE PERSPECTIVE OF THE COMPLEXITY THEORY

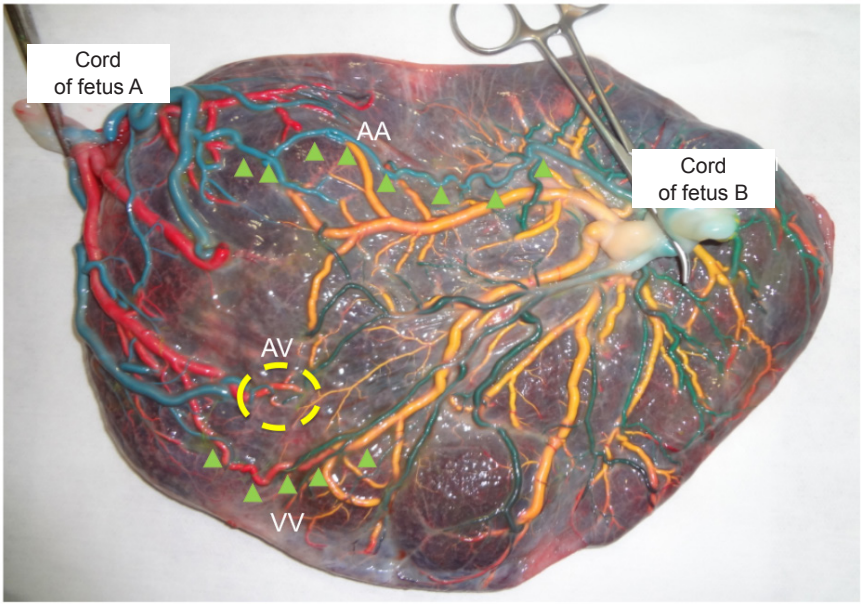
There is a tendency to explain all MC complications based on placental characteristics.

Figure 1. Vascular equator (yellow line) in an uncomplicated monochorionic twin pregnancy



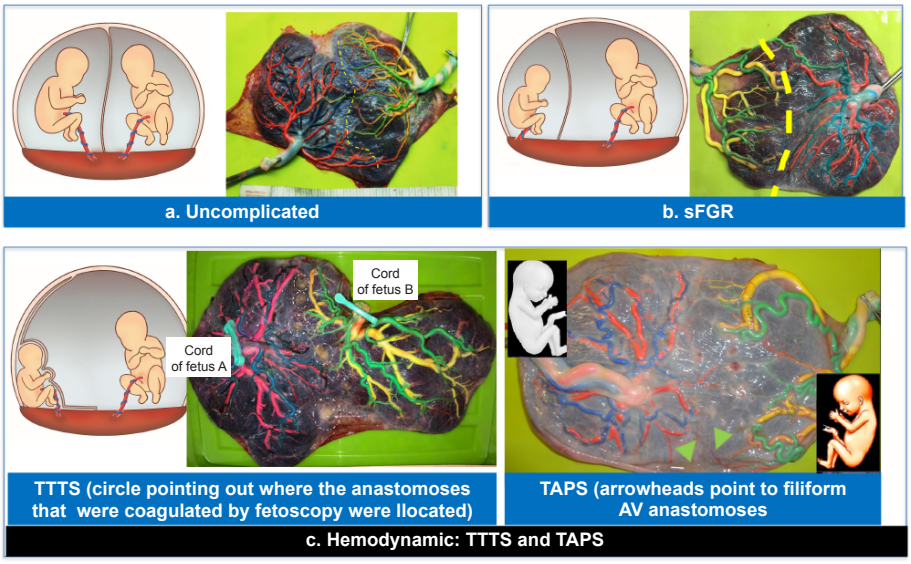
Note the fair distribution of the placental territory and the type of insertion similar in both cords.
Source: Developed by the authors.

Figure 2. Examples of superficial anastomoses (arrowheads), arterioarterial (AA) anastomosis, venovenous (VV) anastomosis, and deep arteriovenous (AV) anastomosis (circle)



Source: Developed by the authors.

Figure 3. Placenta of a monochorionic twin pregnancy: a) uncomplicated; b) complicated due to selective fetal growth restriction (sFGR); c) complicated due to hemodynamic instability: twin-to-twin transfusion syndrome (TTTS) and twin anemia polycythemia syndrome (TAPS)



Source: Developed by the authors.

However, seemingly similar pregnancies have very dissimilar outcomes, and strategies for predicting which patient will have a complication perform moderately well.[8–13] Some series found that nuchal translucency discrepancies were markers of TTTS, while others did not.[8,10] Others series described crown-rump length discrepancy as a risk factor for TTTS, sFGR, and perinatal death, with different cut-off points and varying results.[11,12] The same discrepancy has been observed when analyzing cord insertions; some series described an association with TTTS and sFGR, but others did not.[13]

For all these reasons, in an attempt to provide a new perspective, we now offer a different, not classical, approach from the perspective of the complexity theory.

PREGNANT WOMEN WITH A TWIN MONOCHORIONIC PREGNANCY AS A COMPLEX SYSTEM

A complex system is made up of several interconnected or interwoven parts, whose links create additional information not visible to the observer as a result of interactions among the elements. Pregnancy is a complex system in itself, and certain properties and characteristics that allow it to be studied within this theoretical framework will be discussed below.

-It is made up of simple elements that form the complex system: the simple elements (from the macro level of the mother, her partner, each fetus, and the placenta, to the micro level of the cells and tissues) make up the complex system that is the pregnancy. This complex system must show flexibility to adapt and evolve towards a successful pregnancy.

-Self-organization: there is no predetermined direction in the system, but rather the parts adapt as they go along based on local signals that are "turned on or off" in response to different stimuli. In fact, at the beginning of a MC pregnancy, it is not known whether the growth and development of each fetus will go one way or another, but it happens day by day as a result of a quadruple interaction:

- Between the mother and the fetuses: maternal complications (e.g., hypertension) may affect the fetuses while fetal complications (e.g., polyhydramnios or hydrops) may affect the mother.
- Between each fetus and their placental territory: if their corresponding placental territory is small, the fetus will probably (but not always) develop sFGR.
- Between each fetus, the interaction may be negative or positive. A fetus may complicate their twin, for example, due to a chronic transfusion (TAPS) or the death of one of them (*Figure 4*). Or a

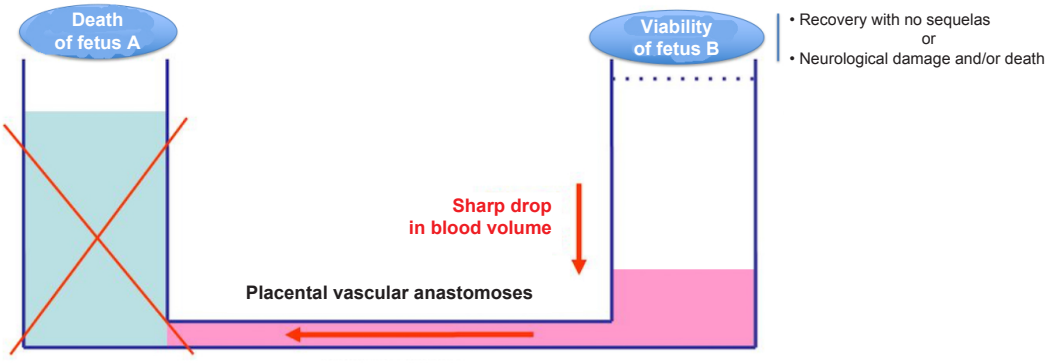
fetus may help their twin, for example, by promoting growth despite having a very small placental territory.
- Among the mother, her partner, and their environment: domestic violence, malnutrition, or environmental pollutants, among others, may cause adverse perinatal outcomes.

-They display emergent properties: as a result of the interactions between the single elements, new properties arise that cannot be explained based on the properties of each isolated element. In summary, the whole is greater than the sum of its parts. In an MC pregnancy, the emergent properties may refer to an uncomplicated gestation or the aforementioned complications, such as TTTS, sIUGR, TAPS, and death. For example, if placental territoriality is analyzed alone, it may be considered that the discrepancy in fetal weights will be very marked when there is evidence of significant discordance in terms of placental territory. However, this may not occur due to the presence of "rescue anastomoses" from one twin to the other. Or it may be considered that fetal growth is going to be normal, but the mother develops preeclampsia that results in sIUGR. In turn, one of the theories of the pathophysiology of preeclampsia is linked to abnormal placentation.

Also, for the study of a complex system, such as the one analyzed here, it is important to take into account certain characteristics necessary to model the system as a form of predictive study of potential emergent factors:

- A complex ***system*** is made up of ***a large number of elements*** (mother, partner, each twin, and the placenta).[14] Each of these components could be a complex system in itself. In turn, the *woman with a MC pregnancy system* is part of other complex systems, such as their extended family and the community.
- Complex systems encompass ***dynamism***:[2] pregnancy is dynamic and a normal check-up does not warrant that the same conditions will be found the next day. Interactions occur at different levels on a continuous basis: from a microvascular and molecular level[15] to a macro mother-fetus level; conditions vary continuously. Such imbalance[2] or dynamic balance actually allows a rapid adaptation to different stimuli.
- ***Penetration***: there is a complex and simultaneous interaction between each of the elements, where small changes or phenomena in one of them may result in large effects on the others. For example, a transient hypotension event in one of the twins may cause severe bleeding in the other twin (*Figure 4*).
- ***Non-linearity***:[2] the interactions between the elements are non-linear. For example, the same stimulus (hypertension) may cause different effects depending on the system (i.e., in another pregnant woman) or even demonstrate a different impact on the twins. For this reason, the same treatment, such as vascular ablation of anastomoses by fetoscopy, even under satisfactory technical

Figure 4. Fetal death of a twin in a monochorionic pregnancy



Acute passage of blood flow from the surviving twin (fetus B) to the deceased twin (fetus A) right before or at the moment of death, at which time blood pressure drops sharply. As a result, twin B may recover without sequelae, suffer from neurological damage or die.

Source: Adapted from Multifetal pregnancies: epidemiology, clinical characteristics, and management. Otaño L, Meller C y Aiello H, in Clinical Obstetrics: The Fetus & Mother, 4th edition, by E. Albert Reece, G. Leguizamon, G. Macones, A. Wiznitzer. Ed. Wolters Kluwer, pp 63-89.

conditions, usually shows surprising results in most patients, but, in some, no benefit is evidenced.

- ***Recursive interactions*:** in the event of a complication such as TTTS, a positive feedback phenomenon in favor of decompensation develops: in the hypovolemic donor fetus, the renin-angiotensin-aldosterone system is activated in an attempt to preserve blood volume. However, the hormones pass through the placental vascular anastomoses to the other twin —the receptor— which is hypervolemic, thus progressively worsening the condition.
- ***Complex systems are open*:**[2] there is a continuous interaction with the environment, both the intrauterine (for the fetuses) and the mother's environment. Obviously, they need this environment to survive and it is not possible to think of the complex "pregnancy" system without imagining it immersed in and dependent on other complex systems, such as society.
- ***Historicity*:** this is a very important factor, since it conditions the system to learn and respond by including all previous events in the response. It is not possible to replicate an event in a system, since the fact of having been previously exposed to a stimulus conditions that system. That pregnancy developed in a certain way (spontaneous versus fertility treatment), between a mother and her partner, who have a certain history. And different nutritional, environmental, and social aspects impact the pregnancy system and condition the emergent "complication" in a unique and unpredictable manner without taking the system for analysis into account.
- ***Local information*:** no element knows the total system complexity, but each element receives information from its immediate environment. The elements of a complex system function based on local information, and the molecular and biochemical stimulus together with the resulting local response determine where the system moves without taking into account the objective and the effect of the whole system.

FINAL COMMENT

From the network of dynamic interactions among the components of a complex system, new properties emerge, called emergent phenomena, which are not governed by a simple cause-effect model. For this reason, we propose the incorporation of tools used in the study of complex systems, such as big data analysis and large-volume complex databases,[16] for the management of MC pregnancies. These data include clinical, lifestyle, imaging, and laboratory aspects feasible for use in machine learning algorithms, such as principal component analysis, penalized regression, decision trees, neural networks, Bayesian analysis, and deep learning, among many others.

Accompanying MC pregnancies may pose a true challenge. Recognizing a MC pregnancy as a complex system, accepting the often frustrating aspects, such as non-linearity and the impossibility of anticipating the emergent phenomena, may help us to improve the quality of care we provide. After all, such unpredictability may even be stimulating. ■

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