UNIVERSIDADE ESTADUAL PAULISTA
"JÚLIO DE MESQUITA FILHO"
FACULDADE DE MEDICINA

HAMILTON DOS PRAZERES TAVARES

Síndrome Metabólica em Gestantes e os Efeitos Perinatais em duas Maternidades: No Brasil e Angola. Prevalência da Nova Epidemia no Século XXI

Tese apresentada a Faculdade de Medicina, Universidade Estadual Paulista "Júlio de Mesquita Filho" Campus de Botucatu, para obtenção do título de Doutor em Ginecologia, Obstetrícia e Mastologia.

Orientadora: Profa. Titular Marilza Vieira Cunha Rudge
Co-Orientadores: Prof. Assistente Doutor Joelcio Francisco Abbade
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BOTUCATU
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Botucatu
2015

FICHA CATALOGRÁFICA ELABORADA PELA SEÇÃO TÉC. AQUIS. TRATAMENTO DA INFORM.
DIVISÃO TÉCNICA DE BIBLIOTECA E DOCUMENTAÇÃO - CÂMPUS DE BOTUCATU - UNESP
BIBLIOTECÁRIA RESPONSÁVEL: ROSEMEIRE APARECIDA VICENTE-CRB 8/5651

Tavares, Hamilton dos Prazeres.
Sindrome metabólica em gestantes e efeitos perinatais em duas maternidades : no Brasil e Angola. Prevalência da nova epidemia no século XXI / Hamilton dos Prazeres Tavares. - Botucatu, 2015

Tese (doutorado) - Universidade Estadual Paulista "Júlio de Mesquita Filho", Faculdade de Medicina de Botucatu
Orientador: Marilza Vieira Cunha Rudge
Coorientador: Joelcio Francisco Abbade
Coorientador: Paulo Adão de Campos
Capes: 40101150

1. Síndrome metabólica. 2. Estudos transversais. 3. Mulheres grávidas. 4. Angola. 5. Gravidez - Complicações. 6. Perinatologia.

Palavras-chave: Angola; Efeitos adversos perinatais; Gravidez; Prevalência; Síndrome metabólica.

DEDICATÓRIAS

Aos meus país, Luís Pereira Tavares e Augusta Georgina Job Chilembo Tavares,

Exemplos a seguir, pelo apoio incondicional, colaboração.

A minha esposa, Suelma Beatriz Marques Prata Tavares,

Companheira, amiga, cumplice, colega, que apesar das dificuldades, distancia pela formação entre outras questões, esteve do meu lado de forma incondicional, me apoiando em tudo

Aos meus irmãos, Job Monteiro Tavares, Ana Tchoconumbi Tavares, Mariana Sandalawa Tavares, Marlene da Gloria Tavares, Isabel da Felicidade Tavares, Evalina Mavilde Tavares, Antunes das Saudades Tavares e Silvina Georgina Tavares,

Que sempre me apoiaram em todos os aspectos, de forma incansável ajudaram a resolver todos os problemas ligados a vida familiar, pessoal e acadêmica.

Aos Meus Sogros, António Saudades Rodrigues Prata e Eva de Figueiredo Marques Prata,

Pelo carinho e incentivo dado para que a formação se concretizasse

AGRADECIMENTOS

A Deus,

Todo poderoso, criador do Céu e da terra, dono da vida, por permitir guiar meu caminho.

À Professora Dra. Marilza Vieira Cunha Rudge,

Orientadora do trabalho, que de forma incondicional aceitou conhecer-me e orientar-me via internet sem termos um contacto prévio, orientadora que se entregou de forma inigualável, a disponibilidade de receber-me em qualquer lugar e a qualquer altura, com uma atuação incomparável. Realçar o facto de me ter tornado membro da família e ser recebido no mesmo meio sempre que necessário

Ao Professor Dr. Joelcio Francisco Abbade,

Co-Orientador do Trabalho, que de forma pronta e incondicional entregou-se para que o trabalho fosse um êxito.

Ao professor Dr. Paulo Adão de Campos,

Que doou seu tempo para se dedicar a pesquisa em Angola, Colheita dados, aprovação do projeto no comitê de ética da Faculdade de Medicina da Universidade Agostinho Neto.

Ao Programa Estudo Convenio – Pós Graduação (PEC-PG), via Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES),

Pela Bolsa concedida para que a formação fosse um êxito

Ao Professor Dr. Aristides Cunha Rudge,

Pela sua disponibilidade, apoio incondicional em prol da formação.

Ao Professor Dr. José Eduardo Corrente,

Pela participação na análise Estatística dos dados.

À Professora Dra. Debora Cristina Damasceno Meirelles dos Santos,

Pelo apoio e forma como fui recebido e se predispôs no ensinamento dentro do Laboratório de Pesquisa Experimental em Ginecologia e Obstetrícia

À Professora Dra. Eliana Aguiar Petri Nahas,

Pelo apoio na resolução dos problemas administrativos ligados a formação.

Aos Professores Drs. Roberto Antônio de Araújo Costa e Claudia Garcia Magalhães,

Que prontamente aceitaram participar na banca do exame de Qualificação e deram seus contributos para a feitura da tese.

Às Professoras Dras. Ana Glória Pontes e Izildinha Maesta,

Pelos ensinamentos incansáveis no estágio docência, transmitindo como deve-se dar aulas teóricas e práticas (sala de aulas, Enfermaria e Ambulatórios) aos estudantes da Faculdade de Medicina de Botucatu

Ao Professor Dr. Antônio Braga Neto,

Companheiro, amigo que sempre está disponível para ajudar-me em prol do desenvolvimento acadêmico.

Ao Professor Carlos Antônio Barbosa Montenegro,

Pelo apoio acadêmico no desenvolvimento da pesquisa.

Ao Dr. Frederico João Carlos Juliana,

Diretor Provincial da Saúde do Huambo, que é uma pessoa em prol da formação profissional e acadêmica, que sem hesitar sempre me recebeu para tratar assuntos ligados a formação e permitiu que desse continuidade a formação.

Ao Drs. Welema Cipriano da Fonseca e Dra. Natércia de Almeida,

Diretor Geral e Diretora Cientifica e Pedagógica do Hospital Geral do Huambo respectivamente, por terem aceite, colaborado para que a pesquisa fosse possível dentro da Instituição e dando apoio de forma sistemática.

Aos colegas de Laboratório de Pesquisa Experimental em Ginecologia e Obstetrícia,

Que me receberam de forma carinhosa, profissional e acadêmica, transmitindo seus saberes de forma incondicional.

Aos funcionários da secretaria de Pós Graduação, do programa de Ginecologia, Obstetrícia e Mastologia,

Que de forma muito profissional resolveram todos os problemas administrativos, facilitando a progressão para o sucesso.

Às Pacientes que participaram neste estudo,

Graças a elas a pesquisa foi possível e obrigado por terem aceitado participar de modo a criar políticas públicas de saúde que visam melhor assistência médica e medicamentosa às usuárias dos serviços de saúde de Angola.

Aos colegas profissionais de saúde que participaram na colheita de dados,

Aos Licenciados em analises Clinicas: Osvaldo Ribeiro Undembe, Abel Capaliculia Chimbonde, Ilda Vaica Cunga, Carmen Noemi Lopis Molina, Paulina Clara Londaca,

Aos Enfermeiros: Rosalina Celeste, Sabina Sandabongo, Ângelo Mussili, Viera Honório, Adriano Camunele Chicanalo, Paulina Cassova, Iracelma Elisa André, Ermelinda Ayondela, Mariete Leniniana, Firmino Cangila.

de forma incansável colheram dados e os analisaram todos os dias nos três períodos, participando de forma ativa na pesquisa de forma a contribuir no desenvolvimento qualitativo das pesquisas em ciências de saúde.

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LISTA DE ABREVIATURAS E SIGLAS

MS	Metabolic Syndrome
CCD	Cardiac coronary disease
CVD	Cardiovascular diseases
EGIR	European Group for the Study of Insulin Resistance
TG	Triglicerídeos
C - HDL	Colesterol - lipoproteínas de alta densidade
JIS	Joint Interim Statement
CC	Circunferência da Cintura
PAS	Pressão Arterial Sistólica
PAD	Pressão Arterial Diastólica
DM2	Diabetes Mellitus do tipo 2
DM	Diabetes Mellitus
NCEP ATP III	Third Report of the National Cholesterol Education Program Expert Panel on Detection
AHA/NHLBI	American Heart Association/National Heart, Lung and Blood Institute
IDF	International Diabetes Federation
INCO	Comitê Nacional da Obesidade Iraniano
ES	Espirito Santo
MG	Minas Gerais
LDL	Lipoproteínas de baixa densidade
MetS	Metabolic Syndrome
WHO	World Health Organization
IR	Insulin Resistance
GDM	Gestational diabetes mellitus
T2DM	Diabetes mellitus type 2
PGGOM	Pos Graduate in Gynecology, Obstetrics and Mastology
MSG	Metabolic Syndrome in Pregnancy
LGA	Large for gestational age
SGA	Small for gestational age
IGF	Growth factors insulin-like
BMI	Body Mean Index

INDICE

Capítulo 1

Metabolic syndrome: Consensus and Controversy. State of the art

Open Journal of Endocrine and Metabolic Diseases (OJEMD)

Metabolic syndrome: Consensus and Controversy. State of the art.

Síndrome Metabólica: Consenso e Controvérsias. Estado da Arte

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Abstract

Background: Metabolic syndrome is an epidemic that affects more and more people, increasing the probability of suffering metabolic and cardiovascular diseases in the short, medium or long term depending on the severity. The purpose of this article is to review the metabolic syndrome, assessing consensus, controversy and prevalence. The methodology was the preparation of a literature review on various health care databases, which were from 43 articles published from 2010 to 2015, in the general population. SM rate ranges from 0 % to 90 % depending on genders, ages and regions. There is still lack of consensus on cutoffs of diagnostic criteria. Thus, it is concluded that the prevalence of metabolic syndrome is being increased, urging the need for early diagnosis and treatment to promote the health of the global population.

Keywords: Metabolic Syndrome X, Prevalence, Consensus.

Resumo

A síndrome metabólica é uma epidemia que afeta cada vez mais a população, aumentando as chances de desenvolver doenças metabólicas e cardiovasculares a curto, médio ou longo prazo dependendo da gravidade. O objetivo do presente artigo é revisar a Síndrome metabólica, avaliando consenso, controvérsia e prevalência. A metodologia utilizada foi a elaboração de uma revisão da literatura em várias bases de dados da área da saúde, onde foram incluídos 43 artigos publicados entre 2010 a 2015, na população em geral. Dos 43 estudos, a taxa de SM variou de 0 % a 90 % dependendo do sexo, idade e região. Ainda existe falta de consensos nos pontos de corte dos critérios de diagnóstico. Hoje recomenda-se o uso dos critérios harmonizados (JIS).Com isso, conclui-se que a prevalência da Síndrome metabólica é cada vez mais alta, urge a necessidade do diagnóstico e tratamento precoce, com objetivo de promover a saúde da população global.

Palavras-chave: Síndrome X Metabólica, Prevalência, Consenso.

Introduction

As the profile of the population in the world is being changed and researchers are trying to understand the causes involved in Metabolic Syndrome. A lot of researches have been developed to understand the situation. In the 30 studies they have been developed in an attempt to understand the sensitivity that some people (thin, fat and old) had used insulin [1].

The metabolic syndrome (MetS) is a set of metabolic abnormalities that give the individual a number of risks for metabolic and cardiovascular diseases [2].

This study is to demonstrate the very latest on conduct in metabolic syndrome and respectively their disputes.

Metabolic Syndrome

Metabolic syndrome is considered as the new epidemic of the twenty-first century. Its appearance depends on several factors that are being studied and gathered on clinical criteria for investigation.

This has been addressed in several studies, since the biophysical profile of the population has being changed and influenced by lifestyles, market demands, industrialization etc. Researchers are still trying to understand the situations about the metabolic syndrome, receiving assignments according to the findings, reasons why their names have been changed over the years, even when having a confluence point.

The association among high blood pressure, hyperglycemia and gout was described by Kylim in 1923 [1]. Following these surveys, it's conventionally to get specific treatment for diabetes, since they knew about the insulin resistance and continued studies [3].

In 1966 Welborn and Modan studied and realized that the population concerned (Fat/thin/diabetic/resistant/insulin), besides these elements were hypertensive and had impaired glucose tolerance, describing association between hypertension and glucose intolerance [1] [4].

In addition to the signs and symptoms previously reported, hyperinsulinemia and dyslipidemia, have been described as X syndrome, characterized by insulin resistance, glucose intolerance, hyperinsulinemia, blood hypertension and dyslipidemia. These problems appear frequently in one person, this situation makes greater risk of cardiovascular events, and this phenomenon is called syndrome X [5].

Those people with this clinical picture had high mortality rates, especially sudden conditions, therefore, they were subjected to autopsy to try to understand what was happening and was described as deadly quartet. During the examination of the corpses, atheromatous plaques found in coronary arteries, the deadly quartet characterized by central obesity, glucose intolerance, hypertriglyceridemia and arterial blood-pressure disease coronary [6].

This population has metabolic complications, in presenting cardiovascular clinical conditions in three to four times or more on all the perimenopause period, hence the designated of cardiovascular metabolic syndrome [7] [8].

In describing the SM and making the clinical diagnosis of the population, it was noticed that the metabolic change was registered in the human body as a whole and not in a specific place, designed as plurimetabolic syndrome, characterized by: Centripetal obesity, glucose intolerance, hypertension characterized with compromised coronary arteries, hypertriglyceridemia [9].

In 1998 the first official definition and a list of criteria for the diagnosis of MetS was published with the cutoff assessment of insulin resistance or disorders in glucose metabolism. The criteria that caused the diagnosis of the syndrome were: hyperglycemia and/or insulin resistance with two or more of the following criteria: abdominal obesity, dyslipidemia, hypertension and microalbuminuria [10].

MetS increases the risk of suffering cardiovascular disease (atherosclerosis and its complications) and metabolic secondarily morbidity and mortality by them.

For the people with diabetes mellitus, cardiovascular disease is a key element in your prognosis [11].

Settings

The literature has been changing the concept and what it encompasses to make diagnoses. Metabolic syndrome is characterized by the presence of hyperinsulinemia, insulin resistance, obesity, dyslipidemia, hypertension, type 2 diabetes mellitus and/or glucose tolerance decreased [12] – [15].

Metabolic syndrome is defined by a set of interconnected factors that directly increase the risk of coronary heart disease (CHD), other forms of Atherosclerosis Cardiovascular Diseases (CVD) and diabetes mellitus type 2 [16].

Diagnosis

The consensus is that the diagnosis of metabolic syndrome needs to change at least 3 variables. The glucose intolerance and insulin resistance are key components in WHO [10], settings and EGIR17. Insulin resistance or fasting hyperinsulinemia plus two of the following- Hyperglycemia > 110 mg/dl but < 126 mg/dl, blood pressure ≥ 140/90 mm/Hg, Dyslipidemia > TG 180 mg/dl or C-HDL < 40 mg/dl, Central obesity (waist ≥ 94 cm with the men and ≥ 80 cm in women [10] [17].

For Joint Interim Statement (JIS) it takes the presence of three or more of the following components: WC ≥ 94 cm (men), 80 cm (women); SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg and/or treatment of reducing blood pressure; triglyceride fasting levels ≥ 150 mg/dl (1.70 mmol/L) or treatment for hypertriglyceridemia; HDL-C <40 mg/dl (1.04 mmol/L) (men), 50 mg/dl (1.30 mmol/l) (women) or treatment for dyslipidemia; Fasting blood glucose levels ≥ 100 mg/dl (5.55 mmol/L) or drug antidiabetic [18].

Some experts defined as SM-bearing individuals with three of the followings: arterial hypertension, dyslipidemia, obesity, glucose intolerance (DM2) or impaired glucose tolerance, or insulin resistance plus two changes [19].

Or as any individual with: Central Obesity (waist ≥ 90 cm with the men and ≥ 80 cm in European women, with values for the various ethnic groups plus two of the following criteria: TG > 150 mg/dl or therapy for Hypertriglyceridemia, C < of HDL 40 mg/dL in humans and < 50 mg/dl in women, or treatment for this anomaly, systolic BP ≥ 130 mm/Hg or diastolic ≥ 85 mm/Hg, fasting blood glucose > 100 mg/dL or previously diagnosed DM, dyslipidemia TG > 80 mg/dl or C-HDL < 40 mg/dl [8].

The frequently used definitions in clinical practice are proposed by the NCEP ATP III (IDF) and American Heart Association/National Heart, Lung and Blood Institute (AHA/NHLBI)[12].

While the Latin American consensus Diabetes defined as criteria for diagnosis: Obesity Central Perimeter waist men = 94 cm, women = 88 cm, plus the following four factors: Triglycerides> 150 mg/dl, HDL c = Men <40 mg/dl, Women <50 mg/dl, blood pressure: Men> 130/85 mm Hg, specific treatment for certain disorders, abnormal blood glucose, oral tolerance test changed or Diabetes glucose [20].

The International Diabetes Federation (IDF) recently recommended settings for metabolic syndrome in children and adolescents, which is to have abdominal obesity and at

least two of the other four components: hypertriglyceridemia, low HDL cholesterol, hyperglycemia and hypertension [8].

Consensus and Controversies

Just to WHO and to the IDF, impaired glucose tolerance or insulin resistance are key components in the settings, whereas for other classifications no components considered fundamental, just have three elements changed.

A variety of classifications and cutoff points for the diagnosis of metabolic syndrome is an obstacle to propaedeutic. The consensus in the use of criteria for the diagnosis of metabolic syndrome is: changes in lipid profile, blood pressure, fasting hyperglycemia, obesity [21].

However, the criteria is set for different populations of the same world, means that there is difference in prevalence rates, however waist circumference (WC) was recommended as a simple screening tool to measure abdominal obesity, in contrast to body mass index or other anthropometric measures. The cutoff point proposed by the ATP III was the subject of debate. This mainly depends on the ethnicity and gender. Several studies in Asian population particularly in China, Turkey and Iran show that the regional cutoff for proposed CC could have been more appropriate. The Iranian National Committee of Obesity (INCO) also proposed revised criteria ATP III regional value DC cut > 95 cm for men and women, these differences cutoffs cause even if there is consensus on the variables, there will still be the cutoff points. Also, there is a difference in blood glucose cutoff NCEP ATP III (Glucose ≥110 mg/dl) for JIS (Glucose 100 mg/dl) [22].

These days, it is recommended the use of harmonized criteria (2009) for the diagnosis of metabolic syndrome, Joint Interim Statement (JIS) [22].

Risk factors

More and more people in the world suffer obesity disease, and especially about 60% population in the North American. This growth also relates to higher incidence of Type 2 diabetes mellitus (DM2) in world [23].

Thus, the rate of cardiovascular disease and mortality increase dramatically. Changing lifestyles toward modernization and urbanization is directly proportional to the growing body

rate of obesity and abdominal obesity. These factors are the main contributors to metabolic syndrome in adults and adolescents [24].

A similar situation is observed in Africa, where most countries are under development, as the prevalence of MS is higher in first world countries and industrialized. In Africa, obesity, diabetes type2 (T2DM) and atherosclerotic cardiovascular disease (CVD) are chronic diseases that affect the health system. In 2006, it was estimated that 10.8 million Africans suffered DM, and in 2025, it would be 18.7 million [25].

Yet with respect to the risks, relative aspects such as lifestyles and food [26]. The MS is usually associated with cardiovascular and metabolic diseases, and is the direct cause of morbidity and mortality in the United States and Brasil[27]. The prevalence of MS has been globally increased. It is estimated that 20-25% of the world population is carrier of this syndrome [8].

In short the risk factors for metabolic syndrome are: less physical exercise; Poor diet; Abdominal obesity; dyslipidemia; dysglycemia and smoking [28].

Epidemiology

The prevalence of MS in adults in the United States, according to the diagnostic criteria of NCEP, was 6.7% in the age group 20-29 years 43.5% 60-69 years and 42% largest among 70 years[29]. Independent of criteria for assessing the SM, it is estimated that nowadays about 100 million people on the planet suffer SM metabolic [7].

The SM prevalence ranges from 20-25% among individuals with adequate weight for height, 50% in patients with dysglycemia 80% in patients with diabetes type2; 12.4 to 28.5% in men and from 10.7 to 40.5% in women, the syndrome is more prevalent in women than men [11].

The prevalence of metabolic syndrome (MS) in childhood and adolescence this estimated at more and 3.3% in the world [30].

The prevalence of MS is still unknown in Brazilian samples. Research conducted in adults in the cities of Vitória-ES and Virgin of Grace-MG, showed prevalence of MS of 29.8% (men: 29.3%; women: 30.1%) and 21.6% (men: 7 7%; women: 33.6%), respectively, and 28% Brasilia [23].

In 2010 the prevalence of the syndrome in the clinic in the state of Rio de Janeiro by the IDF criteria was slightly higher than the NCEP (61.1% vs 55.6%) 30. They found frequency of metabolic syndrome in women 89.66% and 42.86% of men [31].

In 2011 it became public that about 8.9% of the adult men were already obese against 13.1% of women [32].

In 2013, while studying the number of components of the metabolic syndrome in a Brazilian adult population in a rural area it was more frequent among women (23.3%) than among men (6.5%) [33]. The prevalence of metabolic syndrome in Africa varies 0-50% of the population in general [34].

Having been found in Angola crude prevalence of metabolic syndrome in two criteria: JIS (27.8% adjusted for age 14.1%) than with the definition of the ATP III (17.6% adjusted for age 8.7%) [35].

Conduct

Given the situation we need to take necessary actions, especially in relation to public health, it is the responsibility of the public. It is noticed that the developed countries and non-governmental organizations have helped systematically those who in need. Today it needs more investment in research, health promotion and disease prevention. The population or individual with metabolic syndrome should be evaluated and oriented mainly on issues relating to the change of lifestyle and medication.

Regarding the lifestyle changes, regular physical activity is a change in lifestyle that may influence favorably the results of cardiovascular health, including cardiovascular disease, stroke by stroke, hypertension, diabetes mellitus type 2, obesity and improvement in the lipid profile. However, if you want to promote and maintain health, 30 minutes of daily physical exercise, 5 days per week for adults 18-65 years of age, children and adolescent of 5-17 years of age, should do exercise at moderate intensity, for 60 minutes accumulated days [36].

Although there is no consensus on the most appropriate nutritional strategy to cure metabolic syndrome [30], good nutrition education, sometimes accompanied by nutritionists, especially when you are overweight, a balanced and controlled diet alternating with vegetables intake of leafy greens, fruits, vegetables, milk, and exercise, this behavior would improve MS way, so that even if the ideal weight for height, thus reducing the abdominal girth, blood pressure better, controlling blood glucose, improving LDL and LDH [37].

Individuals at any age presenting changes in lipid profile, metabolic disease (DM2), SM, admitted to outpatient State health services and/or private offices nutrition, medicine, pediatrics, endocrinology and others, should be targeted and/or followed according to actual conditions regarding preventive measures and treatment of diseases, rehabilitation of sequela,

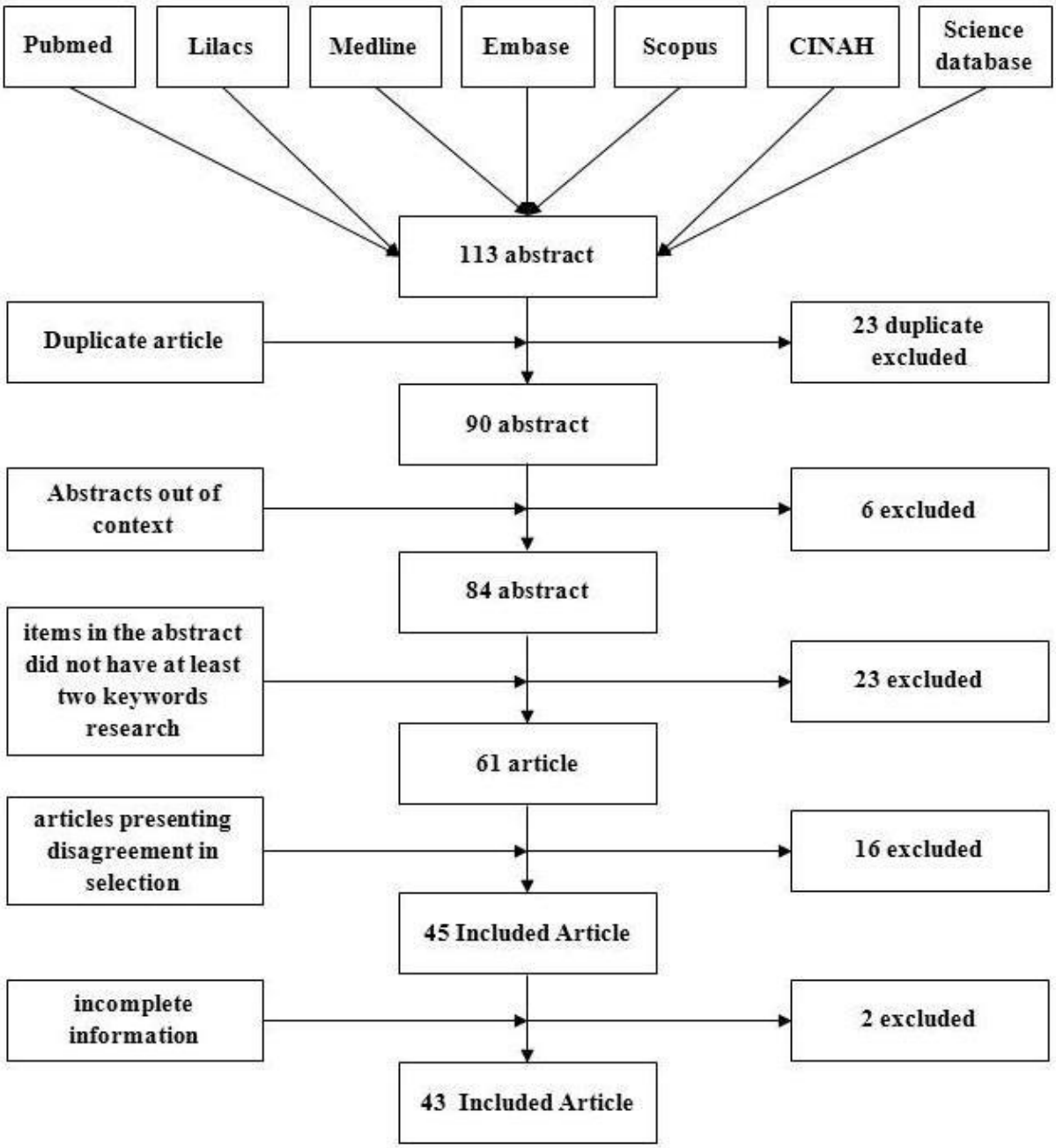
health promotion, as these may increase the longevity, interfering directly in the quality of life. Therapies of modifying the additional lipids such as fibrates, omega-3, polyunsaturated fatty acids, are capable of improving the lipid profile and further reducing the risk of CVD in those patients [23]. .

Methodology

We reviewed the situation of metabolic syndrome MetS, prevalence, risk factors, consensus, controversies in the literature in the general population. To support this review, surveys were conducted in 43 articles and in two books of obstetric publications from 2010 to 2015. PubMed, Lilacs, Medline, Embase, Scopus, CINAH and Science database were used to search for articles published on metabolic syndrome in general, consensus and controversy. We searched all those databases using the key words: metabolic syndrome, prevalence, 113 articles published in English and Portuguese.

All the identified articles were reviewed to find and avoid possible duplication and then arranged for further survey. By analyzing the titles of the articles, the ones whose design differed from inclusion criteria (metabolic syndrome, syndrome X, Prevalence, Consensus) were identified. Summaries of the articles were read and selected and we excluded those which did not mention the features of metabolic syndrome, prevalence, consensus. The complete text of selected articles were retrieved and reviewed independently. After data extraction, a new review of articles was made as a means to ensure that the data of the selected articles were included only once in the analysis, which resulted in only 43 remaining articles taking part with this review. The results are summarized according to sample size, type of study, the definition used for metabolic syndrome, Prevalence, consensus and controversy.

Search strategy



Results

Metabolic syndrome continues to rise on the planet, even though it is a global concern and considered epidemic of the XXI century where almost all countries regard it as a public health problem. It is more prevalent in adults and females.

While there are several criteria and diagnostics for metabolic syndrome, it is agreed that for such an individual has to have at least three elements of the change in the criteria used. There is no consensus on cutoffs.

The investigation of the presence of risk factors for the syndrome is an opportunity to prevent disasters on public health.

Despite the power of intervention of discord on the benefits of certain foods for the prevention of cardiovascular events in people with the installed phenomenon, it is still recommended by most authors.

The consensus is the practice of physical activity for glycemic control, lipid profile, body mass index.

Although there exist many criteria and cutoff points for the diagnosis of metabolic syndrome, a lot of researchers try to cross several criteria, and conclude and harmonize the various definitions and conclude that the most fitting when the JIS (2009).

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Capítulo 2

Metabolic syndrome and pregnancy, its prevalence, obstetrical and newborns complications

Open Journal of Obstetrics and Gynecology (OJOG)

Metabolic syndrome and pregnancy, its prevalence, obstetrical and newborns complications

Síndrome metabólica e gravidez, complicações obstétricas e do recém nascido.

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Abstract

Background: The metabolic syndrome affects more and more the global people. Although it shows increasing prevalence in general population, the syndrome affects more women than men, what makes its risk of being developed during pregnancy period. Also, possible perinatal adverse effects are always lurking. Objective: was demonstrate what's new in literature on metabolic syndrome and pregnancy. Methods: A literature review was performed to extract the articles published on metabolic syndrome and pregnancy, its prevalence, obstetrical complications and its perinatal adverse effects. This review was conducted by online researching in PubMed, Lilacs, Medline, Embase, Scopus, Medscape, Libertas Academica and CINAHL database, Science database and also by researches in books. 27 selected articles on metabolic syndrome after this research were all published between 1988 and 2015. Results: Among those 27 articles and two books studied, SM rate in obstetric population ranged from 3% to 42% depending on the previously manifested components of the syndrome, age and region. Women with previously manifested components showed more adverse perinatal effects. Conclusion: Women with pre gestational DM or SM and SM develop more during pregnancy, obstetric complications and adverse perinatal outcomes.

Key words: Metabolic syndrome , pregnancy , adverse, perinatal outcomes.

Resumo

A síndrome metabólica afeta cada vez mais pessoas a nível mundial. Apesar de mostrar aumento da prevalência na população geral, a síndrome afeta mais mulheres do que os homens, o que faz com que o risco de mulheres desenvolverem a síndrome na gestação seja grande. Além disso, os possíveis efeitos adversos perinatais estão sempre à espreita. Foi feita revisão da literatura realizada a partir de artigos publicados sobre a síndrome metabólica e gestação, prevalência, complicações obstétricas efeitos adversos perinatais. As informações foram obtidas on-line nas bases PubMed, Lilacs, Medline, Embase, Scopus, Medscape, Libertas Academica e banco de dados da CINAHL, banco de dados Ciência e também pesquisas em livros. Após esta pesquisa foram selecionados 27 artigos sobre a síndrome metabólica e gestação, publicados de 1988 e 2015. Entre os 27 artigos e dois livros estudados, a taxa de SM em população obstétrica variou de 3 % a 42 %, dependendo dos componentes manifestados ou existentes antes da gestação, idade e região. Os neonatos de mulheres que têm síndrome metabólica pré gestacional tiveram mais efeitos perinatais adversos . As diabéticas pré gestacionais e as com SM mostrou prevalência aumentada de complicações obstétricas e resultados perinatais adversos

Palavras Chaves: Síndrome Metabólica, Gravidez, efeitos adversos perinatais.

Introduction

Metabolic syndrome (MS) is a complex disorder that affects more and more the people nowadays. It´s considered as the epidemic of the 21st century. Nowadays, it´s a cause for concern in both today, considered as the epidemic of XXI century. Today is a matter of concern in both developed and developing countries [1].

MetS was first described as a syndrome by Reaven in 1988 [2]. With the increasing worldwide prevalence of obesity and of MS, pregnant women with preeclampsia have many of the characteristics of MS, which makes it a provocative subject [3].

The prevalence of MS is commoner in females and increases with age and urban housing [4].

It is associated with the rising incidence of obesity in developed and developing countries and is reaching epidemic proportions affecting between 24% and 34% of the US population (4) and up to 36% of Europeans aged 40–55 years [5].

In a recent study in Greece, the prevalence of metabolic syndrome was 25% in adult men and 15% in women according to the National Cholesterol Education Program, Adult Treatment Panel III [6].

Metabolic syndrome is not a universally-accepted entity and, although certain cardiovascular risk factors undoubtedly occur together more often than expected by chance, the underlying pathophysiology of the syndrome is unclear [7]. However, so far several definitions have been proposed [8], namely by the World Health Organization (WHO), the International Disease Federation (IDF), the National Cholesterol Education Program (NCEP), and the fourth was the modified definition of the NCEP/ATP III (ATP III/ American Heart Association (AHA)/ National Heart, Lung and Blood Institute (NHLBI)) [1] [2] [14]. Among these, the report of the panel of NCEP called “Adult Treatment Panel III (ATP III)” has been widely used as a common definition in literature [9] – [11]. Now, the JIS proposed is frequently used when we couldn’t find metabolic syndrome [12].

The ATP III method for diagnosing MetS is the presence of three or more of the five criteria-emphasis on high waist circumference (WC>102 cm in men and WC>88 cm in women), high blood pressure (BP>130/80 mm/Hg), high triglyceride (TG>150 mm/dl), high glucose (FBG>110 mg/dl, and low HDL (HDL<40 mg/dl in men and HDL<50 mg/dl in women) [2]. On the other hand, abdominal obesity, defined by high WC is a compulsory criterion on two or more of the other four criteria in IDF definition [11].

SM is defined by an interconnected set of factors that directly increases the risk of cardiovascular disease - coronary heart disease (DCC), other forms of atherosclerotic cardiovascular disease (CVD) - and metabolic diseases (diabetes mellitus type 2 (T2DM).

Its main components are: dyslipidemia, characterized by elevated triglycerides and apolipoprotein B (apoB), containing lipoproteins, low and high density lipoproteins (HDL cholesterol), elevated blood pressure (BP) and hyperglycemia, abdominal obesity and/or insulin resistance (IR).

As the research was developed, other abnormalities have been found in people with this syndrome such as pro-inflammatory state, pro-thrombotic non-alcoholic fatty liver disease and sleep apnea [13].

In the United States, about a quarter of the adults suffer from Metabolic Syndrome [14].

The SM setting in pregnancy is controversial because the criteria for detection of SM overlap to the physiologic changes of pregnancy. During pregnancy, a woman experiences a set of periodic transformations that disappear after delivery, among many quoted phenomena: insulin resistance, increased anabolism in the first half of pregnancy, increased adiposity, hyperlipidemia, prothrombotic state [15]. Studies published on Diabetes Care, shows that women who have not lost the weight gained during pregnancy up to twelve months after the birth of the baby or put up on weight at this stage, are at serious health risks [16].

The role of insulin resistance in the pathophysiology of pregnant women with SM components (pre-eclampsia, eclampsia, gestational diabetes) or even SM allow healthcare professionals to intervene properly and on time in pregnant women to prevent obstetric and neonatal disasters.

The prevalence of SM markers (obesity, high levels of glucose, triglycerides, total cholesterol and LDL cholesterol) shows increasing trend with the evolution of pregnancy.

There are various diagnosing criteria for metabolic syndrome, but just Bartha and Chatzi presented modifications to diagnosis of the metabolic syndrome in obstetric people. Bartha introduced changes to the criteria of WHO and NCEP-ATP III, while Chatzi did it in the criteria of the NCEP ATP III and the NHLBI/AHA [17].

Table 1 – NCEP-ATP III adaptation of MS settings to pregnancy

Clinical NCEP - ATP III for defining SM	Proposal for Adaptation of MS definition of the NCEP - ATP III to pregnancy(Bartha et al, 2008)
Any of the following 3	Any of the following 3
Visceral obesity , defined as waist circumference > 88 cm (in women)	Visceral obesity , defined as waist circumference > 2SD for gestational age in the 1st half of pregnancy or pre- pregnancy BMI > 30 kg / m2
Plasma triglicérides ≥ 150 mg/dl	Plasma triglycerides ≥ 2 SD for gestational age
< HDL cholesterol 50 mg / dl (in women)	HDL cholesterol < 2 SD for gestational age
Blood Pressure ≥ 130 / ≥ 85 mm / Hg	Blood Pressure ≥ 130 / ≥ 85 mm / Hg
Fasting glucose ≥ 110 mg / dl	Fasting glucose ≥ 110 mg / dl

Table 2 – WHO adaptation of MS settings to pregnancy

WHO clinical criteria for defining SM	Proposal for Adaptation to Pregnancy SM definition of WHO (Bartha et al, 2008)
Resistance to insulin by one of the following	Resistance to insulin by one of the following
Type 2 Diabetes	Type 2 Diabetes
Impaired fasting glucose	Impaired fasting glucose ≥ 105 mg / dl
Impaired Glucose Tolerance	-
Insulin resistance defined euglycemic hyperinsulinemic clamp using the	Insulin resistance defined using the euglycemic hyperinsulinemic clamp or other sensitivity measuring method insulin , adjusted for gestational age
More any two of the following	More any two of the following
Antihypertensive and / or high blood pressure (systolic or diastolic ≥ 140 ≥ 90 mm / Hg)	Antihypertensive and / or high blood pressure (systolic or diastolic ≥ 140 ≥ 90 mm / Hg)
Plasma triglycerides ≥ 150 mg / dl	Triglicerídeos plasmáticos ≥ 2 DP para a idade gestacional
< HDL cholesterol 39 mg / dl (in women)	Cholesterol HDL < 2 DP for gestational age
> BMI 30 kg / m2 and / or the waist / hip > 0.85 (in women)	IMC pré-pregnancy> 30 Kg/m2 and/or waist/hip ratio > 0,85
Urinary albumin excretion rate ≥ 20 g / min or albumin creatinine ratio ≥ 30 mg / g	-

In 2009, Chatzi et al also submitted proposals for diagnosis of metabolic syndrome in obstetric population. Based on the NCEP ATP III and on the NHLBI/AHA criteria, waist circumference is not considered as obesity and neither criterion. While obesity is defined as a body mass index greater than pre-pregnancy - 30 kg/m^{2} -, in particular, metabolic syndrome is diagnosed if 3 or more of the following risk factors are present: pre-pregnancy body mass index >30 kg/m^2; level of triglyceride ≥150 mg /dl; cholesterol level HDL<50 mg/dl; fasting plasma glucose level ≥100 mg/dl, and blood pressure level≥130/85 mm Hg [18] – [19].

Metabolic alteration in pre gestational is a determinant complication factor in pregnancy, post-pregnancy, in life after birth and adverse perinatal outcomes. High maternal before pregnancy increased the risk of adverse pregnancy outcomes, obesity has been demonstrated to be an independent risk factor for: macrossomia, delivery by cesarean section, pregnancy induced hypertension, congenital malformation and lead to fetal death [20].

The diagnosis of MS during pregnancy identifies women at increased risk for developing cardiovascular and metabolic complications later in life and that are potentially candidate to develop pathologies related to pregnancy, making it a proper situation to evaluate the perinatal adverse effects [21].

Women with MS have a higher risk of developing GDM and because of that they can develop about 30% risk for future development of diabetes type 2(DM2) [22].

There are few studies on metabolic syndrome in pregnancy. In pregnant women with GDM it was reported a prevalence of 10% [17] - [24]. In pregnant adolescents, the prevalence is 3 – 5% [25]. Women with gestational hypertension have increased risk for developing insulin resistance postpartum, thus increasing likelihood of developing the metabolic syndrome. Drebes et al 2009 detected a prevalence of MS in mothers who had been diagnosed pre-eclampsia of 13,9%, [26] 7,6% [27].

In Brazil, a PhD thesis developed in the PG Program in Gynecology, Obstetrics and Mastology (PGGOM) at Unesp by Negrato *et al.* in 2008 found 24 to 36%, while another study conducted by Drebes (2009) “Disease Gestational Hypertension and Metabolic Syndrome” in Pontifical Catholic University of Rio Grande do Sul, found 42% pregnant women with MS [26].

Once diagnosed Metabolic Syndrome in Pregnancy (MSG) or elements of it, it´s possible to provide rapid intervention to prevent complications in pregnancy and adverse perinatal outcomes [28].

Maternal dietary conditions and changes in the intra uterine environment are directly related to the outcome of pregnancy. Childbirth preterm, restricted intra uterine growth and

newborn with low weight have a higher risk of developing cardiovascular disease and insulin resistance in the future. Previous studies have reported associations between pre-pregnancy obesity, chronic hypertension, dyslipidemia, and inflammation in early pregnancy to higher risks of preterm birth and intrauterine growth restriction [18].

Adverse Perinatal Outcome

Concerning the adverse perinatal outcomes, the LGA and SGA neonates have augmented chances of developing metabolic syndrome later [29].

The nourishment of the mother, of the embryo, of the fetus and of the newborn, plays an important condition for a generation in developing or not diseases in future life. Lifestyle and feeding characteristics such as being natural, synthetic, with or without pesticides etc., are directly related to ontogeny and diseases development [19].

Pregnant women with metabolic syndrome components are still considered at high risk despite all the scientific efforts that have occurred along the years to promote quality more and more. Yet, the control of this is lower than desired. Thus, perinatal adverse effects (malformations, neonatal, neonatal hypoglycemia, and neonatal macrosomia jaundice) continue to increase and this increase is directly proportional to the values and Components numbers of MS presented [30].

Pregnant women with "insulin dependent DM" give birth to offspring with risk two to three times superior than the normal rate of having malformation, whereas this risk is not observed in pregnant women with gestational diabetes. Multiple malformations are more frequent in diabetics' offspring than in nondiabetics [22]. The macrosomia newborns have increased rate of hypoglycemia, hyperbilirubinemia, hypocalcemia, respiratory distress syndrome and hypertrophic cardiomyopathy [22].

The high levels of maternal glycemia lead to fetal hyperglycemia, and then to hyperglycemia in both mother and fetus. Subsequently, the augmented insulin production occurred as an attempt of metabolism of the available glucose, causes hypertrophy and hyperplasia of pancreatic b-cells.

Hyperinsulinemia and hyperglycemia in the intrauterine environment is common in pregnancies complicated by diabetes, what cause bigger fetal organs development than they should be and therefore favors the emergence of macrosomia. Moreover, the excessive and continuous supply of glucose, amino acids and lipids from the mother to the fetus stimulates the increase of newborn weight. Other determinant factors of fetal growth and additional

elements such as the presence of some hormones triglycerides, of free fatty acids, ketones, leptin, amino acids and growth factors insulin-like (IGF) and insulin, are recognized as causative agents of exacerbated fetal development [30].

Many studies refer to BMI bigger than 25 kg/m2 interference with parturition newborn great. Other studies make reference to the fact that the pre-gestational hyperglycemia and hyperinsulinemia in the first trimester of pregnancy might be associated with macrosomia. Pregnant women with hyperglycemia in the first quarter, when out of control, have increased in five times the risk of developing newborn great [22].

Hyperglycemia harms the PAX gene-3, which is responsible for the closure of the neural tube. The oxygen free radicals concentration increases because of hyperglycemia and this can have teratogenic effects. Fetal lungs also suffer with this situation and may develop respiratory distress syndrome (20 - 30%) due to the fact that the hyperglycemia and hyperinsulinemia retard fetal lung maturity [31].

Fetal macrosomia is linked to perinatal complications such as: maternal morbidity, trauma at birth, fetal distress during labor (25%), neonatal hypoglycemia (8-22%), hyperbilirubinemia (15-20%) and neonatal mortality [31].

The hyperinsulinemia inhibits the action of cortisol in the lung, what leads to lecithin inhibition production by type II pneumocystis. Lecithin is a phospholipids present in the surfactant, which stabilizes the pulmonary alveoli during the expiration. Its decrease leads to the syndrome of respiratory discomfort, SRD [32].

The neonatal hyperbilirubinemia, defined as bilirubin bigger than 13mg/dl complicates the evolution of newborns in 20% of diabetic mothers and infants. Polycythemia and hyperbilirubinemia set a situation in 3-5% of diabetic mothers and infants. Diabetic pregnancy causes an increase in viscosity, providing clinical sequelae such as heart failure, renal impairment, renal vein thrombosis, necrotizing enterocolitis and damage to the central nervous system, leading to decreased blood oxygenation and stimulation of erythropoiesis [32].

Congenital malformations are commonly more frequent and severe in children born of pregnant women who have gestational diabetes than in the population without this condition. The most common kinds of malformation are: anencephaly, spina bifida, hydrocephalus, rectal/anal atresia, renal anomalies, cardiac hypertrophy, organomegaly and increase in blood volume. These are all associated with gestational diabetes. It´s worthy recalling that children of diabetic mothers have a higher risk of later obesity and often are in obesity class III; they also develop diabetes and problems in psychomotor development [33]. Regarding the

obstetric and neonatal complications related to MS in pregnancy, gestational diabetes, hyperinsulinemia, presence of acute comorbidities or chronic complications are directly related to morbidity and maternal and fetal mortality. For this association is urgent to pay more attention in the treatment and diet to prevent diseases that cause disorders in the lives of mother/fetus and society. 50 to 70% of diabetic pregnant women improve their glycemic rates with dietary improvement [34].

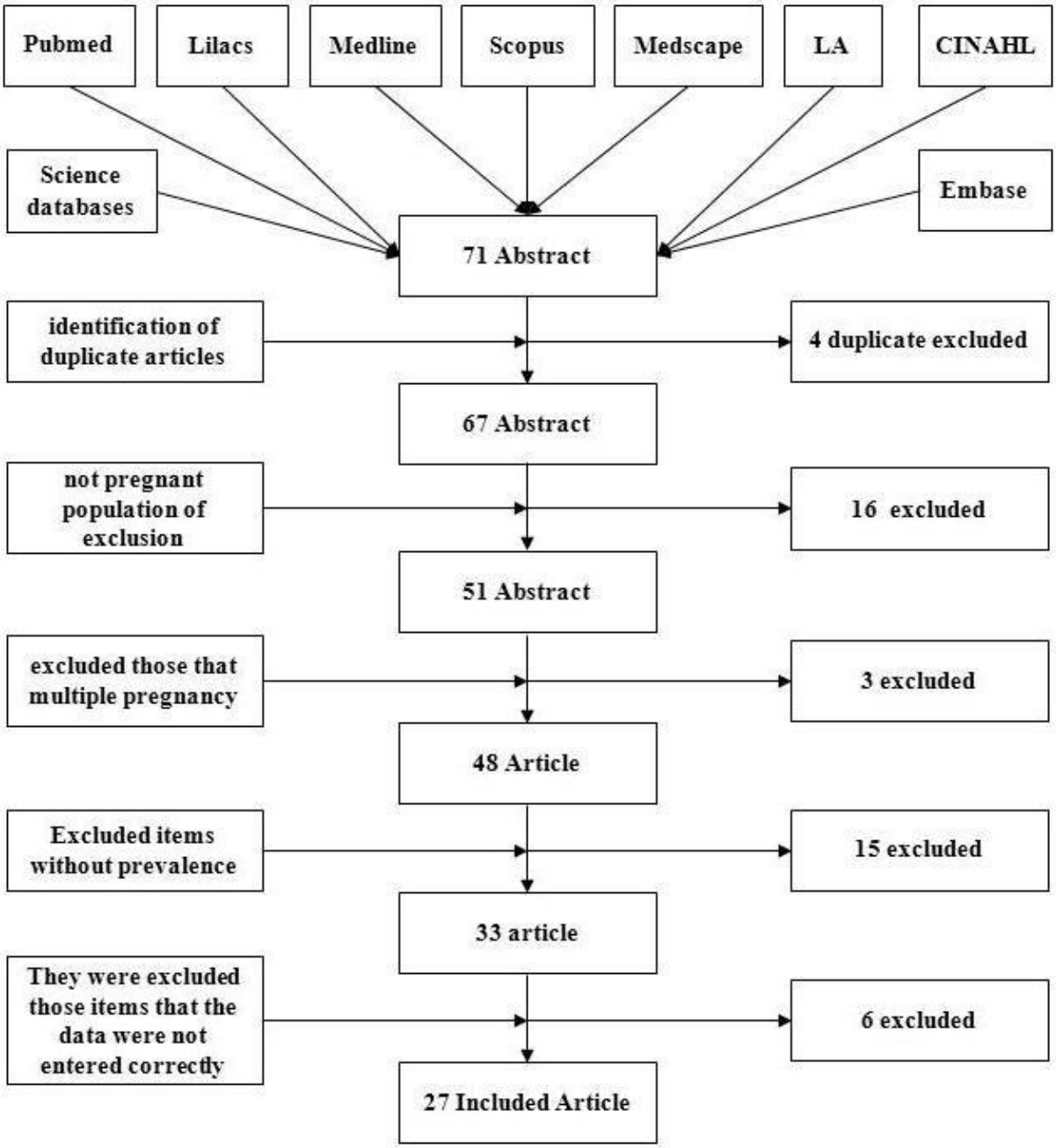
Methodology

We reviewed the literature to demonstrate the current state of metabolic syndrome and pregnancy, its prevalence, obstetric complications and its adverse perinatal factors. To support this review, surveys were conducted in 27 articles and in two books of obstetric publications from 1988 to 2015. PubMed, Lilacs, Medline, Embase, Scopus, Medscape, Libertas Academica, CINAHL and Science databases were used to search for articles published on metabolic syndrome in pregnancy. We searched all those databases using the key words: metabolic syndrome in pregnancy, the MS prevalence in pregnancy, perinatal adverse effects in pregnant women with MS. 71 articles published in English and Portuguese were identified.

All the identified articles were reviewed to find and avoid possible duplication and then arranged for further survey. By analyzing the titles of the articles, the ones whose design differed from inclusion criteria (metabolic syndrome in pregnancy, adverse perinatal outcome) were excluded. Summaries of the articles were read and selected and we excluded those which did not mention the features of metabolic syndrome in pregnancy and its adverse perinatal outcomes. The complete text of selected articles were retrieved and reviewed independently. After data extraction, a new review of articles was made as a means to ensure that the data of the selected articles were included only once in the analysis, which resulted in only 27 remaining articles taking part with this review.

The results are summarized according to sample size, type of study, the definition used for metabolic syndrome in pregnancy and its prevalence. Risk factors were also evaluated. From all of these studies, 27 articles focused mainly on the syndrome definition, its prevalence and its adverse perinatal outcomes.

Search strategy



Results

Women with pre gestational metabolic syndrome are more likely to develop complications during pregnancy, such as pre eclampsia, eclampsia, gestational diabetes, coma. Thereby increasing the possibility of being born a baby with perinatal adverse effects such as malformations, hypoglycemia, newborn great among others, while when this syndrome begins in pregnancy, reduce the harm chances formations because they have relationships with situations that occur in the first quarter pregnancy, with only the chances of having obstetric complications and with respect to the newborn: newborn great, jaundice, hypoglycemia and respiratory distress syndrome.

Recommendation

Metabolic syndrome is an entity that must be diagnosed early so you can provide an opportunity for health professionals to intervene in ways to promote health and prevent complications.

Our Experience at the Experimental Laboratory of Gynecology and Obstetrics of Botucatu Medical University/Universidade Estadual Paulista

The unprecedented identification of pregnant women with mild gestational hyperglycemia – HGL (using the following diagnostic tests: Tolerance Test to normal glucose and glycemic profile changes, proposed by RUDGE, 1983) is now recognized by the international literature (HAPO, 2009; 2010). It was performed by the Diabetes Research Group and Pregnancy: Clinical & Experimental Research (from CNPq) which started in 1983 at the Botucatu University of Medicine/UNESP. In the early projects and publications, the name of this group of pregnant women with abnormal glucose profile was IB of Rudge (RUDGE et al., 1990). Research related to these IB groups of mothers who have HGL, correspond to 13.8% of the pregnant women with positive screening for GDM, which added to 7.0% of the pregnancies complicated by diabetes and augmented the occurrence of hyperglycemic disorders in pregnancy to about 20%. The translational research has guided all

the researches over the years (SGARBOSA et al., 2006; RUDGE et al., 2006, 2007, 2009; CALDERON et al., 2007; CAMPOS et al., 2007, 2008; LIMA et al., 2007; SPINNATO et al., 2008; SIBAI et al., 2008; VOLPATO et al., 2008, 2009; NEGRATO et al., 2008, 2009; DE LUCA et al., 2009; de SOUZA et al., 2009, 2010; PIETRO et al., 2010). Investigations have shown that pregnant women with HGL and DMG have several clinical parameters of MS during pregnancy. The history of DMG (odds ratio 3,75; IC 95% 1,03 – 15,9), and BMI ≥ 25/kg m² (odds ratio 3,63; IC 95%; 1,06 – 12,49)was more relevant for MS occurrence during pregnancy . Determinations HOMA-IR and HOMA- β indicated in pregnant women with HGL an insulin resistance framework that persists 06 weeks postpartum and that associates pregnant women with GDM directly to the occurrence of MS during pregnancy (NEGRATO et al, 2008).

Pregnant women who develop GDM or HGL usually were found to be born with lower weight and shorter legs, showing the fetal programming of MS still in their intrauterine life (NEGRATO et al, 2008). Nowadays, literature alerts to the risks of association between MS and its components in pregnancies complicated by GDM or HGL (NEGRATO *et al*., 2008; 2009), suggesting strong interrelationship between these conditions. Since there is no global definition for MS during pregnancy, Negrato et al, in 2008, adopted the following criteria: any of the three primary criteria (changes in glycemic profile and/or the GTT or hyperinsulinemia) plus at least two of the following criteria: hypertension, dyslipidemia and obesity. The results showed that MS components have great impact on the product of conception, increasing the adverse perinatal events - APO (Adverse Perinatal Outcome) (NEGRATO et al, 2008a and NEGRATO et al, 2008b). The prevalence of MS during pregnancy increased with worsening of glucose tolerance, reflected insulin resistance/hyperinsulinemia leading to increased fetal weight and was precursor of adverse perinatal outcome (APO). The diagnosis of MS in the second half of pregnancy was an important indicator of fetal macrosomia in both DMG and HGL, showing that the sum of MS components identifies a group of high-risk pregnant women about to develop APO (Negrato et al 2008 b).

The results strongly recommend that people with MS during pregnancy need to be compared to the population of other countries in the world to establish general criteria for the MS monitoring.

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Capítulo 3

Prevalence of metabolic syndrome in non-diabetic, pregnant Angolan women according to four diagnostic criteria and its effects on adverse perinatal outcomes

Diabetology & Metabolic Syndrome

Prevalence of metabolic syndrome in non-diabetic, pregnant Angolan women according to four diagnostic criteria and its effects on adverse perinatal outcomes

A prevalência de síndrome metabólica em mulheres angolanas gravidas não-diabéticos, de acordo com quatro critérios de diagnóstico e efeitos adversos perinatais.

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Abstract

Background: Metabolic syndrome (MetS) is a cluster of risk factors for type 2 diabetes (Type2 DM) and cardiovascular diseases (CVD), and its prevalence varies based on region, population, and sex. Newborns of women with MetS have a greater risk of adverse perinatal outcomes. This study explores the prevalence of metabolic syndrome in non-diabetic, pregnant Angolan women and the adverse perinatal outcomes associated with it.

Methods: This cross-sectional study collected the demographic, anthropometric and clinical data of 675 pregnant women in the maternity ward of General Hospital in Huambo, Angola. Metabolic syndrome was defined using four criteria: the third report of the National Cholesterol Education Program Adult Treatment Panel (ATPIII), the Joint Interim Statement (JIS), and definitions by both Bartha et al and Chatzi et al.

Results: The crude prevalence of metabolic syndrome was 36.6% based on the JIS definition, 29.2% based on NCEP ATPIII, 12.6% based on Chatzi et al and 1.8% based on Bartha et al. In general, the prevalence of adverse perinatal outcomes was 14.1% .

Conclusions: There was a high prevalence of metabolic syndrome, depending on the criteria used, and thus a great need to harmonize the criteria and cutoff points. Perinatal adverse outcomes were higher in pregnant women with metabolic syndrome.

Keywords: Prevalence, metabolic syndrome, Angola, Pregnancy perinatal outcome

Resumo

A síndrome metabólica (SM) é um conjunto de fatores de risco para diabetes tipo 2 (DM Tipo 2) e doenças cardiovasculares (DCV) e sua prevalência varia de acordo com o sexo, região e população. Recém-nascidos de mães com SM têm risco maior de resultados perinatais adversos(RPA). O objetivo deste estudo foi determinar a prevalência da SM em grávidas angolanas não-diabéticas e os RPA.

Métodos: Foi um estudo de corte transversal, em que foram coletados dados demográficos, antropométricos e clínicos de 675 grávidas usuárias da Maternidade do Hospital Geral do Huambo - Angola. A SM foi definida de acordo com quatro critérios: o terceiro relatório da National Cholesterol Education Painel de Programa de tratamento para Adultos (ATPIII), o Critério Harmonizado (JIS) e os de Bartha et al e Chatzi et al.

Resultados: A prevalência de SM foi de 36,6% para o critério JIS ,de 29,2% para o NCEPATP III, de 12,6% para o de Chatzi et al e de 1,8% para o de Bartha et al .A prevalência dos RPA foi de 14,1%l.

Conclusões: a prevalência da síndrome metabólica foi elevada, e variou de acordo com o critério utilizado. Impõe-se a necessidade de harmonizar os critérios e pontos de corte. Os RPA foram mais prevalentes nos neonatos de grávidas com SM.

Palavras chaves: Prevalência, Síndrome Metabólica, Angola, Gravidez, resultado perinatal adverso

Introduction

Metabolic syndrome (MetS) is a cluster of risk factors for type 2 diabetes (Type2 DM) and cardiovascular diseases (CVD), with insulin resistance (IR) proposed as the linking factor [1]. It includes dyslipidemia—elevated triglycerides and apolipoprotein B (apoB), containing lipoproteins and low high-density lipoproteins (HDL), as well as elevated arterial blood pressure (BP) and dysregulated glucose homeostasis. Abdominal obesity and/or IR have also gained increasing attention as important components of the syndrome. Despite the many components and clinical implications of MetS, there are still no universally accepted pathogenic mechanisms or clearly defined diagnostic criteria [2] for the syndrome.

Over the past few decades, several definitions of MetS have been proposed using various diagnostic criteria: WHO (1998, 1999) [3,4], the National Cholesterol Education Program Third Adult Treatment Panel (ATPIII) (2001, 2004) [5], and more recently, the International Diabetes Federation (IDF) (2005) [8 – 10]. In an attempt to unify the criteria, in 2009, an additional definition was proposed as a harmonized Joint Interim Statement (JIS) by several organizations. Notwithstanding the various definitions, central obesity, dyslipidemia, hyperglycemia and elevated BP are the key characteristics of MetS [6].

In the same year as the JIS publication, a study conducted in Brazil showed that the prevalence of MetS in pregnancy increases with the decline in glucose tolerance. The study also demonstrated that the glycemic profile is a useful diagnostic tool for identifying metabolic abnormalities related to MetS in pregnancy and predicting the occurrence of adverse perinatal outcomes (APO). The authors concluded that MetS diagnosed during mid-pregnancy is a predictor of APO, both in women with gestational diabetes (GDM) and in those with mild gestational hyperglycemia (MGH) who are not currently classified as having GDM. These results reinforced the importance of screening for the components of MetS to identify pregnant women who are at high risk for APO [7].

During the same period, research was published studying different populations and showed an association between maternal MetS in early pregnancy and higher risk for both preterm birth (Chatzi et al 2009a) [8] and GDM [9].

In 2008, Bartha et al modified the NCEP ATPIII for pregnancy, establishing a new cutoff for several parameters: pre-pregnancy BMI > 30 kg / m2, Plasma triglycerides ≥ 2 SD for gestational age, HDL cholesterol > 2 SD for gestational age, blood pressure ≥ 130 / ≥ 85 mm / Hg, and fasting glucose ≥ 110 mg / dL [10].

Recognition of MetS during pregnancy could help identify a subgroup of women who may not only develop a pregnancy-related condition but are also potentially at an increased risk for either metabolic or cardiovascular adverse conditions later in life.

Adverse outcome indexes were designed to measure the quality of perinatal care [11 - 13].

The clinical outcomes are a function of both the received healthcare and the basic health status of the patient [14].

In sub-Saharan Africa, many countries are experiencing a rapid demographic and epidemiological transition [15].

Angola is a country in sub-Saharan Africa that has undergone significant political changes over the last several years, accompanied by rapid economic growth and an increased urbanization rate. These changes may be implicated in the increasing prevalence of MetS caused by the rise in obesity due to insufficient physical activity, dyslipidemia, hypertension and hyperglycemia [15]. However, the prevalence of the MetS in pregnant Angolan women, the specific factors contributing to its occurrence, and its perinatal implications remain unknown. Despite the diversity of definitions, the prevalence of MetS is well known in several populations worldwide [2]. To date, however, no such information is available in communities in low- to mid-income countries, such as non-diabetic, pregnant Angolan women. There are also no studies on the association between APO and maternal MetS in pregnancy.

Our hypothesis is that in a country with a high prevalence of MetS, norm glycemic pregnant women may also exhibit a high prevalence of MetS, which has direct effects on the perinatal results. The detection of MetS during pregnancy has not been established in the literature, and it merits a comparison between different diagnostic criteria.

This study aimed to 1- gather data on the prevalence of MetS in a subset of non-diabetic, pregnant Angolan women; 2- estimate the prevalence of MetS according to four diagnostic criteria: NCEP ATP III (2001) [5], the Joint Interim Statement (JIS) definition (2009) [6], and the modification of criteria for pregnancy proposed by Bartha et al (2008) [10] and Chatzi et al (2009) [8,9]; 3- determine the level of agreement and disparity among these four criteria for the diagnosis of MetS and APO; and 4- compare the effects of MetS in non-diabetic, pregnant women on APO.

Methods

Study population

This mother-child, cross-sectional study examined a sample population of non-diabetic pregnant women from the public General Hospital of Huambo, Angola, to estimate the prevalence of metabolic syndrome (MetS) in pregnancy and its effects on APO. During the study period, which lasted from December 2014 to February 2015, a total of 675 single, non-diabetic pregnant women with complete data were selected and enrolled in this study.

The study was conducted according to the tenets of the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the Faculty of Medicine, Agostinho Neto University, Huambo, Angola.

All non-diabetic pregnant women in the maternity ward during this period were invited to participate and were included after an informed consent form was signed. Patients with established cardiovascular diseases, thyroid dysfunction, excessive alcohol or other drug abuse, current or recent psychiatric treatment (up to 4 months) during pregnancy and cesarean section were excluded. Eight nurses were trained on the structured guide for the survey. The interview guide was divided into three sections: socio-demographic characteristics, anthropometrics and biochemical evaluation.

On the test day, all consenting subjects provided information for a structured questionnaire, underwent an anthropometric examination and provided blood samples for biochemistry tests. Maternal characteristics such as age, parity, ethnicity, educational level, family income, smoking status, alcohol consumption and alimentary habits, weight and pre-pregnancy body mass index (BMI) were recorded.

All biochemical analyses were carried out within 2 h of blood sampling in the laboratory of the General Hospital of Huambo, which adheres to strict internal and external standards of quality control techniques.

Pre-gestational BMI and waist circumference (WC) were obtained to quantify obesity. Body weight (kg) was measured to the nearest 0.1 kg using a previously calibrated mechanical scale (SECA GmbH & Co, Germany) with a maximum capacity of 200 kg. Standing body height (cm) was measured to the nearest 0.2 cm using a portable wall stadiometer (Seca, Germany). WC was measured in cm at the level of the navel using a flexible, non-distensible tape without exerting pressure on the tissues. Pre-gestational BMI

was calculated as weight in kilograms divided by the square of the height (kg/m^2). Three consecutive measurements of sitting blood pressure at a minimum of 5-min intervals were recorded using Omrom® MX3 with an automated oscillometric Blood Pressure Monitor (O-HEM-742-E) (Matsusaka, Japan) [16].

After the participants had Been sitting for at least 30 minutes, were measures Systolic blood pressure (SBP, mmHg) and diastolic blood pressure (DBP, mmHg). Hypertension was defined as systolic blood pressure ≥130 mmHg and diastolic blood pressure ≥ 85 mmHg.

In addition, venous blood samples were drawn from the forearm using standard techniques and were processed immediately using commercially available kits (BioSystems SA, Costa Brava 30, Barcelona, Spain) to measure fasting plasma glucose (FPG, mg/dl), triglycerides (TG, mg/dl), total cholesterol (TC, mg/dl), low-density lipoprotein cholesterol (LDL-C, mg/dl), and high-density lipoprotein cholesterol (HDL-C, mg/ dl). All biochemical analyses were carried out within 2 h of blood sampling in the central laboratory of Huambo Hospital. This lab adheres to strict internal and external standards of quality control techniques.

Definition of metabolic syndrome in pregnancy

All participants were classified as either having or not having MetS according to four criteria, as indicated in Table 1 NCPE ATP III 2001 [5], JIS (2009) [6] and two modified definitions for pregnancy: Bartha et al (2008) [10] and Chatzi et al (2009) [8,9].

The definition of the four criteria was based on the presence of three or more of the five components (Table 1).

The ATP III (2001)[5] components are WC > 88 cm; SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg and/or BP-lowering treatment; fasting triglyceride levels ≥ 150 mg/dl and/or treatment for hypertriglyceridemia; HDL-C < 50 mg/dl and/or treatment for dyslipidemia; and fasting glucose level ≥ 110 mg/dl and/or on antidiabetic medication.

The Joint Interim Statement (JIS) definition (2009) [6] components are WC > 80 cm; SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg and/or undergoing BP-lowering treatment; fasting triglyceride levels ≥ 150 mg/dl and/or treatment for hypertriglyceridaemia; HDL-C < 50 mg/dl and/or treatment for dyslipidemia; and fasting glucose level ≥ 100 mg/dl or on antidiabetic medication.

The Bartha et al (2008) [10] modified criteria of NCEP APTIII characterize MetS by abdominal obesity, given WC > 2 S.D. for gestational age in the first half of pregnancy or pre gestational BMI > 30 Kg/m^2; triglycerides ≥ 2 S.D. for gestational age; HDL-Cholesterol < 2 S.D. for gestational age; blood pressure ≥ 130/85 mm/Hg; and fasting glucose ≥ 105 mg/dl.

The Chatzi et al (2009 a,b) [8,9] criteria, which modify HNLBI/AHA and NECP ATP III, are as follows**:** pre gestational BMI > 30 Kg/m^2; triglycerides ≥ 150 mg/dl; HDL cholesterol < 50 mg/dl; BP ≥ 130/85 mm/Hg; and fasting glucose ≥ 100 mg/dl.

Adverse perinatal outcomes

Newborn data collection included birth weight, length, sex, gestational age at delivery, the first and fifth minutes' perinatal morbidity and congenital malformations. Births were defined as pre-term if the gestational age was <37 weeks. The relation between the newborns' weight and gestational age was defined according to Lubchenco's criteria [17].

APO was diagnosed in the presence of any morbidity factors, such as prematurity, a low Apgar score, malformations, respiratory distress syndrome, jaundice, infections, large for gestational age (LGA), small for gestational age (SGA) and macrosomia.

Statistical analysis

Data analyses were performed using the **SAS 9.3 Foundation for Microsoft® Windows®** (Copyright © 2012, SAS Institute Inc., Cary, NC, USA). Data for categorical variables are expressed as the number and percentage. Continuous variables are reported as the means ± standard deviation and compared using the independent samples t-test. Categorical variables were expressed as proportions and compared using the chi-square test or Fisher's exact test if appropriate. The prevalence of MetS was determined according to the four criteria (NCEP ATP III 2001, the harmonized definition, the Bartha et al (2008) criteria that modified NCEP APT III and the Chatzi et al (2009) criteria that modified HNLBI/AHA). The kappa coefficient was calculated to evaluate the concordance among the definitions—NCEP ATP III, the harmonized criteria, Bartha et al and Chatzi et al—in detecting MetS and APO.

The agreement among the four definitions was determined by kappa statistics (k). The level of agreement was considered poor for k≤0.20, fair for k=0.21-0.40, moderate for

k=0.41to 0.60, substantial for k=061 to 0.80 and excellent for k≥0.80 (Landis & Koch, 1977) [18].

The percentage of socio-demographic and obstetric variables, the prevalence of MetS, and the APO of non-diabetic pregnant women with MetS were calculated and grouped as independent and dependent variables.

Independent variables: with or without MetS

Dependent variables: with or without APOs. Comparisons between 'with' and 'without' MetS were made using a difference of proportions test for all criteria.

Sensibility, specificity, and positive and negative predicted values were also calculated for all of the criteria used to diagnose of MetS and for APO.

A *p*-value < 0.05 was considered statistically significant.

Results

A total of 675 non-diabetic pregnant women consented to participate in the survey. Full data sets were available from all participants and are the basis of this report. The mean values for the socio-demographic and various anthropometric, clinical and biochemical parameters of the study patients are presented in Table 2.

The mean age of the patients was 24 ± 6.7 years, and the mean gestational age was 39.2 weeks. In terms of educational background, 8.0% were illiterate, 84.7% had completed secondary education and 7.3% had completed high school. One hundred forty-nine patients (22.1%) were from urban areas, and 572 (84.7%) were from rural areas. Only one patient was a smoker at the time of the study.

The major occupations of the patients were business (460, 68.1%), student (141, 21.0%) and public officials (74, 11.0%). One hundred eighty-eight (27.8 %) were nulliparous.

In our study, the mean values of particular features of metabolic abnormalities characteristic of MetS among pregnant women are summarized in Table 2. Most of the women studied had normal blood glucose levels (551, 81.6%). Obesity was evaluated by two parameters: the mean pre-gestational BMI was 24.4 ± 4.2, and the mean WC at term was 93.6 ± 9.3 cm. The mean fasting plasma glucose was 83.7 ± 22.9 mg/dl, and the triglyceride, HDL-C, LDL-C and total cholesterol means were 149.3 ± 55.8, 70.9 ± 18.5, 116.9 ± 34.5, 193.2 ±

37.8, respectively. Hypertension was very common among pregnant women and was detected in 54.8% of all patients; 6.5% were taking medication for hypertension.

APOs were diagnosed in 14.1% of the entire population.

The prevalence of MetS was estimated using NCEP ATP III, the Joint Interim Statement (JIS) definition, and the modified criteria for MetS in pregnancy by Bartha et al (2008) and by Chatzi et al (2009). The overall prevalence of MetS during pregnancy varied according to the four definitions: 36.6% for the JIS, 29.2% for the NCEP ATP III, 12.6% for the Chatzi definition and 1.8% for the Bartha definition. These results are shown in Table 3 ($p < 0.0001$).

The prevalence of individual MetS components according to the four criteria varied according to different criteria, and the results are presented in Table 4.

Using the JIS definition, 36.0% had high fasting blood glucose levels, 99.6% had increased WC, 80.6% had hypertriglyceridemia, 19.8% had low HDL-C and 87.4% presented hypertension.

Using the NCEP ATP III criteria, 22.3% had increased fasting glucose levels, 95.9%, had increased WC, 84.3% had hypertriglyceridemia, 22.8% had decreased HDL-C, and hypertension occurred in 90.9%.

Using the Chatzi et al criteria, 47.1% exhibited high fasting glucose levels, 47.1% had a pre gestational BMI > 30, 91.8% had hypertriglyceridemia, 37.6% had low HDL-C and 92.9% exhibited hypertension.

The Bartha et al criteria detected the lowest percentage of MetS in pregnancy, with high fasting glucose levels in 83.3%, pre gestational BMI > 30 in 91.7%, hypertriglyceridemia in 8.3%, low HDL-C in 16.7%, and all patients presenting hypertension.

The frequency of the number of MetS components in the NCEP ATP III, harmonized, Bartha and Chatzi criteria are summarized in Table 5. The majority of non-diabetic pregnant women had a cluster of one or two metabolic abnormalities in the four definitions used in this study.

Table 6 shows the comparison of socio-demographic and various anthropometric, clinical and biochemical parameters between groups with and without MetS components included in the NCEP ATP III, JIS definition, and modified criteria for MetS in pregnancy by Bartha et al (2008) and Chatzi et al (2009).

Non-diabetic pregnant women with MetS were older according to three criteria (NCEP ATP III, the JIS definition and Bartha et al) and were overweight or obese (either with WC or

BMI>30 before pregnancy) according to all four criteria. They had high fasting blood glucose levels, increased serum triglyceride levels, decreased serum HDL-C, increased hypertension prevalence and higher systolic and diastolic blood pressure ($p < 0.05$).

In the entire population, there were 129 APOs in 95 newborns (14.1%). The APOs were analyzed according to the four definitions that identified mothers with and without MetS (Table 7). The prevalence of newborns with APOs from non-diabetic mothers with and without MetS defined by the four definitions were similar. There was no statistically significant difference between any APO from mothers with and without MetS. Detailed APO data between the groups with and without MetS mothers are presented in Table 7.

The agreement and disagreement in the diagnosis of MetS among the four criteria is presented in Table 8. The agreement among these four definitions was ranked from excellent to poor. The agreement was excellent between NCEP ATP III — JIS definition ($\kappa = 0.8332$ (0.7894-0.8771), $p < 0.001$), considerable between Bartha – Chatzi ($\kappa = 0.2232$ (0.1172-0.3292), $p < 0.001$) and Chatzi – JIS definition ($\kappa = 0.4036$ (0.3389-0.4684), $p < 0.001$), moderate between NCEP ATP III—Chatzi ($\kappa = 0.4320$ (0.3076-0.5064), $p < 0.001$) and poor between Bartha – ATP III ($\kappa = 0.0841$ (0.0390-0.1293), $p < 0.001$), and Bartha- JIS definition ($\kappa = 0.0608$ (0.00275-0.0941), $p < 0.001$).

In terms of the diagnostic accuracy of MetS, the Bartha et al, NCEP ATP III and Chatzi et al definitions displayed the highest sensitivity (100%) and negative predictive value (100%), whereas NCEP ATPIII and the JIS definition had the highest specificity (100%) and positive predictive value (100%).

The agreement and disagreement among APO in the four definitions of MetS in non-diabetic pregnant women is presented in Table 9.

The agreement among these four definitions varies from excellent to poor. The agreement was excellent between NCEP ATP III — JIS definition ($\kappa = 0.86$ (0.76-0.9677), p 0.01); considerable between Bartha – Chatzi ($\kappa = 0.38$ (0.11-0.65), p 0.0009); moderate between NCEP ATP III-Chatzi ($\kappa = 0.52$ (0.34-0.71), p 0.003) and Chatzi — JIS definition ($\kappa = 0.47$ (0.30-0.64), $p < 0.001$); and slight between Bartha – NCEP ATP III ($\kappa = 0.17$ (0.02-0.33), $p < 0.001$) and Bartha — JIS definition ($\kappa = 0.13$ (0.01-0.26), $p < 0.001$).

The Bartha, NCEP ATP III, Chatzi and JIS definitions had the highest sensitivity (100%) and negative predictive value (100%), whereas the NCEP ATPIII, JIS definition, and Bartha definitions had the highest specificity (100%) and positive predictive value (100%) for APO.

Table 1 Criteria for clinical diagnosis of metabolic syndrome components according to four definitions

Components of MetS	NCEP – ATP III (2001)	JIS MetS Criteria (2009)	NCEP – ATP III, Bartha et al (2008) Modification	HNLBI/AHA, Chatzi et al (2009) Modification
Prerequisite	None	None	None	None
Nº of other criteria	≥ 3 of:	≥ 3 of:	≥ 3 of:	≥ 3 of:
Obesity	W.C. > 88 cm	W.C. ≥ 80 cm	P.G/B.M.I. > 30 Kg/m^2	P.G/B.M.I. > 30 Kg/m^2
Hypertension	≥ 130/85 mm/Hg	≥ 130/85 mm/Hg	≥ 130/85 mm/Hg	≥ 130/85 mm/Hg
Decreased HDL-C	< 50 mg/dl	< 50 mg/dl	< 2 S.D. (40 mg/dl)	< 50 mg/dl
Hypertriglyceridemia	≥ 150 mg/dl	≥ 150 mg/dl	≥ 2 S.D/ G.A (270 mg/dl)	≥ 150 mg/dl
Increased Fasting Hyperglycemia	≥ 110 mg/dl	≥ 100 mg/dl	≥ 105 mg/dl	≥ 100 mg/dl

Table 2 Frequency analysis of socio-demographic and metabolic parameters of pregnant women

Variables	Media ± Standard deviation
N	**675**
Race	
Black [n (%)]	675 (100)
Other [n (%)]	0 (0)
Maternal age (y)	24.7 ± 6.7
Level of education	
Never studied [n (%)]	54 (8)
Middle [n (%)]	572 (84.7)
Higher education [n (%)]	49 (7.3)
Place of residence	
Urban [n (%)]	149 (22.1)
Village [n (%)]	526 (77.9)
Occupation	
Students [n (%)]	141 (21.0)
Business [n (%)]	460 (68.1)
Public official [n (%)]	74 (11.0)
Smoking habit	
Non-smoker	674 (99.9)
Current smoker (%)	1 (0.1)
Gestational age (weeks)	39.2 ± 1.6
Hypertension [n (%)]	370 (54.8)
Anti-hypertensive drugs (%)	44 (6.5)
Nulliparous	188 (27.8 %)
Glycemic level	
≥ 110 mg/dl	70 (10.4)
≥ 105 mg/dl	90 (13.3)
≥ 100 mg/dl	124 (18.4)
< 100 mg/dl	551 (81.6)
Fasting glycemia mean	83.7 ± 22.9
Obesity	
Mean waist circumference	93.6 ± 9.3
BMI (Kg/m^2)	24.4 ± 4.2
Triglycerides (mg/dl)	149.3 ± 55.8
HDL – C (mg/dl)	70.9 ± 18.5
LDL – C (mg/dl)	116.9 ± 34.5
Total Cholesterol (mg/dl)	193.2 ± 37.8
Adverse Perinatal Outcome (APO)	95 (14.1%)

Table 3 Prevalence of metabolic syndrome according to four definitions and its components in pregnant women.

Components of MetS	NCEPT – ATP III (2001) N = 675		JIS MetS Criteria (2009) N = 675		NCEPT – ATP III Bartha (2008) Modification N = 675		NHLBI/AHA Chatzi (2009) Modification N = 675	
	Cut Points	**N (%)**	**Cut Points**	**N (%)**	**Cut Points**	**N (%)**	**Cut Points**	**N (%)**
Fasting glycemia mean	≥ 110 mg/dl	70 (10.4)	≥ 100 mg/dl	124 (18.4)	≥ 105 mg/dl	90 (13.3)	≥ 100 mg/dl	124 (18.4)
Obesity								
BMI		-	-		> 30 Kg/m^2	75 (11.1)	> 30 Kg/m^2	75 (11.1)
Waist circumference	> 88 cm	497 (73.6)	≥ 80 cm	657 (97.3)		_	-	-
Hypertriglyceridemia	≥ 150 mg/dl	293 (43.4)	≥ 150 mg/dl	293 (43.4)	≥ 270 mg/dl	15 (2.2)	≥ 150 mg/dl	293 (43.4)
Decreased HDL-C	< 50 mg/dl	53 (7.8)	< 50 mg/dl	53 (7.9)	< 40 mg/dl	17 (2.5)	< 50 mg/dl	53 (7.9)
Hypertension	≥ 130/85 mm/Hg	370 (54.8)	≥ 130/85 mm/Hg	370 (54.8)	≥ 130/85 mm/Hg	370 (54.8)	≥ 130/85 mm/Hg	370 (54.8)
MetS prevalence		197 (29.2)		247 (36.6)		12 (1.8)		85 (12.6)

*Differences of the test proporcções - p <0.0001 (a, b, c and d)

Table 4 Prevalence of individual metabolic syndrome abnormalities in pregnant women with metabolic syndrome according to four definitions

Components of MetS	NCEPT – ATP III (2001) and Grundy (2005) N = 197		JIS MetS Criteria (2009) N = 247		NCEPT – ATP III Bartha (2008) Modification N = 12		NHLBI/AHA Chatzi (2009) Modification N = 85	
Increased Fasting Glycemia	≥ 110 mg/dl	44 (22.3)	≥ 100 mg/dl	89 (36.0)	≥ 105 mg/dl	10 (83.3)	≥ 100 mg/dl	40 (47.1)
Obesity								
BMI					> 30 Kg/m^2	11 (91.7)	> 30 Kg/m^2	40 (47.1)
Waist Circumference	> 88 cm	189 (95.9)	≥ 80 cm	246 (99.6)		-		-
Hypertriglyceridemia	≥ 150 mg/dl	166 (84.3)	≥ 150 mg/dl	199 (80.6)	≥ 270 mg/dl	1 (8.3)	≥ 150 mg/dl	78 (91.8)
Decreased HDL - C	< 50 mg/dl	45 (22.8)	< 50 mg/dl	49 (19.8)	< 40 mg/dl	2 (16.7)	< 50 mg/dl	32 (37.6)
Hypertension	≥ 130/85 mm/Hg	179 (90.9)	≥ 130/85 mm/Hg	216 (87.4)	≥ 130/85 mm/Hg	12 (100)	≥ 130/85 mm/Hg	79 (92.9)
Metabolic Syndrome %		29.2 (a)		36.6 (b)		1.8 (c)		12.6 (d)

Table 5 Frequency of individual components of metabolic syndrome according to four definitions

Defenitions / MetS Components Nº	NCEP ATP III (2001) N = 675	JIS MetS Criteria (2009) N = 675	NCEP ATP III (Bartha, 2008) N = 675	NHLBI/AHA (Chatzi, 2009) N = 675
0	48	04	239	141
1	200	150	317	252
2	230	274	107	197
3	165	190	12	71
4	32	56	0	14
5	0	1	0	0

Table 6 Comparison of socio-demographic, clinical and biochemical parameters in pregnant women with and without metabolic syndrome according to four definitions.

Variables	NCEP ATP III (2001)		p Value	JIS MetS Criteria (2009)		p value
	With MetS N = 197	Without MetS N = 478		With MetS N = 247	Without MetS N = 428	
Mean age (y)	26.2± 6.8	24.0 ± 6.6	0.0002	25.6 ± 6.8	24.1 ± 6.7	0.0070
Level of education						
Never studied [n (%)]	21 (10.6)	33 (6.9)	0.1391	24 (9.7)	30 (7.0)	0.2706
Middle	157 (79.7)	415 (86.8)	0.0162	203 (82.2)	369 (86.2)	0.1967
Higher education	19 (9.6)	30 (6.3)	0.1706	20 (8.1)	29 (11.7)	0.6288
Place of Residence						
Urban [n (%)]	50 (25.4)	99 (20.7)	0.2196	61 (24.7)	88 (20.6)	0.2495
Village [n (%)]	147 (74.6)	379 (79.3)	0.2196	186 (75.3)	340 (79.4)	0.2495
Current smoker (%)	0 (0.0)	1	1.0	0 (0)	1 (0.2)	1.0
Mean body mass index	-	-	-	-	-	-
Mean waist circumference	97.4 ± 8.5	92.0 ± 9.1	< 0.0001	95.6 ± 9.0	92.4 ± 9.3	< 0.0001
Known diabetes mellitus (%)	00	00	-	00	00	-
Use of hypotensive drugs (%)	22 (11.1)	22 (4.6)	0.0029	23 (9.3)	21 (4.9)	0.0383
Fasting Glycemia (mg/dl)	90.5 ± 29.1	80.9 ± 19.2	< 0.0001	91.8 ± 27.4	79.1 ± 18.4	< 0.0001
Hipertension	179 (90.9)	191 (39.9)	< 0.0001	216 (87.4)	154 (36.0)	< 0.0001
Systolic Blood pressore	140.8 ± 18.5	124.4 ± 18.0	< 0.0001	138.5 ± 18.7	123.8 ± 18.1	< 0.0001
Diastolic Blood presssure	90.7 ± 14.1	80.4 ± 13.6	< 0.0001	89.3 ± 14.3	80.1 ± 13.6	< 0.0001
Total cholesterol (mg/dl) [$\bar{x}$ ± s]	197.0 ± 42.9	191.4 ± 35.6	0.0810	196.2 ± 43.6	191.4 ± 33.9	0.1364
LDL – C (mg/dl) [$\bar{x}$ ± s]	122.0 ± 37.8	114.8 ± 32.8	0.020	120.2 ± 38.2	114.9 ± 31.9	0.0655
HDL - C(mg/dl) [$\bar{x}$ ± s]	64.5 ± 19.0	73.5 ± 17.7	< 0.0001	65.8 ± 19.1	73.8 ± 17.5	< 0.0001
Tryglicerides (mg/dl) [$\bar{x}$ ± s]	182.0 ± 60.2	135.0 ± 47.7	< 0.0001	179.7 ± 59.5	131.7 ± 45.1	< 0.0001
Variables	**NCEP ATP III (Bartha, 2008)**			**NHLBI/AHA (Chatzi, 2009)**		
	With MetS N = 12	**Without MetS N = 663**	**p value**	**With N = 85**	**Without N = 590**	**p value**
Mean age (y)	28.7± 2	24.6 ± 6.7	0.0377	25.3± 6.9	24.6 ± 6.7	0.3217
Level of education						
Never studied [n (%)]	1 (8.3)	53 (7.9)	1.0	12 (14.1)	42 (7.1)	0.0444
Middle	09 (75)	563 (84.9)	0.588	66 (77.6)	506 (85.8)	0.0744
Higher education	02 (16.7)	47 (7.1)	0.4802	07(8.2)	42 (7.1)	0.8828
Place of Residence						
Urban [n (%)]	04 (33.3)	145 (21.9)	0.55	28 (33.0)	121 (20.5)	0.0145
Village [n (%)]	08 (66.7)	518 (78.1)	0.55	57 (67.0)	469 (79.5)	0.0145
Current smoker (%)	1.0	00	1.0	0	1	1.0
Mean body mass index	31.7± 4.1	24.2 ± 4.0	< 0.0001	27.6 ± 5.0	23.9 ± 3.8	< 0.0001
Mean waist circumference	-	-	-	-	-	-
Known diabetes mellitus (%)	00	00	-	00	00	-
Use of hypotensive drugs (%)	3 (25.0)	41 (6.2)	0.0426	11 (12.9)	33 (5.8)	0.0216
Fasting Glycemia (mg/dl)	126.7 ± 46.4	83.0 ± 21.6	0.0076	96.7±34.1	81.9±20.2	0.0002
Hipertension	12(100)	358 (54)	0.0039	79 ± 92.9	291 ± 49.3	<0.0001
Systolic Blood pressore	148.4 ±20.6	128.8 ± 19.4	0.0006	140.4 ± 17.8	127.6 ± 19.3	< 0.0001
Diastolic Blood presssure	96.3± 12.4	83.2 ± 14.5	0.00019	90.5 ± 15.6	82.4 ± 14.1	< 0.0001
Total cholesterol (mg/dl) [$\bar{x}$ ± s]	174.5 ± 38.1	193.5 ± 37.7	0.043	115.1 ± 36.5	117.1 ± 34.2	0.6155
LDL – C (mg/dl) [$\bar{x}$ ± s]	107.0 ± 34.9	117.0 ± 34.4	0.316	187.8 ± 40.4	193.9 ± 37.4	0.1632
HDL – C (mg/dl) [$\bar{x}$ ± s]	58.0 ± 17.7	71.1 ± 18.5	0.0152	60.0 ± 21.3	72.4 ± 55.3	< 0.0001
Tryglicérides (mg/dl) [$\bar{x}$ ± s]	126.7 ± 46.4	83.0 ± 21.6	0.0076	96.7 ± 34.1	81.9 ± 20.2	< 0.0001

Table 7 Comparison of adverse perinatal outcomes in pregnant women with and without metabolic syndrome according to four definitions.

Adverse perinatal outcome	Entire study group (N = 675)	NCEP ATP III (2001)		p Value	JIS MetS Criteria (2009)		p value	NCEP ATP III (Bartha, 2008)		p value	NHLBI/AHA (Chatzi, 2009)		p value
		With MetS N = 197	Without MetS N = 478		With MetS N = 247	Without MetS N = 428		With MetS N = 12	Without MetS N = 663		With MetS N = 85	Without MetS N = 590	
Visible malformation (%)	1	1 (0.5)	0 (0.0)	0.6468	0 (0)	1 (0.2)	1.0	0 (0.0)	1 (0.2)	1.0	0 (0.0)	1 (0.01)	1.0
Icterus (%)	4	2 (0.1)	2 (0.4)	0.7137	2 (0.8)	2 (0.5)	0.9699	0 (0.0)	4 (0.6)	1.0	1 (1.2)	3 (0.05)	1.0
Macrossomia	28	14 (7.1)	14 (2.9)	0.236	15 (6.0)	13 (3.0)	0.0882	2 (16.7)	26 (3.9)	0.1432	6 (7.0)	22 (3.7)	0.2507
Prematurity (%)	26	7 (3.5)	19 (3.9)	0.9691	9 (3.6)	17 (4.0)	0.9953	1	25 (3.7)	0.9544	5 (5.9)	21 (3.5)	0.4599
Respiratory Distress Syndrome (%)	14	3 (1.5)	11 (2.3)	0.7278	3 (1.2)	11 (2.6)	0.3628	0 (0.0)	14 (2.1)	1.0	2 (2.3)	12 (2.0)	1.0
Stillbirth (%)	15	6 (3.0)	9 (1.9)	0.5192	6 (2.4)	9 (2.1)	0.9952	2 (16.7)	13 (2.0)	0.0148	3 (3.5)	12 (2.0)	0.6305
Apgar Score <7													
1 min (%)	31	6 (3.0)	25 (5.2)	0.3028	9 (3.6)	22 (5.1)	0.4816	0 (0.0)	31 (4.8)	0.9433	4 (4.7)	27 (4.6)	1.0
5 min (%)	10	3 (1.5)	7 (1.5)	1.0	3 (1.2)	7 (1.6)	0.9161		10 (1.5)	1.0	1 (1.2)	9 (1.5)	1.0
Number of newborns with APO	95	30 (15.2) (a)	65 (13.6)	0.6658	36 (14.6) (a)	59 (13.8)	0.8655	4 (33.3) (a)	91 (13.7)	0.1293	15 (17.6) (a)	80 (13.5)	0.3973
Any adverse perinatal outcome APO N (%)	129	42 (21.3) (a)	87 (12.2)	p = 0,4069	47 (19.0) (a)	82 (19.2)	p = 1,000	5 (41.7) (a)	124 (18.7)	p = 0,1021	22 (25.9) (a)	106 (18.0)	p 0,1112

*Difference test of proportions of number of newborns with APO p = 0.3435 (a.a.a and a). *Difference test of proportions of any adverse perinatal outcomes is p=0,1898

Table 8 Agreement and disagreement among metabolic syndrome definitions in pregnant women with metabolic syndrome and the diagnostic criteria according to each definition

Definitions	Concordance			Diagnostic Accuracy (%)			
	k-value (95% CI)	p value	Agreement	Sensitivity	Specificity	PPV	NPV
Bartha vs NCEP ATP III	0.0841 (0.0390 – 0.1293)	< 0.0001	Poor	100	72.1	6.1	100
NCEP ATP III vs Bartha	0.0841 (0.0390 – 0.1293)	< 0.0001	Poor	6.1	100	100	72.1
Bartha vs Chatzi	0.2232 (0.1172 – 0.3292)	< 0.0001	Considerable	100	88.9	14.1	100
Chatzi vs Bartha	0.2232 (0.1172 – 0.3292)	< 0.0001	Considerable	14.1	100	100	88.9
Bartha vs JIS	0.0608 (0.0275 – 0.0941)	< 0.0001	Poor	100	64.6	4.9	100
JIS vs Bartha	0.0608 (0.0275 – 0.0941)	< 0.0001	Poor	4.9	100	100	100
NECP ATP III vs JIS	0.8332 (0.7894 – 0.8771)	< 0.0001	Excellent	100	89.5	79.8	100
JIS vs NECP ATP III	0.8332 (0.7894 – 0.8771)	< 0.0001	Excellent	79.8	100	100	89.5
NCEP ATP III vs Chatzi	0.4320 (0.3076 – 0.5064)	< 0.0001	Moderate	38.1	97.9	88.2	79.3
Chatzi vs NCEP ATP III	0.4320 (0.3076 – 0.5064)	< 0.0001	Moderate	88.2	79.3	38.1	97.9
Chatzi vs JIS	0.4036 (0.3389 – 0.4684)	< 0.0001	Considerable	100	72.5	34.4	100
JIS vs Chatzi	0.4036 (0.3389 – 0.4684)	< 0.0001	Considerable	34.4	100	100	72.5

Table 9 Agreement and disparity among adverse pregnancy outcomes in four definitions of metabolic syndrome in pregnant women

Definitions	Concordance			Diagnostic Accuracy (%)			
	k-value (95% CI)	p value	Agreement	Sensitivity	Specificity	PPV	NPV
Bartha vs NCEP ATP III	0.1739 (0.0214 – 0.3264)	< 0.0001	Slight	100	71.4	13.3	100
NCEP ATP III vs Bartha	0.1739 (0.0214 – 0.3264)	< 0.0001	Slight	13.3	100	100	71.4
Bartha vs Chatzi	0.3798 (0.1095 – 0.6502)	0.0009	Considerable	100	87.9	26.7	100
Chatzi vs Bartha	0.3798 (0.1095 – 0.6502)	0.0009	Considerable	26.7	100	100	87.9
Bartha vs JIS	0.1344 (0.0121 – 0.2567)	< 0.0001	Slight	11.1	100	100	64.8
JIS vs Bartha	0.1344 (0.0121 – 0.2567)	< 0.0001	Slight	100	64.8	11.1	100
NCEP ATP III vs Chatzi	0.5215 (0.3364 – 0.7065)	0.0003	Moderate	93.3	80	46.7	98.5
Chatzi vs NCEP ATP III	0.5215 (0.3364 – 0.7065)	0.0003	Moderate	46.7	98.5	93.3	80
NECP ATP III vs JIS	0.8613 (0.7549 – 0.9677)	0.0143	Excellent	83.3	100	100	90.8
JIS vs NECP ATP III	0.8613 (0.7549 – 0.9677)	0.0143	Excellent	100	90.8	83.3	100
Chatzi vs JIS	0.4701 (0.3005 – 0.6397)	< 0.0001	Moderate	100	73.7	41.7	100
JIS vs Chatzi	0.4701 (0.3005 – 0.6397)	< 0.0001	Moderate	41.7	100	100	73.7

Discussion

This study described, for the first time, the global variation of MetS prevalence and its components in a sample of non-diabetic pregnant Angolan women, according to four definitions of MetS. Two classical definitions for MetS (NCEP ATP- III and the Joint Interim Statement-JIS) and two other classical definitions modified for pregnant women (Bartha et al and Chatzi et al) were evaluated. There are some similarities among the components of the four criteria: none had pre-requisites, 3 of the 5 components of MetS are required to establish a MetS diagnosis; and the level for hypertension diagnosis is the same. However, the cutoff for fasting glycemia varies from 100 to 110 mg/dl.

The assessment of obesity is the greatest difference between the four criteria: some use the classical WC, whereas others rely on pre gestational BMI.

Among non-diabetic, black, pregnant Angolan women, the highest prevalence rate was estimated by the Joint Interim Statement (JIS) definition (36.6%), followed by NCEP ATPIII (29.2%), Chatzi et al (12.6%) and Bartha et al (1.8%). Irrespective of the defining criteria, our study revealed a very high prevalence of MetS in non-diabetic, pregnant Angolan women. The overall prevalence (29.2% by NCEP ATPIII criteria) in pregnant Angolan women is similar to that observed in the Nigerian general population (27.9%), compared to 34.1% in the USA, and is higher than the overall prevalence in Angola (17.6%[15]) and Canada [19].

These results may suggest significant implications for long-term cardiovascular complications, especially in populations of low- to mid-income countries such as Angola. Another explanation for this high prevalence of MetS could be the pregnancy itself, due to the increased abdominal circumference determined either by the gravid uterus or by maternal adaptations to pregnancy as metabolic and hematological changes occur. Many of the parameters involved in the definitions of MetS are part of the maternal adaptations to pregnancy [20].

The significantly different prevalence rates among the four definitions likely arise due to the different criteria used for obesity parameters—WC cut-off points and pre gestational BMI. It is well established in the literature that different components of the criteria impact the MetS prevalence rates and may complicate the interpretation of epidemiological studies [21]. Another aspect that should be considered is the apparent similarity between the normal development of pregnancy to MetS, including a fraction of women showing increased blood glucose levels, higher triglycerides and higher blood pressure levels. GDM and preeclampsia,

which are considered features of MetS, are associated with exaggerated dyslipidemia, insulin and glucose metabolism abnormalities during and even after pregnancy. Women with MetS have a higher risk of developing preeclampsia than do those without MetS [22]. An increased prevalence of MetS was found to correspond with the worsening of glucose tolerance in Brazilian hyperglycemic mothers [7].

Pregnancy offers a unique window of time to inform women of the long-term implications of predictive factors such as anthropometric, biochemical and clinical parameters of MetS during pregnancy, which are not only transient metabolic abnormalities but may also be the first manifestation of a serious disease such as Type 2 DM or CVD [7].

The high prevalence of MetS among our patients was surprising because they were low-risk, pregnant women, were at term and had vaginal delivery. This finding indicates that in pregnant women, the criterion used to assess obesity by WC represents a confounding factor because the gravid uterus undermines the measurement. The WC has been proposed as a useful screening tool in many primary care settings, although in pregnant women, the WC is potentially problematic because the uterine size could interfere in this measurement. This has led to some confusion on the part of obstetricians regarding how to identify pregnant women with MetS. During pregnancy, the characterization of central obesity is difficult due to uterus enlargement. The suggested WC cut-off points to define MetS result from experts' consensus and, in our view, justify additional clinical and epidemiological prospective studies on pregnant women by using adverse perinatal outcomes as a dependent variable.

Recent guidelines released by the Joint Interim Statement (JIS) 2009 [6] stressed the need to adopt ethnicity-specific values of WC to measure central obesity. For a given WC, Asians, blacks, and Caucasians showed different levels of intra-abdominal adiposity, thus putting the subjects at different levels of risk for CVD and type2 DM [23,24].

However, these guidelines did not determine how to evaluate MetS during pregnancy, which cut-off points should be used to define abdominal obesity, the prevalence of MetS during pregnancy worldwide, and the impact of MetS both in pregnancy and in the perinatal period. The various diagnostic criteria have led to some confusion on the part of clinicians regarding how to identify pregnant women with MetS.

This issue suggests the need to reconsider the current cut-off points for WC to establish specific recommendations for pregnant women.

Although the two classical definitions of MetS were introduced in 2001 and 2005 and the consensus statement was established in 2009 [2], disagreement remains regarding their use

in clinical practice. This debate is caused by disparities in the results, as evidenced by the review by Oguoma, VM 2014 in *Prevalence of cardio-metabolic syndrome in Nigeria: a systematic review* [19].

Conversely, the two definitions that have modified the classical consensus for MetS in pregnancy detected the lowest levels of MetS in non-diabetic, pregnant Angolan women (Chatzi et al (12.6%) and Bartha et al (1.8%)). The definition proposed by Chatzi was based on an adaptation of the NHLB/AHA criteria, and obesity is defined as a pre gestational BMI>30 kg/m². The authors analyzed the association between MetS characteristics before pregnancy and early in pregnancy and concluded that women with these MetS components were at a high risk of GDM development. The definition of obesity according to the WHO criteria (BMI>30 kg/m²) was used in four other studies evaluating MetS in pregnant women (Chatzi et al 2009 preterm; Bartha et al 2008). These studies showed that MetS is not only directly responsible for the development of atherosclerotic cardiovascular disease but that it has additional impacts on human pregnancy, such as preterm delivery, low birth weight infants, and the development of diseases such as diabetes, preeclampsia and hypertension.

Considering the apparent disagreement surrounding the evaluation of central obesity in the diagnosis of MetS, we found a substantial degree of agreement between the JIS definition and the NCEP ATPIII (0.83), which indicates that the requirement of abdominal obesity did not generate significant discrepancies in the prevalence or the classification of the MetS; instead, the WC cut-off points did. Similar results were found in a large Chinese population,[25] other Caucasian populations [26,27], and in Luxembourg [28].

The definitions using pre gestational BMI in pregnancy exhibited considerable (0.22) agreement.

African pregnant women with MetS were older according to three criteria (NCEP ATP III, the JIS definition and Bartha et al) and more overweight or obese either with the WC or BMI>30 before pregnancy variables based on all four criteria. They had higher fasting glycemia, increased serum triglyceride levels, decreased serum HDL-C, increased hypertension prevalence and higher systolic and diastolic blood pressure.

Among the four definitions used, the JIS definition was found to be the most sensitive, and the NCEP ATPIII definition was found to be most specific in identifying cases of MetS.

APO represents a group of maternal diseases and/or neonatal morbidity that interfere in perinatal results. It is well known that perinatal outcomes and quality of prenatal care are separate but related issues. Furthermore, perinatal outcomes depend in part upon the quality of

care, the complexity of the case mix and maternal complications [14]. In a low-risk pregnant population from Africa, the prevalence of APO (14,1%) was similar in mothers with and without MetS based on all four definitions. These results conflict with those found by Negrato et al (2009) in a Brazilian cohort of hyperglycemic mothers who had or did not have MetS. The offspring of the hyperglycemic mothers with MetS presented significantly higher prevalences of Large for Gestational Age (LGA), overweight (ponderal index), Apgar scores (<7 at 1 min and 2 min) and any type of APOs.

Our study had a cross-sectional design and was conducted among low-risk pregnant women from Huambo Hospital, which is located in the central highlands of Angola, a sub-Saharan area in Africa that does not necessarily represent the entire pregnant population of Angola.

However, several points of strength do need to be highlighted. First is the high prevalence of MetS according to four definition criteria, considering the increased risk of future CVD diseases among non-diabetic, pregnant Angolan women. Second, this study describes the similarities and differences among the classical definitions for MetS currently used outside pregnancy and those used in pregnancy to establish maternal and perinatal risks of MetS. This adverse maternal metabolic profile contributes to the epidemiological mapping of MetS in Angola and can serve as baseline data for low-risk pregnant women.

The completion of the JIS meeting to harmonize the criteria for the diagnosis of MetS emphasize that the new diagnosis elements, especially the WC, need to be addressed in the near future (JIS 2009). In our view, it is also necessary to establish correct and harmonized criteria of MetS in pregnancy, which can be accomplished by longitudinal studies comparing pregnant women who are at low and high risk for MetS.

Our results show the importance of strategic efforts to improve prenatal care to avoid maternal and perinatal long-term consequences. This includes focusing on interventions such as whole family lifestyle modification with weight control, physical activity, and nutrition to control the MetS epidemic of the 21st century both during and after pregnancy.

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Capítulo 4

Building the next generation of African Health researchers in Africa with Brazilian Government and University co-operation - a case report

Bulltein of the World Health Organization

Building the next generation of African Health researchers in Africa with Brazilian Government and University co-operation - a case report

Construir a próxima geração de pesquisadores de saúde africanos para África com o Governo brasileiro em cooperação com as Universidades - relato de caso

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Abstract

An efficient Brazilian co-operation program within the undergraduate and post graduation courses was created in 1981 to enable students coming from developing countries to take on their postgraduate courses. So far, about 1,600 undergraduate and postgraduate students were selected, from that 20% comes from Africa.

We have reviewed the strengths and weaknesses to emphasize the impact of PhD research training agreement between Brazil and Angola within the scientific community. Also how Angolan PhD works will have an effect on Brazilian students.

It took several steps in Angola to make possible to research, such as to meet a relevant research subject for the country, as well as for the undergraduation program, the sponsorship and the project manager, the responsibility to maintain this co-operation between countries in a long term and, finally, to enhance a powerful network among Angola, Africa and Brazil.

Key words: PhD cooperation program Brazil-Africa, research strength and weakness,

Resumo

Em 1981 foi criado um programa de cooperação brasileira nos cursos de graduação e pós-graduação para a participação de estudantes provenientes de países em desenvolvimento. Até o momento, cerca de 1.600 estudantes de graduação e de pós-graduação foram selecionados e destes 20% vieram da África. Revisamos os pontos fortes e fracos para enfatizar o impacto do acordo de treinamento pesquisadores de doutorado entre o Brasil e Angola no seio da comunidade científica. Também como a presença e o trabalho dos doutorandos angolanos terão efeito sobre os estudantes brasileiros.

Foram discutidas as várias etapas para a elaboração do projeto de pesquisa: o tema que deveria ser relevante para o país e também para o programa de pós - graduação, o financiamento do projeto , as dificuldades e facilidades no desenvolvimento da pesquisa e a possibilidade de manter este tipo de cooperação entre os dois países a longo prazo estruturando uma rede entre Angola e Brasil.

Introduction

In 1981, the Brazilian Government developed a program involving three ministries: of Foreign Affairs, of Education and of Science & Technology to enable students coming from developing countries to take on a postgraduation course in Brazilian Universities. This international program has contributed to prepare researchers in the developing world. Brazilian Higher Education Personnel Training Coordination (Capes), the Ministry of Foreign Affairs through the Division of Educational Topics (DET) and the National Council for Scientific and Technological Development (CNPq) have turned into public interest to select new candidates every year from developing countries, the ones Brazil has a cooperation agreement (1).

Brazilian universities with postgraduate courses recognized by Capes have to accept such students, which will receive all the support needed in order to study in that country, e.g. flight tickets, scholarship and diploma nationally recognized . In the last decade, more than 1,600 postgraduate students were selected, 75% of which comes from North and South America, 20% from Africa and 5% from Asia, particularly from East Timor (1). From 2000 to 2014, the first author of this written paper is one of 465 African postgraduate students, as well as one of 59 Angolan students to take part of the Brazilian PhD Program. , which empowered a strong international research network. (1)

Within my four-years ‘experience as a Brazilian advisor to Angolan PhD students, I have had difficulties that involved meeting a relevant research topic to his country, financial support and project management, as well as the responsibility to build and maintain this project.

To address a relevant research topic for Angola and postgraduate program

Several methods were used to collect relevant information, including literature review from the international speech made by the Ministry of Foreign Affairs (MFA) through the Division of Educational Topics (DET) in 2011, candidate application, acceptance letter by UNESP within the Women´s Health postgraduate program, focused on diabetes and pregnancy , as it is the last author and student tutor area .

To complete the course, meeting these co-operation program requirements, any student should take some lectures and develop a research project together with his tutor.

Data were also drawn from the Brazilian Higher Education Personnel Training Coordination (Capes) and from Unesp Pro-Vice-Chancellor for undergraduate and postgraduate studies in documents/ website. http://www.fmb.unesp.br/#!/pos-graduacao

The financial support and project management

This project aimed at better National Health Service in Angola, taking into consideration the maternal health index.

However, there were limitations to manage the project caused by the visa refusal, which did not allow the advisor to come to Angola Huambo Motherhood to supervise the samples´ collection. Then, the patients submitted to cesarean section was excluded of the project since this surgery procedure was made outside the Motherhood.

Firstly, we chose to study Metabolic Syndrome (MetS)/HIV associated, but many challenges were found. Meanwhile, considering the high prevalence of MetS in many African countries and its influence on maternal health and adverse perinatal outcome (2), having MetS as one of the research subject in postgraduate program, led us choose for MetS research project in non-diabetic pregnant women in Angola.

Another challenge faced throughout the project was purchasing the necessary kits for laboratory analysis.

Also, international border challenges sending biological samples from Angola to Brazil, which had a great impact on the decision of the diagnostic criteria to be used in Angolan pregnant women to confirm MetS. Literature review showed the possibility to choose four different criteria for MetS diagnosis, two of them are currently used outside pregnancy and the other two are for pregnancy.

Responsability to build and maintain the next generation of African researchers

The PhD findings could be seen by the advantages of these programs to empower: African researchers, Brazilian advisors, scientific community of Women Reproduction field and strengthening the international research network between Unesp and Angola´s Universities (1,3).

The success of this mixed country PhD research training could be confirmed by two scientific papers published by the research group that was formed in Huambo Motherhood supervised by the PhD student that started after this cooperation. (4,5)

Building the next generation of African researchers has provided innumerous gains, such as the relationship between student and his tutor, as the tutor experienced different practices and conditions than the ones she had known before (6,7).

The four year work between Angolan PhD student and Brazilian tutor has improved the quality of supervision and doctoral education (8), which shows a vital component of the university´s research efforts and contributes significantly to Unesp´s research profile.

The overseas matters funded to be transferred during the course of the project associated with difficulties to send biological samples from Angola to Brazil are hindering aspects of the research development. African scientists need to have greater control over research in their own countries, in order to develop a fruitful research capacity. (9)

After the end of this research, the local conditions of the site for new projects was established; the subject of research be useful not only for individual training, institutional and organizational development, but also for Angola Health System.

Conclusions

In conclusion, this case report carries on the strong Brazilian PhD program for developing countries in terms of human resources development. It is necessary to be linked with local infrastructure in order to strengthening national research systems(3). This competitive fellowship training program offered through bilateral development cooperation is part of global initiatives and Brazilian goals for reducing inequalities among people and represents an effective approach to complement academic degree offerings. Another result of this South to South cooperation is the creation of a network between African (Angola) and Brazil (Unesp) contributing to integrate an African research community from Angola with us. Investments in training more researchers are crucial to enhance regional networks in order to create a synergistic commitment of African and Brazilian researches. With this PhD program, Brazil and its universities are certainly contributing to build the next generation of African researchers.

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Anexos

ANEXOS

Anexo 1 – Parecer do Comitê de Ética da Faculdade de Medicina da Universidade Agostinho Neto – Angola

COMISSÃO DE ÉTICA DA FACULDADE DE MEDICINA DA UNIVERSIDADE AGOSTINHO NETO

DELIBERAÇÃO Nº 1/15

PROJECTO: Síndrome Metabólica em Gestantes e os Efeitos Perinatais em duas Maternidades: No Brasil e Angola. Prevalência da Nova Epidemia no Século XXI

INVESTIGADOR PRINCIPAL: Hamilton dos Prazeres Tavares

ORIENTADORA: Profª. Doutora Marilza Vieira Cunha Rudge, FMB/UNESP - Brasil

CO-ORIENTADORES: Prof. Doutor Joelcio Francisco Abbad FMB/UNESP - Brasil

Prof. Doutor Paulo Adão de Campos, FMUAN - Angola

A Comissão de Ética da Faculdade de Medicina, reunida no dia 20 de Janeiro de 2015, deliberou, de acordo com o Artigo 5º do seu regulamento, que o projecto de investigação acima identificado obedece integralmente aos pressupostos éticos, sendo **APROVADO** por unanimidade.

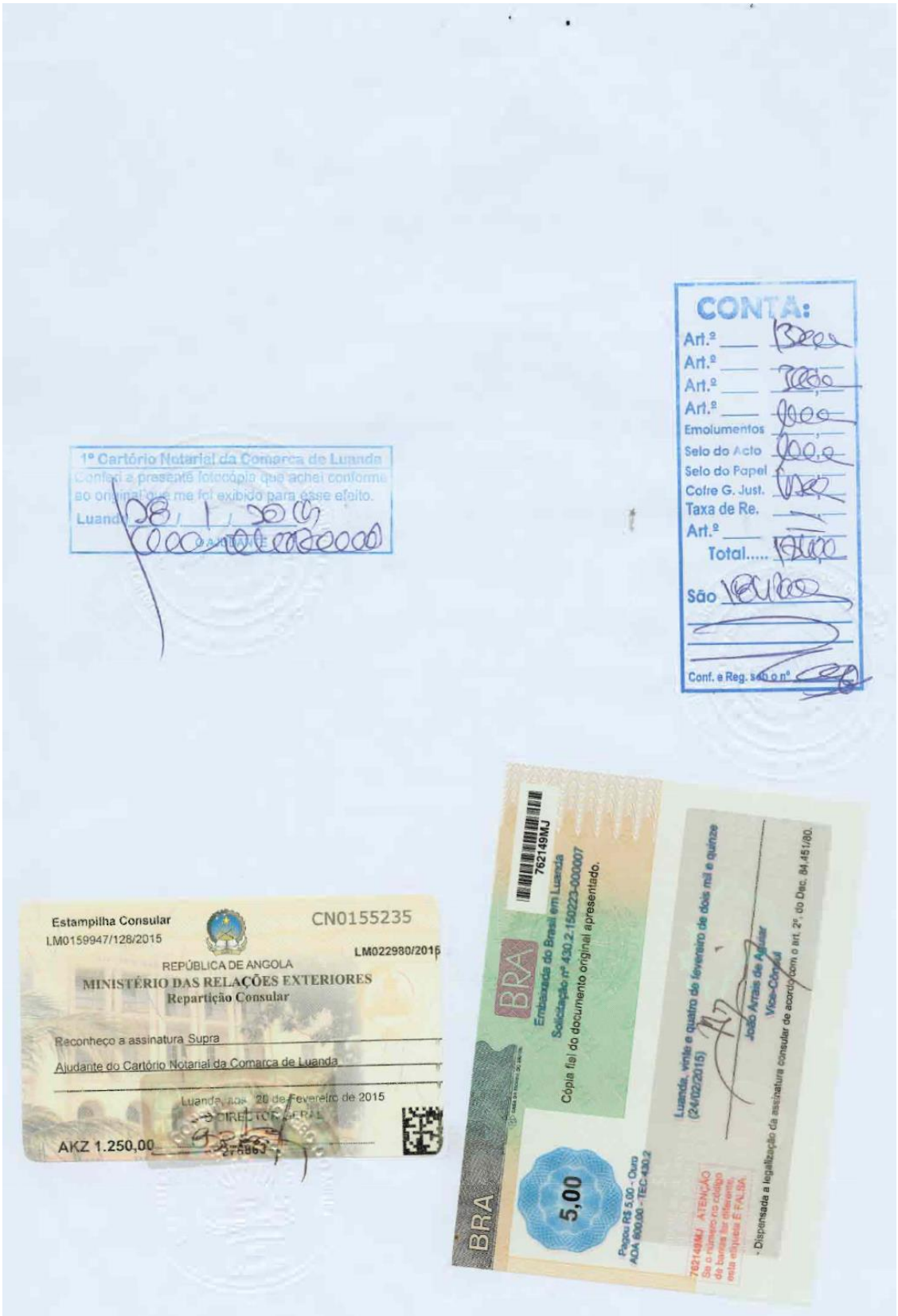
Luanda, 20 de Janeiro de 2015.

A Comissão de Ética

Santos Morais Nicolau, PhD

Joaquim Carlos Vicente Dias Van-Van-Dúnem, MD, MSc, PhD

REPÚBLICA DE ANGOLA Faculdade de Medicina Gab. Director UNIVERSIDADE AGOSTINHO


1º Cartório Notarial da Comarca de Luanda
Confere a presente fotocópia que achei conforme ao original que me foi exibido para esse efeito.
Luanda, 28 / 1 / 2015
O AJUDANTE
CONTA:
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LM022980/2015
REPÚBLICA DE ANGOLA
MINISTÉRIO DAS RELAÇÕES EXTERIORES
Repartição Consular
Reconheço a assinatura Supra
Ajudante do Cartório Notarial da Comarca de Luanda
Luanda, aos 20 de Fevereiro de 2015
DIRECTOR GERAL
AKZ 1.250,00
762149MJ
BRA
Embaixada do Brasil em Luanda
Solicitação nº 430.2.150223-000007
Cópia fiel do documento original apresentado.
Luanda, vinte e quatro de fevereiro de dois mil e quinze
(24/02/2015)
João Arrais de Aguiar
Vice-Cônsul
- Dispensada a legalização da assinatura consular de acordo com o art. 2º, do Dec. 84.451/80.
BRA
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Pagou R$ 5,00 - Ourp
AOA 600,00 - TEC 430.2
762149MJ ATENÇÃO
Se o número no código de barras for diferente, esta etiqueta É FALSA

Anexo 2 – Parecer da Direção do Hospital Geral do Huambo - Angola

V I S T O
O DIRECTOR PROVINCIAL
//FREDERICO JOÃO CARLOS JULIANA//
(Médico Assistente)

Médico Especialista em Ginecologia/Obstetrícia
Ordem Nº 1651

República de Angola
Hospital Regional do Huambo
Direção Geral

Ao
Comité de Ética em Pesquisa da
Faculdade de Medicina de Botucatu
Da Universidade Estadual Paulista,
São Paulo – Brasil

Título: Síndrome Metabólica em Gestantes e os Efeitos Perinatais em Duas Maternidades: No Brasil e Angola. Prevalência da Nova epidemia no Século XXI.

Pesquisador: Hamilton dos Prazeres Tavares, Médico Esp. Em Ginecologia e Obstetrícia. Doutorando em Ginecologia, Obstetrícia e Mastologia pela Faculdade de Medicina de Botucatu, Universidade Estadual Paulista (UNESP). Brasil

Orientadora: Profª Dra. Marilza Vieira Cunha Rudge

Co-Orientadores: Profs. Drs. Joelcio Francisco Abbad e Paulo Adão de Campos.

A Síndrome Metabólica predispõe risco aumentado para o desenvolvimento de complicações Cardiovasculares e metabólicas tardiamente na vida. As gestantes afectadas com esta Sindróme são candidatas potencias a desenvolver patologias durante a gravidez, com repercussão negativa no produto da concepção aumentando os eventos perinatais adversos.

Em conformidade com o disposto pelo ministério da Saúde, mediante consultas pré-natais de qualidade promove-se a maternidade segura e a humanização no atendimento deste grupo especial de pacientes com maior garantia de um binômio, mãe e filho, saudável.

A pesquisa proposta pelo pesquisador enquadra-se dentro dos padrões éticos de investigação em seres humanos e o Conselho Cientifico e Pedagógico do Hospital Regional do Huambo Opta pela **Aprovação** do presente Projeto.

Huambo, aos 16 de Janeiro de 2015

O Director Geral

Dr. Welema Cipriano da Fonseca

Médico Especialista em Cirurgia, Céd. Prof. Nº 1918


Estampilha Consular
M0086398/130/2015
CN0152955
LM018084/2015
REPÚBLICA DE ANGOLA
MINISTÉRIO DAS RELAÇÕES EXTERIORES
Repartição Consular
Certifico e dou fé que este documento é autêntico.
Luanda, aos 10 de Fevereiro de 2015
DIRECTOR GERAL
AKZ 1.500,00
www.caesc.org/public
BRA
762342MJ
Embaixada do Brasil em Luanda
Solicitação nº 410.4.150223-000010
Reconheço verdadeira, por semelhança, a assinatura neste documento de BEATRIZ DE CARVALHO NUNES RODRIGUES - CHEFE DE DEPARTAMENTO, 1ª SECRETARIA, em/no(a) LUANDA - Angola. E, para constar onde convier, mandei passar o presente, que assinei e fiz selar com o selo deste(a) Embaixada.
Luanda, vinte e cinco de fevereiro de dois mil e quinze (25/02/2015)
João Arnaldo de Aguiar
Vice-Cônsul
20,00
Preço: R$ 20,00 - Ouro
AOA 2.400,00 - TEC 410.4
- Dispensada a legalização da assinatura consular de acordo com o art. 2º, do Dec. 84.451/80.

Anexo 3 – Questionário para avaliação da Síndrome metabólica e efeitos adversos perinatais em puérperas assistidas na maternidade do Hospital geral do Huambo

FACULDADE DE MEDICINA DE BOTUCATU (UNESP)
DEPARTAMENTO DE GINECOLOGIA E OBSBTETRÍCIA

Síndrome Metabólica em gestantes e os efeitos perinatais em duas maternidades do Brasil e Angola (África) : prevalência da nova epidemia do século XXI

INSTRUMENTO PARA AVALIAÇÃO DA SÍNDROME METABÓLICA

Nº _____

Nome: _____
Número de registro: _____
Data da colheita _____/_____/_____
Endereço:
Zona urbana ( ) zona sub urbana ( )
Telefone _____
Idade _____
Data da nascimento _____/_____/_____
Raça: Negra ( ) Não Negra ( )
Estado Civil: Solteira ( ), Casada ( ), Marital ( ), Viúva ( ), Divorciada ( ).
Seu Companheiro tem outra (s) Família para além de você? Não ( ), Sim ( )
Nível de escolaridade:
Nunca Estudou ( )
Ensino primário: Completo ( ), Incompleto ( )
Primeiro ciclo: Completo ( ), Incompleto ( )
Segundo ciclo: completo ( ), incompleto ( )
Ensino Universitário: Completo ( ), Incompleto ( )
Pós-graduação: Completa ( ), Incompleta ( )
Natural de: _____
Ocupação/profissão: _____
Funcionaria em empresa Publica ( )
Funcionaria em empresa Privada ( )
Funcionaria autônoma ( )
Vendedora Ambulante ( )
Camponesa ( )
Domestica ( )
Seu trabalho exige esforço físico: sim ( ), não ( )
Peso no momento da admissão: _____
Altura da gestante: _____
Sua mãe teve *Diabetes mellitus* gestacional (DMG) na gravidez?: sim ( ), Não ( ), Não sabe( )
Se sim, fez uso de insulina: sim ( ), Não ( ).
Qual a idade da sua mãe quando você nasceu? _____

Histórico ginecológico e obstétrico

Idade da primeira menstruação (menarca) _____
G ____/ P _____/ A _____, Cesáreas _____
Ciclos menstruais? _____
Já teve diagnóstico prévio de Síndrome do Ovário Poliscístico (SOP) ? _____
Quantos partos? Primípara: ( ), Multíparas ( )
Quantas gestações? Primigesta ( ), Multigesta ( )
Já teve DMG em outras gestações? Sim ( ), Não ( ) se sim quantas vezes?
Fez uso de insulina? Sim ( ), Não ( ), Quantas unidades dias? _____
Abortamentos? Sim ( ), Não ( )
Se sim quantos? _____
Tomou algum medicamento nesta gravidez? Sim ( ), Não ( ), se sim qual (s) _____
Idade na primeira gestação_____
Teve polidramnios Sim ( ), Não ( )
Teve natimortos? Sim ( ), Não ( )
Prematuros? Sim ( ), Não ( ), se sim quantos?_____
Já teve feto com morte intrauterina? Sim ( ), Não ( ), se sim quantos? _____
Teve dificuldade de engravidar? Sim ( ), Não ( )
Teve infecção em gravidez anterior? Sim ( ), Não ( )
Teve alguma infecção na gravidez atual? Sim ( ), Não ( )
Teve vulvovaginites na gravidez atual? Sim ( ), Não ( )
Já teve partos gemelares? Sim ( ), Não ( )
Já teve filho com malformação? SIM ( ), Não ( ).
Se sim, qual tipo? _____
Já teve filhos com problemas respiratórios após o nascimento? Sim ( ), Não ( ), se sim qual? _____
Já teve filhos com hipoglicemia pós-natal? Sim ( ), Não ( )
Já teve filhos com icterícia pós-natal prolongada? Sim ( ), Não ( )
RN com peso igual ou menos que 2500 gramas Sim ( ), Não ( ), se sim quantos? _____
RN com peso igual ou superior a 4000 gramas Sim ( ), Não ( ), se sim quantos? _____
Teve recém nascido que morreu depois do parto? Sim ( ), Não ( ), se sim quantos dias após? _____
Qual foi a causa da morte?_____

Historia da gravidez atual

Fez consultas de pré natal? sim ( ), Não ( ), Se sim quantas? _____, até seis ( ), Menos de seis ( ), Unidade básica ( ), Secundaria ( ), Unidade terciaria ( ), Nome da Unidade: _____, Se não fez consultas, tomou algum medicamento nesta gravidez (Automedicação)? Sim ( ), se sim Natural ( ) de laboratório (sintético) ( ), Não ( ),
DUM_____/_____/_____, Idade gestacional _____
Data provável do parto (DPP)_____/_____/_____
Peso_____

Altura_____
Comprimento das pernas_____

IMC antes de engravidar_____
Peso_____
Altura_____
IMC de 24 – 28 semanas_____
Peso_____
Altura_____
IMC na 36ª. semana_____
Pressão arterial antes da gestação_____
Pressão arterial de 24 – 28ª. semanas de gravidez_____
Pressão arterial na 36a semana _____
Pressão arterial no momento da admissão _____
Altura uterina _____
Circunferência Abdominal _____
Toma algum medicamento para pressão arterial? Sim ( ), Não ( ), se sim qual? _____
Fez algum exame nas consultas de Pré-natal? Sim ( ), Não ( ), se sim qual (is)? _____
Fez exame de HIV nas consultas de pré-natal? Sim ( ), Não ( ), se sim sabe o resultado? Sim ( ), Não ( ). Qual é o resultado? _____
Gostaria de fazer um teste rápido de diagnóstico para HIV? Sim ( ), Não ( ), se sim, Resultado _____

Explicaram a você a importância das consultas de Pré-natal? Sim ( ), Não ( )
Sinais de Parto? Sim ( ), Não ( ), Alimentação? Sim ( ), Não ( )
Aferiram sua pressão arterial? Sim ( ), Não ( )
Foi vacinada na gravidez? Sim ( ), Não ( ).

Dados do Recém nascido

Peso _____
Presença de malformação visível Sim ( ), Não ( ), Se sim qual? _____
Hipoglicemia neonatal Sim ( ), Não ( )
Ictericia neonatal: Sim ( ), Não ( )
Esta com dificuldades de Respirar Sim ( ), Não ( )
O seu bebê está vivo Sim ( ), Não ( ).
Apgar _____

Estilo de vida

Tabagismo? Não ( ), sim ( ), sim quantos cigarros por dia_____, tempo_____
Consumo diário de café_____, Quantas Xicaras (Chávenas) dia? _____
Já teve alterações do colesterol e triglicerídeos? Sim ( ), Não ( )
Se sim a quanto a tempo?_____

Etilismo (Usa bebidas alcoólicas) ?_____Há quanto tempo?_____quanto ao dia?_____
Pratica algum exercício físico pré consulta: _____
Pratica exercício físico pós consulta: _____

Histórico Familiar

Tem algum familiar diabético? Não ( ), Sim ( ), Não sabe ( ).
Pai ( ), Avó Paterno ( ), Avó Paterno ( ).
Mãe ( ), Avô Materno ( ), Avó materna ( ).
Irmão ( ), Tio Paterno ( ), Tio Materno ( ).
Irmã ( ), Tia Paterna ( ), Tia Materna ( ).
Outros_____
Fazem ou fizeram uso de insulina? Sim ( ), Não ( )
Tem casos de obesidade na família? Sim ( ), Não ( ), se sim quem?_____
Tem casos de Hipertensão arterial na família? Sim ( ), Não ( ), se sim quem? _____ , Não sabe ( ).
Tem caso de dislipidemias na família? Sim ( ), Não ( ), se sim quem?_____ Não sabe ( ).

Exames Solicitados durante a Gravidez Atual

Glicemia em jejum_____
HbA1c_____
Colesterol Total_____
LDL_____
LDH _____
VLDL_____
Triglicerídeos _____
Outros exames
Dosagem insulina_____
HIV 1 -2 _____
Ureia _____
Creatinina_____
Urina do tipo 1 _____
Urina do tipo II _____
Hemoglobina_____
Hematocrito_____
VDRL _____
Pesquisa de Plasmodium _____

Doutorando: Hamilton dos Prazeres Tavares
Orientadora: Professora Titular Marilza Vieira Cunha Rudge
Co-Orientadores: Prof. Dr. Joelcio Francisco Abbade
Prof. Dr. Paulo Adão de Campos

Equipe de pesquisa: _____

Anexo 4 – Termo de Consentimento livre e esclarecido

Termo de Consentimento Livre e Esclarecido –TCLE

Convidamos a Sra _____, Portadora do BI nº _____
para participar do estudo intitulado: **Síndrome Metabólica em gestantes e os efeitos perinatais em duas maternidades do Brasil e Angola (África) : prevalência da nova epidemia do século XXI.**

O objetivo é verificar se a senhora tem uma doença chamada Síndrome Metabólica que pode trazer grandes consequências para a senhora e para o seu filho. Essa doença que é a presença de diabetes, (teor de açucar alto no sangue, excesso de peso, pressão arterial alta, e alguns exames laboratoriais alterados) pode ser prevenida e tratada, se o diagnostico for feito precocemente. O estudo terá as seguintes etapas:

1 – Em primeiro lugar, antes de participar do estudo, a senhora será avaliada pelo médico que pedirá alguns exames de sangue e urina e, se houver alguma alteração, será comunicada e encaminhada para tratamento adequado.

2 – O estudo irá verificar e, se necessário tratar as complicações da doença (síndrome metabólica) na sua gestação e prevenir os efeitos dela no seu filho(a).

3 – Haverá necessidade de colher aproximadamente 50 ml de sangue de uma das veias do seu braço. Esse procedimento tem risco baixo podendo deixar um hematoma (mancha roxa) no local. Durante a minha permanência no local da colheita de sangue, receberá todos os cuidados para o seu conforto e o médico responsável fará o acompanhamento dos exames.

4 – No seu sangue iremos verificar quanto tem de glicose, colesterol e frações, triglicerídeos, HbA1c, HB e marcadores da doença chamada Síndrome Metabólica.

5 – Na urina iremos dosar a quantidade de proteínas, ureia e creatinina.

6 – Não haverá administração de nenhum medicamento.

Declaro que fui esclarecida sobre todas as etapas do estudo e sobre o que ocorrerá antes, durante e depois do estudo.

Não haverá benefícios imediatos pela minha participação no estudo. Os resultados poderão beneficiar futuras gestantes que tenham precocemente determinados valores alterados para as dosagens no sangue e na urina.

A sua participação no estudo poderá ser suspensa no momento em que a senhora desejar sem que isso implique em qualquer penalização para a sua pessoa. Tenho ciência que continuarei a ser atendida por esta instituição mesmo me recusando a participar do estudo. Os dados da minha ficha clínica serão mantidos em sigilo absoluto sem identificação da minha pessoa.

Declaro que li e fui esclarecida de todas as etapas do estudo, dos riscos e prováveis benefícios da pesquisas e dos meus direitos, portanto assino este termo de consentimento para o estudo que será feito em duas vias. Uma ficará em meu poder e outra na do médico responsável. Em caso de dúvida poderei procurar o representante da pesquisa pelos telefones: 912 248178, 946 891060 e 926 164334, o CEP da FMB/UNESP no telefone: 55 14 3811 6143.

Paciente: Nome e assinatura _____

Representante no caso de menor de 18 anos: Nome e assinatura _____

Pesquisador: Nome, assinatura e telefone para contato _____

Huambo, aos _____, de _____, 20_____

Anexo 5 – Comprovante do envio do artigo 1 para OJEMD

Scientific Research

Open Journal of Endocrine and Metabolic Diseases

Submission Certificate

August 21, 2015

Dear Dr. Hamilton dos Prazeres Tavares,

Thanks for your contribution to **OJEMD** (Open Journal of Endocrine and Metabolic Diseases).

This is to clarify that the following paper:

ID: 1980180

Title: Metabolic syndrome: Consensus and Controversy. State of the art
Authors: Hamilton dos Prazeres Tavares, Rafael Bottaro Gelaleti, Iracema de Mattos Paranhos Calderon, Marilza Vieira Cunha Rudge

has been submitted to OJEMD on August 21, 2015.

If you have any questions, please feel free to contact us.

Best Regards

Alline Xiao
OJEMD Editorial Board
ojemd@scirp.org
http://www.scirp.org/journal/ojemd

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Anexo 6 – Comprovante do envio do artigo 2 para OJOG

Scientific Research

Open Journal of Obstetrics and Gynecology

Submission Certificate

August 19, 2015

Dear Dr. Hamilton dos Prazeres Tavares,

Thanks for your contribution to **OJOG** (Open Journal of Obstetrics and Gynecology).

This is to clarify that the following paper:

ID: 1431006

Title: Metabolic Syndrome and Pregnancy
Authors: Hamilton dos Prazeres Tavares, Mariana Alvarez Arantes, Suelma Beatriz, Marques Prata Tavares, Joelcio Francisco Abbade, Débora Cristina Damasceno Meirelles dos Santos, Iracema de Mattos Paranhos Calderon, Marilza Vieira Cunha Rudge

has been submitted to OJOG on August 18, 2015.

If you have any questions, please feel free to contact us.

Best Regards

Alline Xiao
OJOG Editorial Board
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http://www.scirp.org/journal/ojog

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Anexo 7 – Comprovante do envio do artigo 4 para Bulltein OMS

MS ID#: BLT/2015/163220
MS TITLE: Building the next generation of African Health researchers in Africa with Brazilian Government and University co-operation - a case report

Dear Hamilton dos Prazeres Tavares,

The file(s) for manuscript BLT/2015/163220 (uploaded by yourself or the Bulletin Editorial Office) has/have been successfully converted to PDF format on the Bulletin on-line submission system.

PLEASE NOTE: that Hamilton dos Prazeres Tavares, as corresponding author, you must now check and approve the converted manuscript.

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Bulletin of the World Health Organization

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Your manuscript has been given the ID BLT/2015/163220. Please use this to refer to your manuscript in any communications.

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