

REVIEW

Metabolic and infectious pathologies in Brazilian medical literature: a review

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OBJECTIVE: This review of original reports on metabolic and infectious diseases that were recently published in Brazilian journals is designed to inform the readership of CLINICS about their content.

METHODS: I conducted a search in PubMed for original research articles (clinical or basic research) recently published (2008–2009) by Brazilian medical and biological periodicals. Papers on metabolic pathologies were retrieved by searching for appropriate keywords such as metabolic syndrome and obesity. Papers on infectious disease were obtained by entering 15 different keywords for the most commonly occurring pathologies. Review articles, editorials, letters to the editor, and case reports were manually excluded. Selected titles were then categorized into appropriate sub-categories.

RESULTS: This search produced a total of 123 articles, which filtered down to 72 articles after eliminating editorials, review articles, letters to the Editor and case reports. Reviewed periodicals were *Arquivos Brasileiros de Cardiologia*, *Arquivos Brasileiros de Endocrinologia e Metabologia*, *Brazilian Journal of Biological and Medical Research*, *Brazilian Journal of Infectious Diseases*, *Jornal de Pediatria*, *Jornal de Pneumologia*, *Revista da Associação Médica Brasileira*, *Revista da Escola de Enfermagem da Universidade de São Paulo*, and *São Paulo Medical Journal*. The articles were then briefly summarized.

KEYWORDS: Metabolic syndrome; Obesity; Brazilian periodicals.

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INTRODUCTION

This review of original reports on recently published metabolic and infectious diseases in Brazilian journals is designed to alert the readership of CLINICS about such reports. As of August 2010, an e-book of each new issue will be made freely available through our site at www.clinics.org.br. Over the next 18 months, we expect to compile e-books dating back to the first issue of CLINICS published in February 2005. In this sense we hope to effectively highlight the production of other Brazilian Medical Periodicals.

METHODS

I conducted a PubMed search for recently published papers (2008–2009) in a nine Brazilian journals which were the most likely sources of original articles on the reviewed subjects. The product of this search was then filtered to eliminate case reports, editorials, letters to the editor, and review articles. Papers on metabolic pathologies were searched for using the keywords “metabolic syndrome” and “obesity” in the abstract. Papers on infectious pathologies

were retrieved with the keywords “AIDS,” “HIV,” “hepatitis,” “pneumonia,” “meningitis,” “staphylococcus,” “streptococcus,” and “syphilis.” The following journals were found using this procedure: *Arquivos Brasileiros de Cardiologia*, *Arquivos Brasileiros de Endocrinologia e Metabologia*, *Brazilian Journal of Biological and Medical Research*, *Journal of Infectious Diseases*, *Jornal de Pediatria*, *Jornal de Pneumologia*, *Revista da Associação Médica Brasileira*, *Revista da Escola de Enfermagem da Universidade de São Paulo*, and *São Paulo Medical Journal*. A grand total of 123 articles were retrieved, leaving 72 after the filtering procedure.

Original research on metabolic pathologies

Diabetes and insulin resistance. As might be expected, diabetes and insulin are the major subjects in these papers. Type 1 Diabetes is analyzed in three papers, while Type 2 Diabetes is the subject of nine articles. Santos et al.¹ evaluated the frequency of metabolic syndrome among adults with type 1 diabetes mellitus according to the criteria of the International Diabetes Federation, the National Cholesterol Education Program, and the World Health Organization and concluded that the latter set of criteria may be preferable in identifying patients in this group, because of better sensitivity. Rollim et al.² prospectively evaluated the efficacy and safety of using insulin glargine to metabolically control type 1 diabetes mellitus in children younger than eight years old and concluded that it was as

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efficacious as Neutral Protamine Hagedorn commonly referred to as NPH but presented a better safety profile, as disclosed by the lower incidence of nocturnal and severe hypoglycemic episodes. **Xavier et al.**³ described the periodontal status of children and adolescents with type 1 diabetes mellitus and concluded that the duration of diabetes and poor glycemic control were significantly associated with periodontal disturbances, suggesting a higher susceptibility of this population in developing probing depth. **Panarotto et al.**⁴ compared the treatment of type 2 diabetic patients from a private clinic with that of patients who were cared for by a public health service and found that the initial A1c and the frequency of visits have a greater impact on the control of diabetes than the place where the patients are treated. **Geloneze et al.**,⁵ **Madeira et al.**,⁶ and **Mendes et al.**⁷ discussed insulin resistance and pancreatic beta cell function and the use of the homeostatic model assessments HOMA1-IR and HOMA2-IR as quantifiers thereof. **Ferreira et al.**⁸ described the epidemiological characteristics of diabetic patients treated in the public health system and suggested that the socio-demographic and clinical characteristics detected in these patients can lead to the proper management and prevention of diabetes in primary health care. **Silva et al.**⁹ described the impact of abdominal fat and insulin resistance on arterial hypertension in non-obese women and concluded that arterial hypertension is associated with insulin resistance, central fat distribution, and higher leptin levels. **Vasques et al.**¹⁰ studied the ability of anthropometric and body composition indicators to predict insulin resistance and found that the anthropometric indicators of central obesity, waist perimeter, and sagittal abdominal diameter show a greater ability to identify insulin resistance in men. Authors indicate that studies in women and elderly people are needed to find the best cut-off points for the entire population. **Caldas et al.**¹¹ described the relationship between insulin and hypogonadism in men with metabolic syndrome and concluded that hypogonadism was associated with insulin resistance and may be a marker of metabolic abnormalities. **Ferreira et al.**¹² described the effects of metformin on blood pressure and glucose metabolism in monosodium glutamate-induced obese, spontaneously hypertensive rats. They also emphasized the role of hepatic insulin resistance on metabolic syndrome and pointed out that beneficial cardiovascular effects and improved insulin sensitivity were observed.

Hormones and signaling. Leptin and adiponectin are highlighted in four papers. **Da-Paz-Filho et al.**¹³ described a decrease in leptin production by adipose tissue in obesity associated with severe metabolic syndrome, suggesting a state of relative leptin deficiency in obesity that is associated with advanced stages of the syndrome. **Hinuy et al.**¹⁴ showed that the polymorphism G2548A in the leptin promoter is associated with increased plasma leptin and body mass index scores in Brazilian women and that it has an important role in regulating plasma leptin levels and body mass index in this population. As mentioned above, **Silva et al.**⁹ showed the impact of abdominal fat and insulin resistance on arterial hypertension in non-obese women and its relation to higher leptin levels. **Geloneze et al.**¹⁵ assessed the relationship between adiponectin and metabolic parameters in severely obese women during surgically induced weight loss and concluded that improvements in insulin resistance and adiponectin levels were related to the

surgically induced weight loss, suggesting an important role of adiponectin in HDL-cholesterol regulation.

Other papers on signaling include a report by **Piccoli et al.**,¹⁶ who performed a case-control study analyzing the association between the 894G>T endothelial nitric oxide synthase gene polymorphism (NOS3) and MS in 616 subjects and found that 894G>T plays a significant role in the mechanistic interaction between metabolic risks such as hypertension and MS, although sex-related differences may exist. **Cercato et al.**¹⁷ studied the N363S polymorphism in the glucocorticoid receptor gene and concluded that its prevalence is low in the Brazilian population; though rare, its presence may contribute to the worsening of the individuals' metabolic profiles. **Madeira et al.**¹⁸ described the impact of obesity on metabolic syndrome components and adipokines in prepubertal children, providing evidence of the influence of obesity on metabolic syndrome components and on adipokine levels in prepubertal children, which in turn indicates that these components may contribute to the onset of cardiovascular diseases.

The interaction of metabolic syndrome with the female reproductive life cycle is discussed in five papers highlighted here: **Buzzinaro et al.**¹⁹ reported on the incidence of high body mass index scores in adolescent offspring among the children of mothers with hyperglycemia during pregnancy, adding that such patients should be followed from childhood. **Rivera et al.**²⁰ evaluated the association between pubertal gynecomastia and body mass index and concluded that a significant correlation occurs between pubertal gynecomastia and a higher body mass index in adult life. **Bonganha et al.**²¹ evaluated the relationship between resting metabolic rate and the body composition of postmenopausal women and concluded that body composition correlates with lean mass and waist circumference. **Tavares et al.**²² studied the effects of physical activity on gestational weight gain and birth weight of pregnant women in Campina Grande, northeast of Brazil, and found that all the pregnant women were sedentary in the third trimester and that there was a significant association between physical activity patterns and gestational weight gain in the second trimester but that there was no association between this pattern and birth weight. **Balen et al.**²³ reported on a murine model of protein restriction in pregnant and non-pregnant rats and concluded that protein restriction in pregnancy modified maternal metabolism, altering lipid synthesis in the liver and hormonal profiles and decreasing the placental and fetal masses.

Epidemiological and other studies. **Silva et al.**²⁴ compared the prevalence of a high body mass index (BMI) and central adiposity in a sample of 287 adult subjects in a rural community of the state of Minas Gerais, Brazil. High BMI was found in 24.8% of the population (37.4% of females; 11.5% of males). Central adiposity was associated with higher total cholesterol, LDL, triglycerides, fasting glucose, lower HDL, arterial hypertension, dyslipidemia, and hyperglycemia. A similar study by **Vedana et al.**²⁵ arrived at comparable conclusions for the extreme south of Brazil. These results confirmed the potential effect of body composition shifting, especially at the abdominal level and on lipids, glucose metabolism, and blood pressure levels in rural populations. **Coltro et al.**²⁶ evaluated cardiovascular risk factors in a population attending a community event on health education and found a significant association between obesity, dyslipidemia, and arterial hypertension,

emphasizing the need for educational programs to promote primary prevention, mainly for the elderly and overweight. Metabolic syndrome was also identified as a risk factor for arterial hypertension by **Nascente et al.**²⁷ in a small Brazilian city. **Fernandes et al.**²⁸ examined risk factors for obese adolescents. Excessive weight was associated with the male gender, studying in a private school, and mothers with higher education levels, revealing a need to implement initiatives to fight obesity in the school environment and reach the whole family structure while taking gender-related specificities into consideration. On the whole, these studies show that obesity is spreading from big cities into smaller towns and the rural areas of the country. In contrast, **Coutinho et al.**²⁹ found that risk factors associated with low birth weight included extremes of reproductive age, poor education, low maternal weight, smoking beyond the fourth month of pregnancy, previous cesarean section, an interdelivery interval <24 months or >37 months, a maternal history of hypertension, cardiopathy, premature delivery, few (<5) prenatal visits, initiation of prenatal care late in the pregnancy (after the 3rd month), premature rupture of membranes, increased blood pressure, infectious diseases, and hemorrhages during the current pregnancy; however, maternal obesity was a protective factor. Finally, two studies found that the progressive intermingling of Brazilians of Japanese origin with other cultures led to an increased incidence of metabolic syndrome in the resulting offspring.^{30,31} **Haun et al.**³² compared the waist-height ratio in a population of 968 inhabitants of the city of Salvador, Brazil with a number of other indicators and found that indicators of abdominal obesity are better for discriminating coronary risk than body mass index. Two separate studies noted the effects of physical activity or inactivity on metabolic syndrome.^{33,34} **Santos et al.**³⁵ described associations between weight loss, bone mass, body composition, and dietary intake of post-pubertal obese adolescents. **Prado et al.**³⁶ described the effects of long-term multidisciplinary inpatient therapy (reduced energy intake, dietetic education, physical exercises and psychological therapy) on the body composition of 728 extremely obese adolescents, showing that such a procedure allows a significant reduction in severe obesity; normal growth was preserved and the percentage of fat-free mass. **Fernandes et al.**³⁷ evaluated the effect of nutritional education on the prevalence of high BMI/obesity and foods eaten at primary schools and found that despite its short duration, there were improvements in the quality of the food the schoolchildren who attended the course were eating. **Abulnaja**³⁸ described an association between obesity and acne in Arabian adolescents.

Diehl et al.³⁹ described an interesting association between lipodystrophy and AIDS/HIV. **Serpa Neto et al.**⁴⁰ compared waist-height ratio to other indicators of obesity as predictors of high coronary risk. **Volterra et al.**⁴¹ described the effects of neuroendocrine obesity induction on systemic hemodynamics and left ventricular function in normotensive rats. **Orpheu et al.**⁴² detected a time dependent increase in the demand for body contour surgery in massive weight loss patients from pretreatment through bariatric surgery and subsequently over a three-year follow up. **Kurebayashi et al.**⁴³ analyzed nurses' perceptions about diseases that are treated by acupuncture and found that it was used to treat obesity among other morbid situations.

Diagnosis. **Rech et al.**⁴⁴ carried out a validation study for the use of bioelectric impedance to measure fat-free body mass. **Rodrigues et al.**⁴⁵ analyzed resting metabolic rate by indirect calorimetry in obese patients and found that a tendency towards underestimation of self-reported caloric intake exists among obese women and that the failure to lose weight in some patients can be due to their low level of physical activity. **Chaves et al.**⁴⁶ used abdominal ultrasound and magnetic resonance imaging to evaluate non-alcoholic fatty liver disease diagnoses in morbidly obese patients and found significant agreement between the ultrasound method and the hepatic biopsy, which indicates a need to implement and perform more research on the use of ultrasound and to validate these methods. Reliance of such procedures could minimize the need to perform biopsies to detect and diagnose such diseases.

Original research on infectious diseases

As might be expected, the pandemic of HIV/AIDS is the most frequently studied pathology in this chapter. Articles fall into various categories, with some articles falling into more than one category.

Epidemiology. **Bassichetto et al.**⁴⁷ estimated the incidence of HIV-1 in the city of São Paulo from November 2000 to April 2001, comparing epidemiological and socio-behavioral data of recently infected individuals with those individuals with long-standing infection. A less sensitive than standard ELISA was employed to identify recent infection. The overall incidence of HIV-1 infection was 0.53%/year, whereas overall HIV-1 prevalence was 3.2% higher among males vs females. Recent infections accounted for 15% of the total infected population and correlated with being younger and male. **Szwarcwald et al.**⁴⁸ described a methodological proposal based on secondary data and the main results of the HIV-Sentinel Study among childbearing women, which was carried out in Brazil during 2006. A probabilistic sample of childbearing women was selected in two stages. In the first stage, 150 health establishments were selected, stratified by municipality size, whereas in the second stage, 100–120 women were selected systematically. Significant differences were found according to race, educational level, and municipality size. The proposed methodology is described as low-cost and easy to apply and permits the identification of problems in routine service provision in addition to monitoring compliance with Ministry of Health recommendations for pre-natal care. **Almeida et al.**⁴⁹ evaluated genotyping and subtyping in antiretroviral-naïve and experienced children and used this information to analyze drug resistance profiles, concluding that rates of primary resistance in antiretroviral-naïve children are low, whereas they are high in children who fail antiretroviral treatment, which is compatible with its use in these patients. **Olajubu et al.**⁵⁰ described the seroprevalence of HIV among blood donors, antenatal women, and other patients in a tertiary hospital in Nigeria and found that though there is a high prevalence rate among in- and out-patients, many of these patients were screened based on manifestations of clinical symptoms. The prevalence of comorbidities is discussed several papers: **Diehl et al.**³⁹ discussed the simultaneous occurrence of lipodystrophy; **Bachur et al.**⁵¹ and **Neto et al.**⁵² described enteric parasitism relating to highly active antiretroviral therapy; **Carvalho et al.**⁵³ evaluated factors related to the development of tuberculosis in HIV-infected patients in

Fortaleza, Ceara, Brazil and discussed strategies to improve the control of tuberculosis in HIV-infected patients; and **Cavasin et al.**⁵⁴ described the incidence of xerostomia, dental caries, and periodontal disease in HIV+ patients.

Risk factors. Two papers cover this subject. **Hofer et al.**⁵⁵ described factors from the neonatal period associated with long-term non-progression of HIV in a Brazilian cohort of vertically infected children; **Mercon et al.**⁵⁶ examined a cross section of HIV-infected patients in Rio de Janeiro and found that risk-based assessment does not distinguish between recent and chronic HIV-1 infection.

Comorbidities are an important aspect of HIV, and we have reports of HIV in association with tuberculosis (Carvalho et al,⁵³ with enteric parasites (Bachur et al, and Neto et al),^{51,52} with lipodistrophy (Monnerast et al),⁵⁷ and cervical intraepithelial neoplasia (Russomano et al).⁵⁸

Perception of HIV by patients is discussed by **Silva et al.**⁵⁹ who researched the perception of female vulnerability to infection among university students in Rio de Janeiro and found that the interviewed women recognize vulnerability factors in other women and realize the risk that others face of acquiring HIV but do not consider themselves to be at risk. **Almeida et al.**⁶⁰ evaluated the knowledge of HIV/AIDS patients concerning antiretroviral drugs and found a lack of general information among users of antiretroviral drugs, and at the same time a need for a better understanding of the problems. They emphasize the need for all health care professionals involved with patients to supply information on prescribed drugs as an ethical component of the treatment that favors and fosters adherence.

Hepatitis

Hepatitis is a frequent occurrence in recent Brazilian medical literature. **Fonseca et al.**⁶¹ developed a Markov model to mirror the natural disease history in cohorts of patients with hepatitis C virus who received peginterferon alpha-2b with ribavirin or interferon alpha-2b and ribavirin treatment for 48 or 24 weeks, according to their viral genotype and liver histology; they concluded that peginterferon alpha-2b with ribavirin is a cost-effective therapy for treating naïve chronic hepatitis C adult patients compared to the interferon alpha-2b and ribavirin regime, regardless of the viral genotype. **Santos et al.**⁶² described fulminant hepatic failure in eight adults and children from a public hospital in Rio de Janeiro, Brazil caused by hepatitis B and one case of severe acute hepatitis caused by hepatitis A. **Veras et al.**⁶³ described the prevalence of chronic hepatitis C virus in the state of Piauí in northeastern Brazil; **Zahdi et al.**⁶⁴ examined the costs and benefits of preventing the disease by utilizing the vaccine for hepatitis A in the southern Brazilian state of Parana. **Schulz et al.**⁶⁵ described the results of cerebral magnetic resonance spectroscopy in patients with hepatic encephalopathy with analysis before and after liver transplantation.

Pneumonia. The prevalence of ventilator-associated pneumonia was studied by **Rodrigues et al.**⁶⁶ in a database of 233 patients on mechanical ventilation, and the investigators concluded that a high incidence of infection with resistant bacteria and inappropriate initial antibiotic therapy with long time on mechanical ventilation and prior use of antibiotics are risk factors for the onset of pneumonia. This study should be analyzed in conjunction with the study by **Fortaleza et al.**,⁶⁷ who described age,

central nervous diseases, and the use of antacids as risk factors for hospital-acquired pneumonia in non-ventilated adults. **Serefhanoglu et al.**⁶⁸ described a prospective case-control study (October 2003 to June 2007) that evaluated risk factors for multidrug resistance among extended-spectrum-β-lactamase-producing *Escherichia coli* and *Klebsiella* spp. (ESBL-EK) isolates in blood cultures. The study included all adult patients (>18 years old) whose blood cultures grew ESBL-EK during the study period and showed that the rate of multidrug resistance among ESBL-EK bloodstream isolates was high and that the duration of hospitalization before bacteremia was the only independent risk factor for the multiple drug resistant ESBL-EK bloodstream infections. **Mukai et al.**⁶⁹ performed a spatial analysis of hospitalizations for pneumonia in the Vale do Paraíba region of Brazil that determined spatial autocorrelations and identified cities in which interventions are necessary regarding the number of hospitalizations for pneumonia in infants under one year of age. **Lopes et al.**⁷⁰ studied the immunization of 139 mothers with pneumococcal capsular polysaccharide vaccine during pregnancy randomly allocated to receive/not receive 23-valent polysaccharide vaccines during or after pregnancy. Their offspring were monitored monthly over the first 6 months of life, and the results showed that providing the mother with a polysaccharide vaccination during pregnancy did not decrease pneumococcal colonization.

Staphylococcus infections are the object of three papers. **Shrestha et al.**⁷¹ described the nasal carriage of *Staphylococcus aureus* among health care workers in a Nepal hospital. **Cury et al.**⁷² studied 151 methicillin-resistant (MRSA) strains isolated from patients admitted to tertiary care hospitals in two metropolitan areas (Campinas City and Ribeirão Preto) in the southeast of Brazil through PCR-based techniques and found that the variability among such strains is larger than previously reported, indicating that the techniques used by these authors can be an alternative to pulsed-field gel electrophoresis.

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