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Research Article

# The Relationship of Weekly Monitoring of the Radial Artery Pulse Harmonics during Pregnancy Process

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## Abstract

**Objectives:** The pulse wave fluctuations during pregnancy exhibit distinct characteristics that represent both the pregnancy and the fetus. However, these fluctuations, which contain more frequency domain information, have not yet been studied for diagnostic purposes. Our objective was to quantify these pulse waveforms and gather empirical evidence regarding their relationship with both pregnancy and fetal sex. **Methods:** We collected wrist pulse data from 36 pregnant women (420 datasets) and 50 nonpregnant women using a pressure sensor. We applied Fourier transformation to analyze these pulse waveforms and extract their harmonics in frequency domain. Subsequently, we conducted a statistical analysis to compare these harmonics between pregnant and non-pregnant women to estimate the differences. To validate our findings, we employed machine-learning techniques to assess the utility of these harmonics. **Results:** We observed a significant increase in the first and second harmonics in the right hand of the pregnant women, with a distinct pattern observed for these harmonics in the left hand. Furthermore, the differences in the top three harmonics between both hands were more evident, particularly in male fetuses, as we analyzed the monthly changes in harmonic differences, revealing stronger magnitudes in the early months. Additionally, our model accurately predicted fetal sex after 12 weeks over 70% accuracy using decision tree techniques. **Conclusions:** The pulse waveforms of the pregnant women displayed distinct signals, and the observed differences in harmonics between both hands were notable, especially with regard to fetal sex. This evidence could inform prenatal care practices and help research the maternal-fetal relationship.

**Keywords:** weekly harmonic monitoring, radial artery pulse, pregnancy process, both hands, gender difference

## Introduction

Elevated blood pressure variability (BPV) may indicate impaired cardiovascular regulation. As a risk factor for various health outcomes, blood pressure exhibits dynamic fluctuations in blood vessels, with systolic and diastolic blood pressures in its waveform [1]. The current evidence regarding its clinical relevance has several gaps and is based on heterogeneous studies with limited standardization of methods for BPV assessment [2]. In traditional Chinese medicine (TCM), practitioners sense the radial artery pulse in the blood pressure waveforms through the fingertips, especially using the "slippery pulse" pattern for fetal sex diagnosis [3]. However, variations in this pattern within the pulse waveform are mainly documented by explanatory words in classical literature. Pulse diagnosis requires apprenticeships and precise tactile sensations of the finger waveform, which are difficult to transmit and lack scientific data. This leads to differences in the interpretation of pulse waveforms. In this study, we employed scientific measurement methods to record pulses in pregnant women and applied machine learning techniques to classify fetal sex with the objective of exploring the impact of pregnancy on wrist pulse waveforms and potentially determining fetal sex.

The use of the "slippery pulse" pattern for diagnosing pregnancy has been recorded in various TCM literature sources. However, these studies mostly focused on explanations that lacked substantial quantitative data. For example, the foundational TCM text Huang-Ti-Nei-Ching indicates pregnancy through a "normal pulse but appearing weak" and "significant movement in the Shaoyin meridian" [4, 5]. Another instance is found in the "differential diagnosis of the Qi," where the pulse can reveal the fetal sex: a larger left pulse indicates a male fetus, whereas a larger right pulse suggests a female fetus. The practice of using TCM pulse diagnosis for pregnancy and sex identification has been employed over time. The current research has delved into digital sensing measurement, revealing that measuring pressure amplitude with position differences in the radial pulse could assist in identifying fetal sex [6]. However, its accuracy remains questionable, owing to its reliance on the tactile sensation of the finger. This reliance on oral tradition, which is susceptible to distortion, adds complexity to discerning the exact meaning of foundational historical texts. Although historical insights are not always conclusive, they offer promising pathways for analyzing pregnant pulse waveforms.

Scientifically measuring and analyzing arterial pulse waves using sensors and computers are essential in clinical practice, encompassing aspects such as understanding how physiological factors impact pulse dynamics, diagnosing diseases, evaluating drug responses, and conducting epidemiological studies [7]. Various devices have been developed to facilitate these measurements [8]. For data preprocessing, the transform-based method, which is one of the four typical methods, delves into the frequency spectrum of the radial arterial pulse using a Fourier transformation [9]. Currently, the application of harmonic modes from transformed pulse data has proven useful in diagnosing conditions, such as abnormal liver function [10, 11], type 2 diabetes [12], coronary artery disease [13], pregnancy[14], and death [15, 16]. Additionally, the authors previously introduced the concept of organs and TCM meridians resonating with specific Fourier components of pressure waves [17, 18], highlighting the detection of disrupted hepatic, renal, or splenic qi in the pulse [16]. Moreover, AI algorithms can go beyond mere classification tasks; they can analyze vast datasets to detect early signs of diseases and conditions, thereby facilitating computational TCM diagnosis [19]. The authors also utilized AI classification techniques in a study of kidney insufficiency [20].

In this study, we addressed the gap in scientifically quantified pulse diagnosis by employing pressure sensors to measure pulses, utilizing a Fourier transform-based method to analyze the signals into harmonic components, and applying machine-learning techniques to support fetal gender classification. Furthermore, by establishing a correlation between harmonic data, monthly pregnancy changes, and fetal sex, our study contributes to a more comprehensive understanding of the intricate dynamics of wrist pulse waveforms during pregnancy. The significance of this study is that it bridges the gap between TCM practices and modern medical techniques but also opens avenues for further research into utilizing pulse waveform analysis for accurate diagnosis and monitoring of pregnancy-related changes.

## Materials and Methods

Data were collected from pregnant women, and measurements were taken simultaneously from both hands of these pregnant women. Simultaneous measurements in both hands increased the complexity of the data collection, particularly considering that pregnant women are a high-risk group. Pregnant women who declined to undergo simultaneous measurements in both hands were excluded from the study. Therefore, a cohort of 86 participants, including 36 pregnant females, were examined using individual monthly measurements. Among them, there were 16 female fetuses and 20 were male fetuses. Measurements were obtained at least once a month, resulting in ten values for both hands. The remaining 50 participants were healthy females who did not menstruate and did not exhibit any apparent symptoms. Measurements were obtained from this group only once and served as the control group.

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This resulted in 420 measurements, comprising 208 among female fetuses and 212 among male fetuses, as depicted in (Figure 1a) for the monthly measurement count and (Figure 1b) for the weekly measurement count. As pregnant participants visited the outpatient department (OPD) between 10 and 30 times during the study, repeated measurements of harmonic magnitudes were linked to the records of individual pregnant women. The entire study was conducted at the OPD over a two-year period. The exclusion criteria were irregular heart rhythms, arterial catheters on the wrists, or sensitive skin conditions. Participants were also required to abstain from consuming alcoholic and caffeinated beverages. One hour before the experiment, participants were instructed to fast and rest. Ten minutes before the test, blood pressure and heart rate of the pregnant participants were recorded. The results of these recordings are shown in (Figures 1c and 1d), respectively. All experiments were conducted with the permission of the participants, and informed consent was obtained after explaining the research purpose. The study was approved by the ethical committee of China Medical University Hospital, Taiwan (No. CMUH108-REC1-135). All the procedures performed in this study were in accordance with the relevant guidelines and regulations of the ethical standards of the institutional research committee and the Declaration of Helsinki.

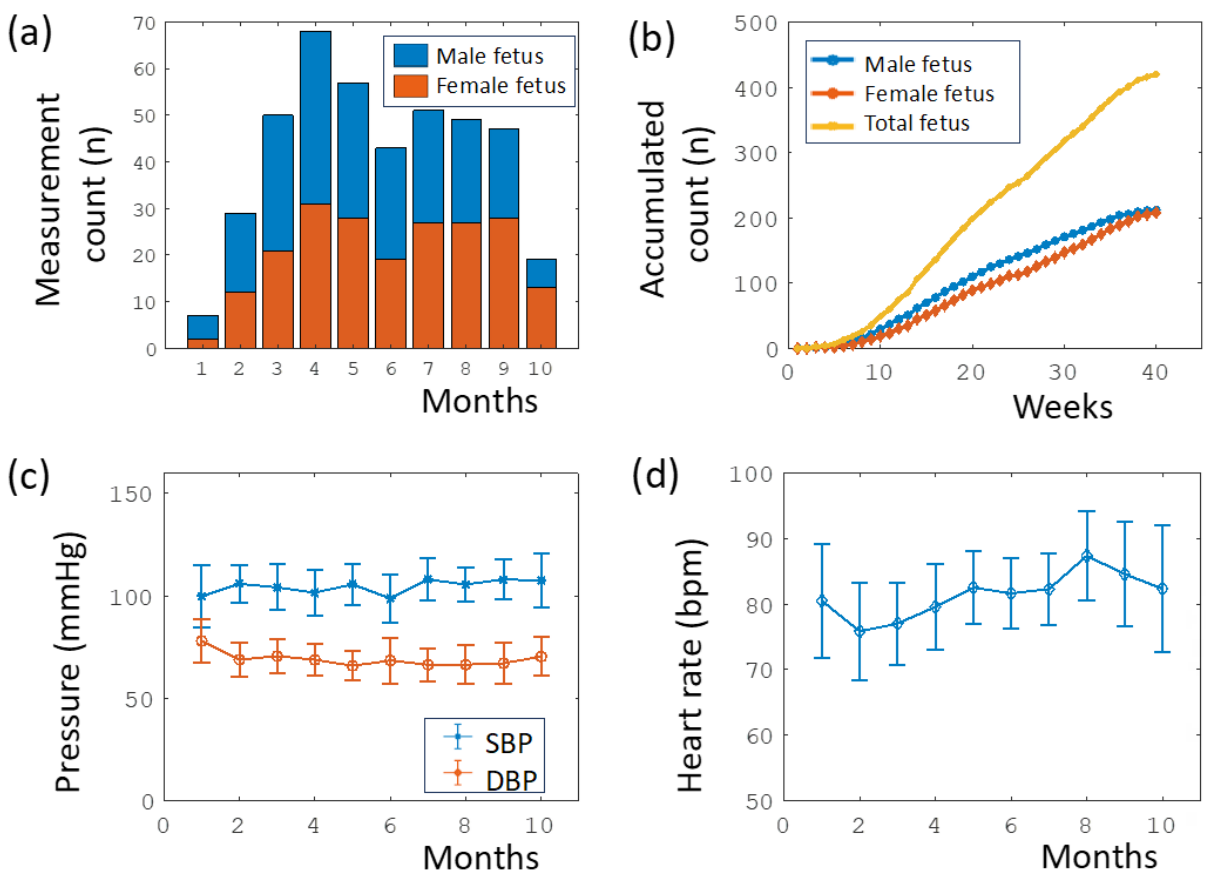


**Figure 1:** The number of participants and their basic physiological data statistics. Statistical data on the number of (a) monthly and (b) weekly measurements. Monthly variations in (c) blood pressure and (d) heart rate were measured for all the participants.

Non-invasively measured pulse pressures of the right and left radical arteries were synchronously obtained for each participant using a pressure transducer (PSL-200GL, Kyowa Electronic Instrument Co. Ltd., Japan). The device was fixed on the participant's skin using Scotch™ tape along with an adjustable belt with a small button to provide a suitable pressure on the transducer. Pulse pressure readings were recorded for both the left and right hands. Precise measurements were obtained by identifying the position at which the wrist bone and tendon on the thumb side (known as the "Guan" point in TCM) exhibited the highest pulse magnitude, as shown in (Figure 2a). Subsequently, the sensor was placed at this specific location. Our successful measurement criterion was to capture the pulse with the highest magnitude [11, 18].

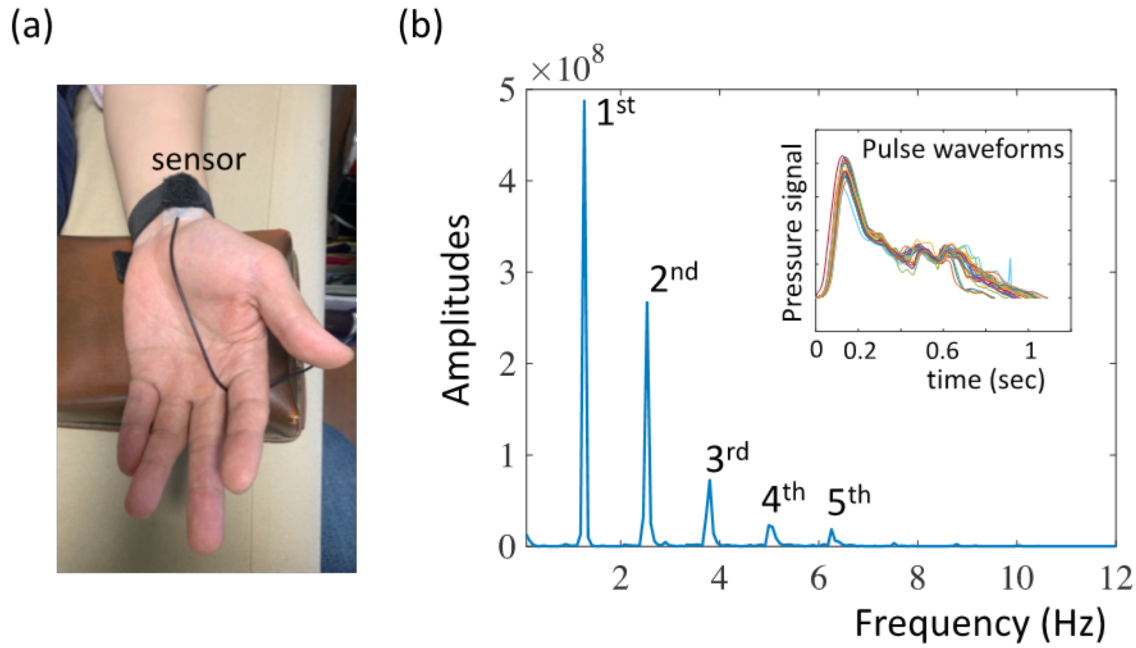


**Figure 2:** Experimental setup and pulse waveform analysis. (a) Measurement setup for detecting pulse waveforms, achieved by placing a pressure sensor on the wrist to obtain signals. (b) The inset figure illustrates the pulse waveform. Each independent waveform can be transformed into the frequency domain through Fourier transformation to obtain various peaks. Each peak is sequentially numbered, representing individual harmonics.

The transducer output was connected to an Apple MacBook for analysis, using an A/D converter with a sampling rate of 500 data points/s. The pulse spectrum was subjected to Fourier transformation using a one-pulse period within a 6-second interval [17], as depicted in the inset of (Figure 2b) (inset). Following the Fourier transformation, we examined the magnitudes (Figure 2b) and corresponding phases of the harmonics along with their mean values. We developed analysis codes using MATLAB (MathWorks, 2022b, USA) and subsequently compared the magnitudes and phases of the first ten harmonics among each group, as shown in (Figure 3). Statistical analyses of these outcomes were conducted using SigmaPlot 14.0. We constructed a two-level hierarchical linear model (HLM) [21, 22] or a mixed model [23] to analyze the harmonic magnitude and group differences. The level-one is used to estimate the means of longitudinal intensive data (repeated harmonic magnitudes) and the level-two is used to estimate the gender differences in the average harmonic magnitudes. Descriptive analyses of harmonic magnitude data were performed using the SPSS 22.0 software package (SPSS Inc., Chicago, IL, USA), and the SPSS mixed module was used to conduct the HLM. For the machine learning components, MATLAB functions were applied, including predictor importance estimates by permutation using a random forest of regression trees, trained regression containing boosting 100 regression trees, and k-nearest neighbor classifier.

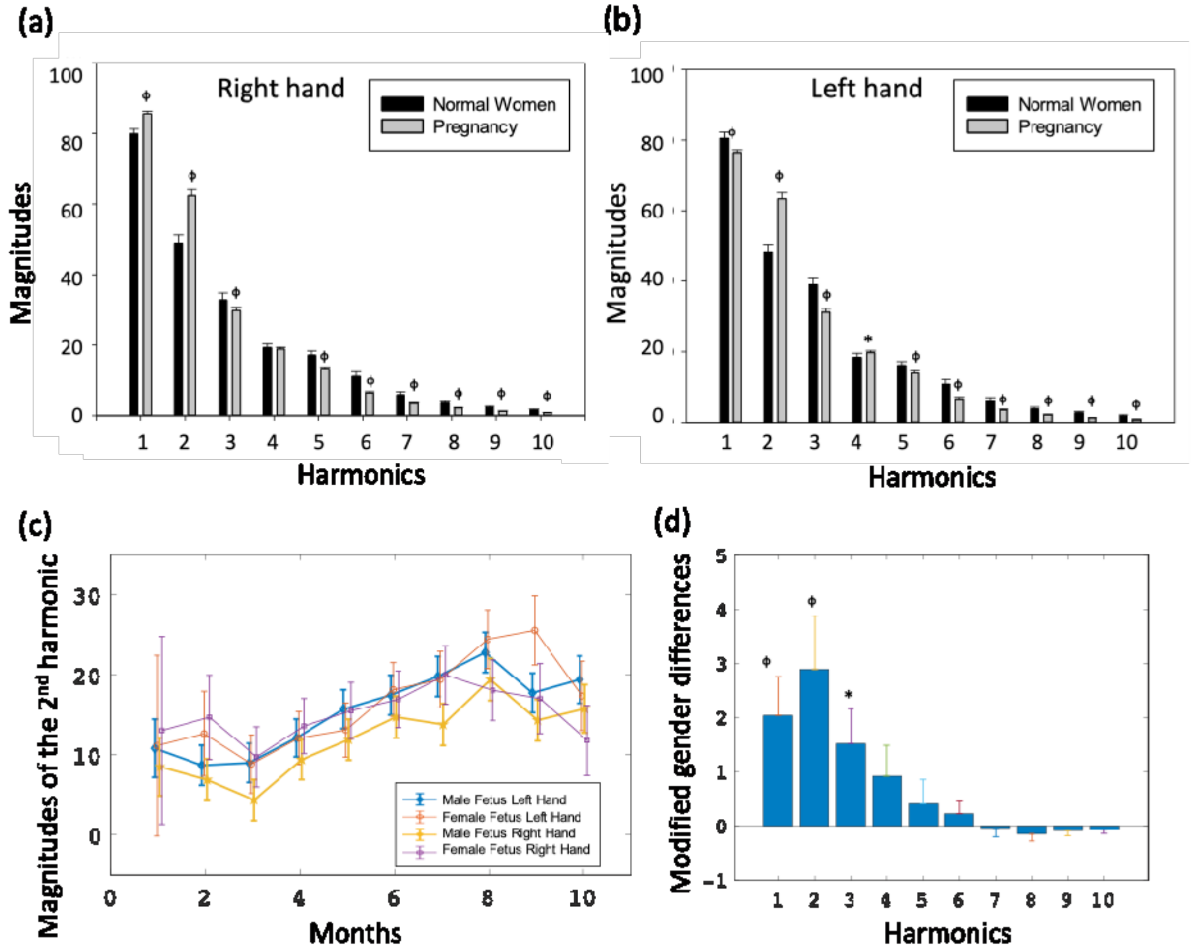


**Figure 3:** Top 10 Harmonics for normal women and pregnancy and their variation. (a) Right hand measurements and (b) Left hand measurements. (c) Monthly variation of the second harmonic based on fetal gender and hands. (d) Average and standard deviation of modified gender differences with harmonics. Here, 'ϕ' denotes $P < 0.01$, and '*' denotes $P < 0.05$.

In this study, we hypothesized that utilizing a highly accurate sensor at the 'Guan point' could effectively capture the necessary information to replace the three-position detection method mentioned in TCM [3]. This assumption is based on the idea that organs and their associated meridians resonate with specific Fourier components of the pressure waveform [17, 18]. Although other studies have often utilized different positions and pressures to obtain pulse signals, we argue that acquiring signals from various positions with varying pressures merely changes local boundary conditions. Consequently, these changes in the boundary conditions result in different local resonance behaviors, enabling the filtration or enhancement of signals in different frequency bands. Therefore, we assumed that employing a high-resolution sensor would be sufficient to compensate for these changes in boundary conditions and strengthen the signal.

Additionally, we considered the potential influence of various external factors on the participants, such as stress levels, physical activity, eating habits, sleeping patterns, and environmental conditions, which were not controlled for in this study. From a TCM perspective, these external factors may influence changes in harmonic values, potentially affecting the accuracy of our measurements. However, owing to the high-risk nature of pregnant women, we were unable to impose strict control over their lifestyle.

## Results

Over a span of two years, we gathered pulse pressure data from both the left and right hands of 36 pregnant women and 50 normal women. After applying the Fourier transformation to these pulse pressure waveforms, the magnitudes of the top ten harmonics for these measurements are depicted in (Figure 3a (right) and 3b (left). Analyzing the results on the right-hand side, we observed that the magnitudes of the 1st and 2nd harmonics were elevated in pregnant women, whereas the magnitudes of the remaining seven harmonics were lower. After conducting t-tests, all these differences were found to be significant (t-test, $P<0.01$, denoted by ϕ), except for the 4th harmonic, which showed nearly equal values between the normal and pregnant groups. On the other hand, in the case of the left hand, it was observed that the 2nd harmonic exhibited higher values among pregnant women, and a minor elevation was seen in the 4th harmonic. However, the remaining eight harmonics exhibit lower values. Subsequent t-tests yielded significant results for all these differences (t-test, $P< 0.01$, denoted by ϕ); the sole exception was the fourth harmonic ($P<0.05$, denoted by *). This result highlighted the distinct nature of the 2nd harmonic. Furthermore, this harmonic emerged as a pivotal indicator after the third month, vividly mirroring the monthly trajectory of fetal growth and gender distinctions (Figure 3c). Notably, all second-harmonic magnitudes experienced significant increases until night. Additionally, pregnancy can be identified in conjunction with the 1st, 3rd, and 4th harmonics, and there is the potential to identify pregnancy [24].

To explore fetal sex distinctions, we collected data synchronously from both the left and right hands of the pregnant women. Mean values and standard errors of the mean (SE) were computed for the male and female fetal groups and are presented in Supplementary Tables S1 and S2, respectively. We assessed the sex differences by subtracting the harmonic magnitudes of females from those of males (sex difference= male–female). These gender differences in harmonic magnitudes are delineated in the corresponding columns of these tables for both the individual left- and right-hand groups. It is important to note that no statistically significant gender differences emerged in either the individual left- or right-hand group. Additionally, we initially obtained the differences between the hands and then computed the modified sex differences. Hand differences were derived by subtracting the harmonic magnitudes of the right hand from those of the left hand (hand difference= left-right). Subsequently, we utilized the individual participants' hand differences to calculate the modified gender difference obtained by subtracting the magnitude of the female hand difference from that of the male hand difference (modified gender difference=Male(L-R)-Female(L-R)). Notable sex differences were observed (Table S3 in the Supplementary). In particular, the differences in the values of the 1st ($P < 0.01$), 2nd ($P< 0.01$), and 3rd ($P< 0.05$) harmonic components were significantly higher in male fetuses, as depicted in Figure 3d. To assess monthly variations, we also considered modified sex differences. The outcomes for identifying modified sex differences based on each harmonic and comparison within each month are presented in (Figure 4), accompanied by the detailed raw data in Supplementary (Table S4).

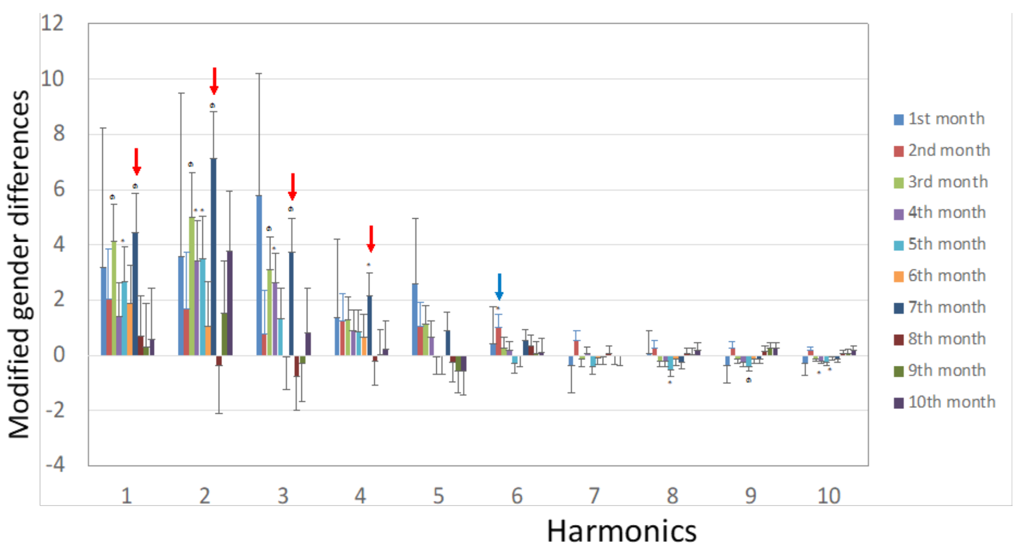


**Figure 4:** Illustrating the monthly differences of modified gender differences with harmonics. The red arrows indicate the seventh month, which served as a turning point, with monthly changes particularly evident in the first four harmonics. Blue arrows indicate the earliest signs of male fetal identification. Here, 'ϕ' denotes $P < 0.01$, and '*' denotes $P < 0.05$.



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We input the ten harmonic values contained in the left hand, right hand, and the difference between the two hands into the decision tree analysis to obtain a streamlined method for distinguishing between male and female fetuses. We also focused on the differences between the first three months (Figure 5a) and months four–ten (Figure 5b), and these figures show the original results of the classification tree view. In the analysis of the first three months, very high prediction probabilities can be achieved, especially for female fetuses. Male fetuses also exhibited discrimination rates of approximately 0.945, except for a small portion of branches with discrimination rates of approximately 0.667, but this accounted for only three out of 68 cases. The estimated probability for female fetuses was 1.0 (28/28), whereas that for male fetuses was 0.925 (37/40). Moreover, in the analysis from months 13 to 40, the discrimination rates were not as ideal as those in the first three months. The discrimination rates for female fetuses ranged from 0.682–0.939, whereas those for male fetuses ranged from 0.753–0.886. In total, the estimated probability of female fetuses was 0.84 (123/146), while that of male fetuses was 0.77 (127/165).

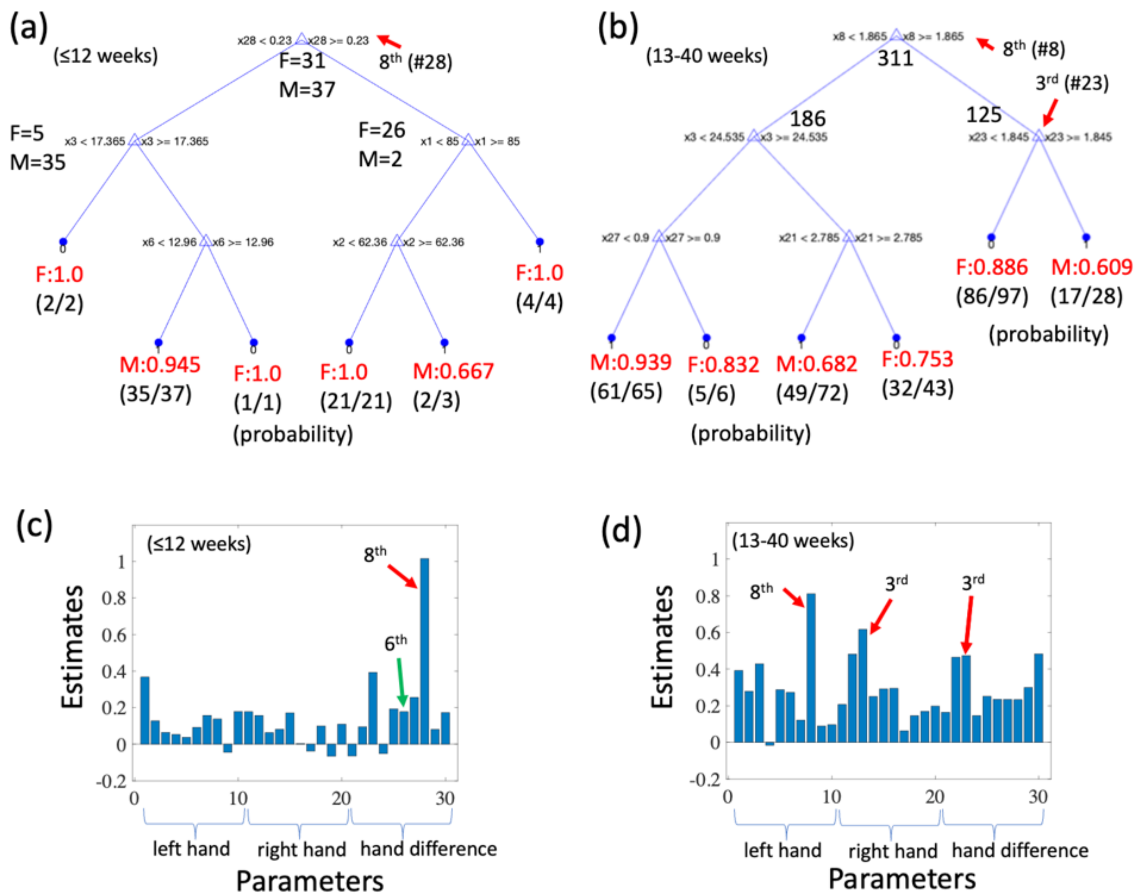


**Figure 5:** The decision tree analysis for classifying fetal genders. (a) Results of the first 12 weekly decision tree. (b) Displays the 13-40 weekly decision tree results. The importance estimates for the 30 harmonics are presented in (c) for the first 12 weeks, and in (d) for weeks 13-40. Here, ‘F’ and ‘0’ denote female fetus, ‘M’ and ‘1’ denote male fetus, and (n/N) denotes ‘n’ for the correct number and ‘N’ for the total number. For example, the values, “F: 0.832” and “M: 0.682” represent probability. The coding is as follows: the left hand (x1-x10), the right hand (x11-x20), and the difference between both hands (x21-x30) represent their ten harmonics.

We also used the out-of-bag predictor importance estimation method, specifically, a random forest of regression trees, to validate the important parameters (Figures 5c and 5d). The results indicate that the difference between the left and right hands plays a crucial role in distinguishing between fetal sexes during the first three months. However, in the analysis of months four–ten, the parameters of the left and right hands individually also showed a significant importance. The most crucial parameter in the first three months is the 8th harmonic of the difference between both hands, while in the later months, the 2nd, 3rd, and 8th harmonics also play important roles. In addition, we analyzed the cumulative weekly data, starting from the seventh week, using both the decision tree and K-nearest neighbors (KNN) methods to statistically analyze the recognition of fetal sex (see Supplementary Material).

## Discussion

Various changes in the cardiovascular system occur during pregnancy, such as increased cardiac output and reduced blood pressure [25]. Examining the trend across different months, as shown in a previous study [26], the mean blood pressure gradually decreased during pregnancy, with the most significant decrease usually occurring at approximately 4–5 months. Comparing this finding with the results shown in (Figure 1c), we observe a similar decreasing pattern. For a more detailed analysis of the pulse measurements 8 taken from both hands, it was observed that the majority of harmonic magnitudes in the pregnant group exhibited a decrease across all ten harmonics, except for the 2nd harmonic as shown in (Figure 3). In the study [3, 27], they observed 1st harmonic outcomes during pregnancy, echoing our findings depicted in (Figure 3c). Additionally, we observed a notable increase in the 2nd harmonic as the months progressed, as illustrated in (Figures 3c and 4). Interestingly, in the broader differences depicted in (Figure 4), the seventh month shows a notable peak (and turning point) in the process for the top four harmonic modes (indicated by the red arrows). This evidence illustrates the potential applicability of these harmonics in observing pregnancy phases, similar to that observed during the dying process [15, 16].

The 2nd harmonic, with a period half that of the 1st harmonic [9], effectively contained two waves within a single pulse. From the perspective of the circulatory system, the frequency at the 2nd harmonic (140 beats per minute) plays a crucial role in fetal growth. This is primarily because the fetal heart rate is nearly twice that of the mother, ranging from 120 to 180 beats per minute. This harmonic serves as the fundamental frequency of the fetus and as a conduit for effective resonance with the maternal circulatory system. This observation suggests that the waveform illustrated in the study [3, 27] for the slippery pulse was reasonable, with the 2nd harmonics potentially elucidating the distinct signal of the "Chi" position in pregnant women. Moreover, from the perspective of TCM, this wrist position is related to the "Foot Shaoyin renal meridian," which is associated with the 2nd harmonic [28]. This evidence could also be related to the concepts of "significantly moving in Shaoyin meridian, pregnancy" and "normal pulse but appears weak, pregnancy" mentioned in TCM classical literature [4].

The significance of the modified sex difference underscores the importance of distinguishing between both hands, as depicted in (Figure 3d), in contrast to the lack of significance observed when analyzing each hand individually, as shown in (Figure 3a). Notably, the 1st, 2nd, and 3rd harmonics exhibited notably higher values in pregnancies with male fetuses than in those with female fetuses (Figure 4). The positive values of the modified sex difference indicated that the harmonics in the left hand were greater than those in the right hand. This aligns with the concept stated in TCM classical literature 4 that "differential diagnosis of the Qi in pulse can detect the sex of the fetus, with the left hand being larger than the right indicating a male fetus, and the right hand being larger than the left indicating a female fetus." Moreover, this pronounced sex difference became significant in the second month of gestation in the 6th harmonic (P<0.05, blue arrow), as illustrated in (Figure 4), and after the third month, it was found in the 1st, 2nd, and 3rd months, as shown in (Table 1).

| Harmonics / Months | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| M1 | | | | | | | | | | |
| M2 | | | | | | * | | | | |
| M3 | ϕ | ϕ | ϕ | | | | | | | |
| M4 | | * | * | | | | | | | * |
| M5 | | * | | | | | | * | ϕ | * |
| M6 | | | | | | | | | | |
| M7 | ϕ | ϕ | ϕ | * | | | | | | |
| M8 | | | | | | | | | | |
| M9 | | | | | | | | | | |
| M10 | | | | | | | | | | |
| ϕ denotes P < 0.01 and * denotes P < 0.05 | | | | | | | | | | |

**Table 1:** Significance of fetal gender based on months and compared within each harmonic

Several interesting features emerged when conducting the decision tree analysis. Notably, within the first three months, the difference between both hands was particularly significant for gender classification, as shown in (Figure 5c). Among these features, the importance estimates of parameters 21–30 are relatively high. As shown in (Figure 5a), this appears to be the largest classification feature of the initial branches. The 8th harmonic served as a crucial indicator for distinguishing between genders, with the left branch showing a probability of (35/40) for males and the right branch showing a probability of (26/28) for females. However, when compared with (Figure 4), the significance of the 8th harmonic was not particularly pronounced, highlighting a potential inconsistency between the decision tree and human judgment. Additionally, in (Figure 4), we observed a higher resolution for the 6th harmonic in the second month, which was also emphasized in the decision tree algorithm (as indicated by the green arrow in (Figure 5c). Additionally, in (Figures S1c and S2d), it is evident that both the decision tree and KNN methods can achieve considerable resolution in identifying fetal sex after the 12th week (12 weeks for ultrasound) [29].

This study had three potential limitations. First, the relatively small sample size may have limited the generalizability of our findings to a broader population. This limitation could be addressed in future research by replicating the study with a larger sample, conducting stratified analysis, and fostering collaboration and data sharing. Secondly, the study utilized a specific measurement technique 8 involving a sensor placed on a specific position, the 'Guan point,' on the wrist, in alignment with the earlier mentioned hypothesis. However, the choice of sensor placement, applied pressure, and potential sources of interference could potentially introduce variations in the measurement accuracy. Therefore, validation of the measurement technique and standardization of the protocol are essential for addressing this limitation in future studies. Third, the influence of various external factors on participants, such as stress levels, physical activity, and environmental conditions, could introduce variability in blood pressure readings and subsequently impact the study's outcomes. These external factors were not comprehensively controlled in the study design and were assumed to not influence them.

## Conclusion

We collected radial artery pulse waveforms from both the pregnant and non-pregnant groups and compared their harmonic differences to bridge the gap caused by the lack of quantified evidence in slippery pulse diagnoses. This study makes two significant contributions to the field. First, comparing Fourier-transformed harmonics greatly enhances our understanding of measuring radial artery pulse waveforms in pregnant individuals, surpassing the insights provided by systolic and diastolic blood pressure information alone. Second, differences in harmonics between both hands enable the determination of fetal sex. With the assistance of machine learning, pronounced sex differences became significant after the 12th weeks of gestation with over 70% accuracy (12 weeks, the same as applying ultrasound), and simple results from the decision tree could aid in early sex classification.

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**Ethical Considerations:** All experiments were conducted with the permission of the participants, and informed consent was obtained after explaining the research purpose. The study was approved by the ethical committee of China Medical University Hospital, Taiwan (No. CMUH108-REC1-135). All the procedures performed in this study were in accordance with the relevant guidelines and regulations of the ethical standards of the institutional research committee and the Declaration of Helsinki.

**Conflict of Interest:** The Authors declare that there is no conflict of interest.

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