Auscultatory Changes Identified through Digital Stethoscope and Echocardiographic Findings Associated with Healthy Pregnancy

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Abstract: The hyperkinetic hemodynamic pattern and the low viscosity of the blood are typical during pregnancy and cause a number of auscultatory changes. The main goal of this study was to describe hemodynamic and auscultatory changes in normal pregnant women and compare them to those of non-pregnant women. Digital heart auscultation and Doppler echocardiography tests were performed in 29 pregnant and 27 non-pregnant women, both healthy. Changes in the digital stethoscope auscultation and Doppler echocardiographic findings were compared between the groups. The low-intensity systolic murmur was statistically more frequent in the pregnant group (69.0% x 40.7%, p=0.034), as well as B1 Hyperphonesis (51.7% x 7.4%, p<0.001), B2 Hyperphonesis (69% x 18.5%, p<0.001) and B1 Split (89.7% x 29.6%, p<0.001). In pregnant women, no associations were found between auscultation findings and Doppler echocardiogram changes (mitral-murmur x mitral-regurgitation, p=0.675; tricuspid-murmur x tricuspid-regurgitation, p=1.000; pulmonary-murmur x pulmonary-regurgitation, p=1.000). The digital heart auscultation of healthy pregnant subjects was able to detect frequent and numerous alterations, confirming the importance of knowing the physiological changes of pregnancy. The normal Doppler echocardiogram in all healthy pregnant women with heart murmur indicates that such test has limited applicability for healthy pregnant subjects, only in cases of suspicion of a heart disease or when it does occur.

1 INTRODUCTION

1.1 The Importance of Tracking and Diagnosing Heart Diseases during Pregnancy

Maternal mortality rates are some of the most critical indicators of quality of life for the population of any given country, while mainly reflecting on the quality of health care provided to prenatal pregnant women. (Cardoso, 2012) Heart disease is universally considered the main cause of indirect maternal deaths in the pregnancy-puerperal cycle (Reidy and Russell, 2011); (Huisman et al., 2013); (Cantwell, 2011). More specifically in Brazil (Saúde., 2006), failure to eradicate rheumatic disorders contributes to high incidence of heart disease during pregnancy - reference centers estimate that up to 4.2% of pregnant patients are affected, eight times more when compared to international estimates (Tedoldi, 2009).

Early diagnosis of heart disease during pregnancy depends a great deal on the understanding of adaptive physiological alterations during pregnancy. That assessment is part of the routine in prenatal care, whose main actions focus on establishing the distinction between adaptive physiological processes and pathological conditions associated to pregnancy. In that context, it is known

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that the common signs and symptoms in regular pregnancy may simulate those of heart diseases and, on the other hand, diagnosing these diseases may become difficult due to the several transitory and adaptive physiological hemodynamic changes during pregnancy (van Mook, 2005).

Heart auscultation is a highly important clinical tool in diagnosing heart disease (Chizner, 2002); (Chizner, 2008). In pregnant patients, it can allow for the early detection of maternal heart disease, as well as timely interventions that can prevent these conditions to evolve during the pregnancy, partum and postpartum periods. However, this detection is still a challenge for professionals that work directly in prenatal health care. It is estimated that internal medicine and family practice physicians were able to recognize only 20% of the most common heart sounds and murmurs that could be diagnosed using a stethoscope (Mangione, 1997).

Instruments that allow for better quality in heart auscultation, analyzing and classifying sounds with resources that enhance the human hearing capacity and at the same time make it easier to detect normal and abnormal heart sounds, are a great asset to tracking and diagnosing maternal heart diseases.

1.2 The Origin and Meaning of Heart Sounds

The vibrations generated by the heart and the great vessels travel to the surface of the human body. The sounds and murmurs produced in the cardiovascular system correspond to sound phenomena with specific characteristics of intensity (loudness), frequency (pitch) and quality (timbre). Most sounds relevant to the heart auscultation process are below the 20-500 Hz frequency, a range with a relatively high audibility threshold (Pazin-Filho, 2004).

The origin of human heart sounds is attributed to a set of hemodynamic changes that occur during the cardiac cycle. A rhythmic sequence of pressure variation in the heart chambers, propelled by myocardium contractions, makes the heart valves move (Hanifin, 2010).

The first heart tone (B1) features two main sound components, originated at the atrioventricular valves: the first one is comprised of intense high-frequency vibrations caused by the closure of the mitral valves (M1); while the second one, is also comprised of high-frequency vibrations caused by the closure of the tricuspid valve (T1), which takes place 30 ms later on average. The second tone (B2) reflects the blocking of the semilunar aortic (A2) and pulmonary (P2) valves. Most normal individuals produce a sole sound during expiration, while during inspiration it is possible to observe its physiological splitting (Pazin-Filho, 2004).

It is critical to identify and characterize B1 and B2 in the auscultatory process, since they define the cardiac cycle intervals: the ventricular systole interval and the beginning of ventricular diastole, respectively. The systolic interval is shorter than the diastolic one, but the difference becomes less noticeable as the cardiac frequency is elevated. (Hanifin, 2010) The first tone is more intense in the apex and the lower-left sternal border, while the second tone tends to be more prominent at the base. (Chizner, 2008)

Heart murmurs are the set of much longer vibrations that arise when the blood changes its flow standard and becomes turbulent (Hanifin, 2010). Turbulence may occur as a result of an excessive increase in blood flow speed in relation to the dimensions of the structures through which it runs (Shaver et al., 1985).

Changes of sound intensity in B1 and B2, the occurrence of B3 and B4, noise, murmurs, clicks, gallops, place of auscultation and radiation, the starting point of the cardiac cycle, are all sound variations used in cardiac semiology to diagnose cardiovascular diseases (Chizner, 2002).

1.3 The Role of the Stethoscope

The stethoscope is an instrument designed for capturing and conducting vibrations from the heart and vascular structures that reach the surface of the chest and the hearing device of the examiner, reducing environment noise and helping to diagnose several heart diseases. (Segall, 1963); (Kindig and OBJ, 1982); (Kindig, 1982). The stethoscope is relatively inexpensive and widely available, and it still remains a qualitative and subjective method of evaluating heart sounds, murmurs and other cardiac noises. (Zuhlke et al., 2012)

More recently, electronic stethoscopes have become available, equipped with sound amplification and environment noise reduction technology, featuring display, recording, storage and reproduction of these sounds, as well as transmission capacity (Hedayioglu et al., 2007); (Tavel, 2010); (Tavel, 2006).

The signs captured electronically through this digital auscultation system may be submitted to objective numeric and visual analysis, transmitted to local remote places or stored in medical records (Dahl et al., 2002). Analysis of signs constitutes a promise that may contribute to clinical application,

as in the assessment of aortic stenosis and the classification of physiological murmurs (Tavel and Katz, 2005). Its real importance and advantages in comparison to traditional stethoscopes are still to be determined; however, digital heart auscultation may potentially tackle current challenges in teaching heart auscultation.

1.4 Maternal Heart Auscultation and Physiological Changes of Pregnancy

The profound cardiovascular adaptive changes that pregnant women undergo may seriously affect heart auscultation (Hanifin, 2010). The hyperkinetic hemodynamic state and low blood viscosity are characteristic to pregnancy and favor the occurrence of low-intensity systolic murmurs in over 95% of pregnant women (Teixeira, 2010). On the other hand, a similar situation may be observed in other hyperkinetic conditions such as fever, anemia, exercise, excitement and hyperthyroidism. In healthy pregnancies, a low murmur intensity (1- 2/6 in the Levine scale) is frequently observed in the beginning or the middle of the systole, increasing-decreasing, many times with a musical, vibrating or rumbling quality. It is more audible over the pulmonary area or the medium-left sternal border, but it may also be heard on the apex or the aortic area. It is frequently accompanied by an physiological splitting of S2 (Stout and Otto, 2007); (Tavel, 1977).

Blood volume increases during pregnancy to facilitate the delivery of nutrients and oxygen to the fetus, however, the increase in plasma volume exceeds the increase in red blood cell mass resulting in a state of hemodilution with lower average hemoglobin and hematocrit concentrations (Chapman et al., 1998). This physiological anemia tends to be more intense in the second trimester (Teixeira, 2010), when the systolic murmur is accentuated (Kaaja and Greer, 2005).

A normal pregnancy also causes frequent tone (B1 and B2) hyperphonesis, B1 split and the occurrence of B3 (Silversides, 2007). Diastolic murmurs during pregnancy are normally associated with anatomic heart injury (Stout and Otto, 2007); (Tedoldi, 2009).

Echocardiogram shows left ventricular hypertrophy with 50% increase muscle mass at full term. Hypertrophy is eccentric, similar to the one acquired through physical exercise. An increase may be observed in the diameter of the mitral, tricuspid and pulmonary valves. The aortic ring does not dilate (Campos, 1993). With the cardiac overload from the great increase in blood volume caused by pregnancy, this period is particularly prone to show heart diseases that were previously asymptomatic or aggravate pre-existing ones (Fujitani and Baldisseri, 2005).

The main goal of this study was to describe hemodynamic and auscultatory changes in normal pregnant women detected by digital auscultation system and to compare them to those of non-pregnant women. This research also aimed at creating a library of heart sounds, clinical data and echocardiogram images obtained during auscultation of healthy pregnant women, which may be used to teach heart auscultation and analysis of signs.

2 METHODOLOGY

This is a cross-sectional study in humans, performed in a Brazilian university hospital. The Ethics Committee of the institution approved the study and all the volunteers signed a letter of consent.

2.1 Research Subjects

From January 2012 to April 2013, 30 healthy pregnant women, in the second trimester of pregnancy and 30 healthy non-pregnant women, aged 18 to 40 years old, without any signs or symptoms of cardiovascular disease or anemia, treated at the Habitual Risk Prenatal and General Gynecology Clinic at Hospital das Clínicas of Universidade Federal de Minas Gerais, were selected by convenience sample, according to pre-established eligibility criteria.

Exclusion criteria were poor quality of the recorded sound signal, presence of cardiac abnormalities detected by Doppler echocardiography or anemia (hemoglobin concentration < 10,5mg/dL (Rasheed et al., 2008) in pregnant women and 12mg/dL in non-pregnant women).

Four women were excluded from the study, one pregnant woman due to moderate mitral regurgitation and three non-pregnant women, due to loss or poor quality of the recorded signal. Therefore, 56 women, (29 pregnant and 27 non-pregnant) were included for the statistical analysis.

2.2 Clinical Evaluation and Complementary Exams

In addition to the routine obstetric consultation, an experienced cardiologist performed a clinical and

cardiac evaluation with all pregnant women. Healthy women were also submitted to a specific cardiac evaluation. During the exam, the specialist carried out auscultation and described every heart sound change detected. That evaluation has become the gold standard for describing abnormal cardiac sound findings in both groups. On the same day, their blood pressure was measured with a manual sphygmomanometer in the right arm, with the women sitting.

A hemoglobin dosage was achieved in all pregnant subjects that did not do a blood test recently. A complete two-dimensional (2-D) Doppler echocardiography examination was performed in each participant at the time of enrollment to ensure normal cardiac structure and function.

2.3 Digital Auscultation

In order to perform the digital auscultation with simultaneous recording of the heart sounds, an electronic stethoscope (Littmann® Model 3200, 3M) was used. A touchscreen laptop (ASUS EEE PC T101MT) was used to capture the heart sounds wirelessly via Bluetooth technology, storing the sound library and clinical data.

The technique used for auscultation of heart sounds with the digital system was the same used in the routine cardiac examination. With women sitting and reclined, and afterwards in the left lateral decubitus, the recording sequence took place in the classic areas of auscultation. For each of these areas (1st, 2nd, 4th and 5th) the recording lasted for about 15 seconds.

The electronic information system used to store clinical data and heart sounds was developed by the DigiScope project team (Pereira et al., 2011).

2.4 Echocardiographic Protocol

Cardiac ultrasound examinations were performed with the women in the left lateral decubitus position with an M-Turbo portable ultrasound machine (SonoSite, Bothwell, WA, USA) equipped with 3-5 MHz phased-array transducers. A complete two-dimensional (2-D) echocardiographic Doppler evaluation was performed in each participant at the time of enrollment to ensure normal cardiac structure and function. The study protocol included imaging of the LV from standard parasternal long- and short- axis views and from apical four- and two-chamber views. Qualitative access of mitral, tricuspid, aortic, and pulmonary valve competence

by pulsed and color-flow Doppler mapping was made. In order to assess LV systolic function, 2-D-directed M-mode tracing of the LV minor axis between the papillary muscle tips was recorded. In order to determine LV diastolic function, mitral inflow was sampled by pulsed Doppler from the apical four-chamber view and analysis of the pulsed tissue Doppler of the mitral angle. All study images were video-recorded for further analysis.

2.5 Statistical Method

In order to estimate the sample size, we used the GPower 3.1.3 statistical software, with a standard significance and test power α=5% and β=80%, respectively. Bearing in mind that the expected prevalence of healthy pregnant subjects with some functional changes of heart auscultation is 95% (Tedoldi, 2009), and that the expected prevalence of functional auscultation sounds of the general population is 77.9% (Bloch and Jaussi, 2001), these two populations are expected to be differentiated with at least 52 women, 26 healthy non-pregnant women and 26 healthy pregnant subjects.

The variables chosen to compare the both groups in the study were the clinical findings of the heart auscultation and the Doppler echocardiographic abnormalities, both observed by the same cardiologist.

For the statistical analysis, each variable was statically described and compared between groups of study. For quantitative variables, the minimum and maximum values were observed and means, medians and standard deviations were calculated. The mean values obtained in the two groups were compared by independent samples t-test for normally distributed variables and the Mann-Whitney U test for not normally distributed ones. Proportions were compared using chi-square and/or Fisher's exact test. The statistical software used was SPSS ® 21.0 for Macintosh (2013).

The significance level was established at 5%.

3 RESULTS

Some demographic and clinical characteristics of the study and control groups are summarized in Table 1. The blood pressure levels in pregnant subjects were shown to be lower than the ones from the control group. Changes identified in the clinical auscultation happen more frequently in pregnant women, except for the B2 split.

Women aged from 19 to 40 years old, mean age

(SD) of 29 (5.5) years and the median was 29 years. With regard to pregnant women, age ranged from 19 and 36 years old, mean (SD) of 27 (5) years and the median was 27. In non-pregnant women, age ranged from 21 to 40 years old, mean (SD) age was 30 (5.4) years and median was 31 years (Table 1).

Weight of the patients ranged from 45.4 kg to 101.5 kg, with a mean (SD) weight of 65.6 (12.78) kg and a median of 62.5 kg. In pregnant women, weight ranged from 45.4 kg to 93.3 kg with a mean (SD) of 67 (12.39) kg and a median of 66 kg and in non-pregnant women it ranged from 49.3 kg to 101.5 kg, with a mean (SD) weight of 64.1 (13.25) kg and a median of 62kg.

Height ranged from 1.47m to 1.77m, mean (SD) height was 1.61 (0.065) and median was 1.62m. In pregnant women height ranged from 1.47 to 1.77m, the mean (SD) height was 1.60 (0.067) and median 1.60 m. In non-pregnant women, height varied from 1.50 to 1.72m, mean (SD) was 1.62 (0.062) and median 1.63m.

Considering all women, mean body mass index (BMI) was 25 kg/m2 (ranging from 17.7 - 40.3 kg/m2; Median: 24.3 kg/m2). In pregnant women, the mean value for body mass index (BMI) was 26 kg/m2 (ranging from 18.3 - 40.4 kg/m2; Median: 25.7 kg/m2). In non-pregnant women, the mean value for body mass index (BMI) was 24.3 kg/m2 (ranging from 17.7 - 36.5 kg/m2 and median 22.6 kg/m2).

No significant differences were found when comparing the two groups regarding weight, height and body mass index.

The group of pregnant women had median (minimum-maximum) values of systolic blood pressure, and diastolic blood pressure of 102 (90-128), and 68 (50-78), respectively. Concerning the mean arterial pressure, it's mean (SD) value was 79.4 (6.5). The control group had median (minimum-maximum) values of systolic blood pressure and diastolic blood pressure of 113 (90-130) and 80 (60-102), respectively, and the mean (SD) mean arterial pressure was 89.6 (9.2). Systolic blood pressure, diastolic pressure and systolic murmur were seen to have significantly higher values in the control group (Table 1).

The chance (95% CI) to detect the systolic murmur was estimated as 3.2 (1.1-9.7) times higher in pregnant than in non-pregnant women. The chance (95% CI) to detect B1 hyperphonesis was 13.4 (2.7-67.3) times higher; while for B1 split it was 20.6 (4.8-88) times higher and for B2 hyperphonesis it was 9.8 (2.8-34.1) times higher.

Regarding Doppler echography, the occurrence of physiological valvular regurgitation was similar in the study and control groups. Pulmonary regurgitation, 25% versus 18.5% (p=0.561); tricuspid regurgitation, 86.2% versus 92.6%, (p=0.671); and mitral regurgitation, 72.4% versus 74.1% (p=0.889), respectively.

In healthy pregnant subjects, no significant association was found among the occurrence of heart murmur with the digital auscultation system and the corresponding echocardiogram alterations, mitral murmur versus mitral regurgitation (p=0.675; tricuspid murmur versus tricuspid regurgitation, (p=1.000) and pulmonary murmur versus pulmonary regurgitation (p=1.000). Even though 20.7% of pregnant women showed aortic murmur, none of them had corresponding changes in the echocardiogram.

4 DISCUSSION

Heart auscultation by means of a stethoscope has been historically considered a symbol of medical care.

Table 1: Clinical characteristics, regarding groups of study.

Caracteristics	Healthy pregnant women (n=29)	Control group (n=27)	p-value	
Mean age (years) (SD)	26.8 (5.0)	30 (5.4)	0.011	*
Mean weight (kg) (SD)	67.0 (12.4)	64.1 (13.3)	0.402	*
Mean height (m) (SD)	1.6 (0.06)	1.6 (0.06)	0.249	*
BMI (kg/m^2) median/range	25.7 / 22.1	22.6 / 18.8	0.129	**
Systolic blood pressure (mmHg) median/range	102 / 38	113 / 40	0.009	**
Diastolic blood pressure (mmHg) median/range	66 / 28	80 / 42	<0.001	**
Mean mean arterial pressure (mmHg) [a] (SD)	79.4 (6.5)	89.6 (9.2)	<0.001	*
Systolic murmur n (%)	20 (69.0)	11 (40.7)	0.034	#
B1 hyperphonesis n (%)	15 (51.7)	2 (7.4)	<0.001	##
B1 split n (%)	26 (89.7)	8 (29.6)	<0.001	##
B2 hyperphonesis n (%)	20 (69.0)	5 (18.5)	<0.001	#
B2 split n (%)	27 (93.1)	27 (100)	0.492	##

[a]Mean arterial pressure: (Systolic+2Diastolic)/3 *T-mean Test, ** Mann-Whitney Test, #Chi-square Test, ## Fisher Test

Even though complementary tests are currently fundamental to diagnose cardiovascular diseases, the clinical semiology associated with anamnesis is still the first step in a complete and accurate cardiovascular evaluation. During prenatal care, the auscultation of heart sounds is especially important to track heart diseases, which are serious pregnancy complications and a relevant cause of maternal death.

This study has shown that heart sounds change significantly in the second trimester of pregnancy - describing the most relevant adaptive changes. Echocardiography performed in all studied cases was critical to discard possible unsuspected diseases. In addition, a specialist allowing us to infer that these changes have a physiological nature performed a complete cardiovascular examination. And even though they may be mistaken for heart disease sounds, they are not enough to justify additional routine tests such as echocardiography for those cases. This is not a recent notion. In order to avoid making inappropriate use of echocardiography in pregnant women showing heart murmur, it is recommended to limit exam requests only for those patients with a history of an underlying heart disease, clear heart symptoms, systolic murmur equal or over 3/6 in the Levine scale or diastolic murmur (Bonow et al., 2008) (Stout and Otto, 2007).

Significant findings on echocardiography have also been reported in other studies. In a longitudinal Doppler echocardiographic study, in four gestational periods and the puerperium, a progressive increase in the prevalence of physiologic tricuspid and pulmonary regurgitation, as well as the transient development of trivial mitral regurgitation have been observed (Campos, 1993). In another study, 79% of women were clinically thought to have benign flow murmurs during pregnancy, and the echocardiographic and Doppler results were normal in all of them (Mishra, 1992).

However, one of the limitations in the present approach is related to the design of the transversal study. It is known that with a longitudinal analysis, in which a group of pregnant subjects could be monitored throughout the pregnancy and puerperium, a more complete and temporary view of the intense physiological changes through heart auscultation are more likely to occur. In order to overcome the current impossibility of the approach, we chose the second trimester of pregnancy to perform the evaluation, since that is when blood volumes hit their highest level, causing a significant hemodilution and a characteristic hyperdynamic state associated with the changes in sounds.

But it can still be considered an innovative evaluation if we consider the fact that a digital system was used, allowing us to store each pregnant subject's heart sounds, subsequently to reevaluate auscultations as often as necessary and to classify them properly. We hope that the library of sounds, images and clinical data created with the study can contribute to the education of health care professionals, providing better resources to detect heart diseases. Similarly, the digital sonograms stored may be used in establishing the difference between heart disease standards through a study involving the analysis of digital signals in order to compare sonograms stored with the ones generated by heart diseases.

Another important asset was to set up a multidisciplinary group of medical informatics, consisting of medical and information technology researchers from different areas. This variety of professionals is essential for further analysis, as it brings important computer tools to help solve some of the greatest challenges in medicine.

Since Brazil is a country of continental proportions, and part of the population lives in areas with no access to health care or specialized health professionals, the digital heart auscultation technology would help combine information technology and the promotion of health care, shortening distances between isolated populations and large urban centers. UFMG is connected to the University Telemedicine Network through Tele-health System (Ribeiro, 2010), with 817 connection points available in the state of Minas Gerais (www.telessaude.hc.ufmg.br), with a potential of using the results from this investigation to achieve the goals of telemedicine. With a future perspective yet to be planned, digital heart auscultation technology can become part of the propedeutics of heart diseases in teleconsultations, validating these findings in a large number of subjects. Early diagnosis of heart disease during pregnancy using transmitted digital signs could be a potential advantage of this technology.

5 CONCLUSIONS

Digital heart auscultation performed in healthy pregnant subjects was able to detect frequent and numerous changes and results confirm the importance of understanding the physiological changes that take place during pregnancy. The normal echocardiogram in all healthy pregnant women with heart murmur indicates that such test

has limited applicability for healthy pregnancy, only in cases of suspicion of a heart disease or when it does occur.

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