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Serum and Salivary Levels of Glucose and Urea in Pregnant and Non-pregnant Women: A Comparative Study

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Abstract

Background: Pregnancy is one of the most critical periods in the life of most women. Since it is necessary to be aware of the health of the mother and fetus, serum markers (i.e., glucose and urea) need to be monitored during pregnancy. A routine strategy in this area is venipuncture which is applied to measure the level of these markers. It is also a stressful procedure for pregnant women. The purpose of this study was to determine the salivary level of these markers as a stress-free method in pregnant women.

Materials and Methods: The samples were collected from 30 pregnant and 30 non-pregnant fasting women. Then, the serum and salivary levels of glucose and urea were measured, analyzed, and compared by photometry.

Results: Results indicated that the mean salivary glucose level was 10.2 ± 1.4 mg/dL and 6.4 ± 0.9 mg/dL in non-pregnant and pregnant women, respectively. In addition, the mean serum glucose level was 106.5 ± 5.3 mg/dL and 82.9 ± 4.5 mg/dL in non-pregnant and pregnant women, respectively. Further, the mean salivary urea level was 37.1 ± 3.3 mg/dL in non-pregnant women and 27.1 ± 1.9 mg/dL in pregnant women. Moreover, the mean serum urea level was 26.9 ± 1.9 mg/dL and 19.5 ± 2.3 mg/dL in non-pregnant and pregnant women, respectively.

Conclusion: Serum and salivary levels of glucose and urea in pregnant women were lower than those in non-pregnant women, and there was a positive correlation between serum and salivary levels. Therefore, it seems that saliva can be a substitute for serum regarding the measurement of glucose and urea levels.

Keywords: Saliva, Urea, Glucose, Pregnant

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Introduction

Certain changes occur during a woman's life due to hormonal fluctuations, affecting the overall physiology of the body such as the oral cavity. Therefore, different periods such as menstruation, pregnancy, and menopause can directly affect the composition and flow rate of saliva (1). Pregnancy is a condition in which a woman carries a fetus in her uterus, which lasts for nine months in a human being and ends with the birth of a baby through a process called childbirth, also known as labor or delivery (2, 3). One of the most common problems during this period is gestational diabetes with obvious harmful effects on the mother and fetus. Hence, constant monitoring of serum glucose levels is required during this period. According to previous findings, glucose is found in nature in free form or in combination. It is not only the most common sugar but also the most abundant chemical compound in nature. This molecule is found in the free state in tallest plants, and can move easily through the membranes of blood vessels, pass from the blood plasma to the gingival crevicular fluid, and reach the saliva through the gingival sulcus (4). Some studies have suggested that increased levels of salivary glucose may be attributed to high blood sugar (2). Another serum marker required for monitoring is urea, which plays an important role in the metabolism of nitrogen-containing compounds in animals' bodies. It is also the main nitrogen-containing substance in mammalian urine. Urea is a hard, colorless, and odorless compound (although the resulting ammonia in the presence of water contains water vapor in the air and has a pungent odor), which is neither acidic nor alkaline and is relatively non-toxic and highly soluble in water. It is one of the serum markers also found in saliva. On the other hand, the oral problem is recognized as another common pregnancy disorder, the most prevalent of which is tooth decay in many cases. According to previous studies, urea is one of the effective markers on saliva buffering, which is also a serum marker (2, 5-7).

The method used today to measure these serum markers is venipuncture, which is both painful and stressful for pregnant women. Given the adverse effects of such stress on the mother and fetus, efforts have been made to achieve a non-invasive and stress-free method for measuring these markers in pregnant women. Evidently, saliva is the most available and non-invasive body fluid with a large amount of organic and inorganic compounds which can be collected using a non-invasive and low-cost method. It acts as a mirror of the body's health which is capable of showing local and systemic changes so that the components of saliva can be related to a person's hormonal, immunological, neurological, nutritional, and metabolic conditions. The ability to use saliva to monitor patient health is a desirable goal for health promotion and healthcare research. Accordingly, qualitative and quantitative alterations in salivary secretion can have local and secondary effects on the oral cavity. Therefore, there are compelling reasons to use saliva as a diagnostic fluid for health and disease monitoring (8, 9). Due to the invasive nature of venipuncture techniques for determining such markers, finding a relationship between serum and salivary levels of these markers may help to achieve a non-invasive method for their measurement through saliva that both accelerate the examination and reduces the pregnant women's discomfort and stress (10). Therefore, the present study was designed to evaluate levels of glucose due to the prevalence of gestational diabetes as well as urea owing to its buffering effects on saliva which can reduce tooth decay during pregnancy.

Materials and Methods

According to the formula for determining sample size and previous studies, the sample size included 30 women in each group, a total of 60 women in two groups (N = 60). After the study was approved by the ethics committee, the necessary permission and coordination were first made with maternity hospitals in Ardestan and Aran va Bidgol county, Isfahan province, Iran. The participants of the study were people who were referred to a hospital laboratory for a blood test prescribed by a gynecologist although they were not addicted to alcohol, cigarettes, and drugs. Furthermore, they had no history of radiotherapy in the head and neck area. The methodology and objectives of the study were fully explained to the research units, including the lack of any intervention and the absence of any complications as a result of saliva collection from the patients. All participants signed an informed written consent after explaining all the inserted details, including entering and leaving the project voluntarily, maintaining the confidentiality of personal information, not imposing any costs on participants, not using any drug, as well as complete safety of individuals. In coordination with maternity hospitals in Ardestan and Aran va Bidgol county, 30 pregnant women and 30 non-pregnant women were monitored for this study. Then, the participants' medical history was explored to exclude diabetic cases and any systemic conditions that could affect saliva secretion such as Sjogren or sicca syndrome in these centers (6, 7, 11). These individuals were asked to use a toothbrush and mouthwash on the day of sampling after waking up and to visit our office without eating breakfast after at least 90 minutes of oral hygiene (12). To prevent the effect of circadian cycles on saliva, all saliva samples were collected in sterile graduated vials for each person in a quiet environment between 9:00 am and 12:00 at noon. After referral, the subjects took a rest, and their saliva samples were collected in plastic vials by spitting method. Thus, the saliva in the mouth was swallowed, and subsequently, the accumulated saliva was poured into the sterile graduated vial by bending the head forward with the eyes open and with minimal movement of the body and head. It should be noted that the saliva samples were frozen in the freezer immediately after collection to prevent the effect of oral microorganisms on saliva glucose (7, 13). After completing saliva collection for each individual, blood samples were also taken inside gel-coated test tubes containing coagulants, then centrifuged to extract sera, and were later stored in the freezer. After the sample collection process was completed, the research team paid all the costs of the hospital tests to appreciate the participants for their cooperation and also donated them an oral hygiene pack (e.g., mouthwash, toothbrush, toothpaste, and floss). To measure glucose and urea levels, the saliva and serum samples were placed in special ice boxes and transferred to the physiology laboratory of Aja University of Medical Sciences. In the measurement phase, the serum and salivary levels of glucose and urea were measured separately for all participants by photometry using a glucose kit (Pars Azmoun company, Tehran, Iran) and urea kit (Fars Biorex Company, Tehran, Iran) based on the manufacturer's instructions. Finally, the results were recorded for statistical analysis. Data were analyzed by SPSS version 22 software using unpaired Student's t test and Pearson's correlation coefficient.

Results

In this study, the salivary and serum glucose and urea levels were measured in both groups. The first group consisted of 30 non-pregnant women within the age range of 16-40 years and a mean age of 25.5 years. The second group included 30 pregnant women within the age range of 20 to 38 years and a mean age of 25 years. There was no significant difference in the mean age between the two groups ($P < 0.50$). In the pregnant women group, the mean number of deliveries was 1.7 with a range of 1-3 times.

The number of pregnant women by pregnancy trimester included 4, 7, and 19 people in the first, second, and third trimesters, respectively. The results of the measurements are presented in Table 1.

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Analytical Findings

The findings of the unpaired student's t test are as follows ($P < 0.05$):

According to Figure 1, the mean serum glucose level in pregnant women was lower than that in non-pregnant women ($P = 0.001$); likewise, the mean salivary glucose level in pregnant women was lower than that in non-pregnant women ($P = 0.029$). Figure 2 illustrates that the mean serum urea level in pregnant women was lower than that in non-pregnant women ($P = 0.014$), and the mean salivary urea level in pregnant women was lower than that in non-pregnant women ($P = 0.011$). Furthermore, a moderate positive correlation was observed between serum and salivary glucose levels ($P = 0.000$). Similarly, a moderate positive correlation was found between serum and salivary urea levels ($P = 0.038$). Data were expressed as means $\pm$ SEM, which were statistically analyzed by unpaired Student's t test.

Discussion

There are obvious changes in a woman's life due to hormonal fluctuations affecting the overall physiology of the body, including the oral cavity. Accordingly, various stages such as menstruation, pregnancy, and menopause can directly influence the composition of saliva and its flow rate (1, 14, 15). One of the most common problems during pregnancy is gestational diabetes, the harmful effects of which on the mother and fetus are obvious (16). Hence, monitoring the serum glucose levels during this period is constantly needed. Another common disorder during pregnancy is oral problems, the most prevalent of which is tooth decay. One of the effective markers on saliva buffering is urea that is also a serum marker (1). Blood samples are the most common biological fluid used to diagnose and monitor diseases. However, saliva can be useful for diagnostic purposes instead of blood samples. The saliva contains substances produced by the salivary glands as well as serum components that can be collected to diagnose a variety of systemic diseases and to understand their oral manifestations. Of the undeniable benefits of saliva testing, we can refer to its cost-effectiveness and non-invasiveness for screening large populations (6, 11).

Lasisi & Abdus-Salam and Shimada et al reported changes in salivary markers during pregnancy and found that salivary levels of glucose and urea decreased during pregnancy (7, 17). This finding is consistent with

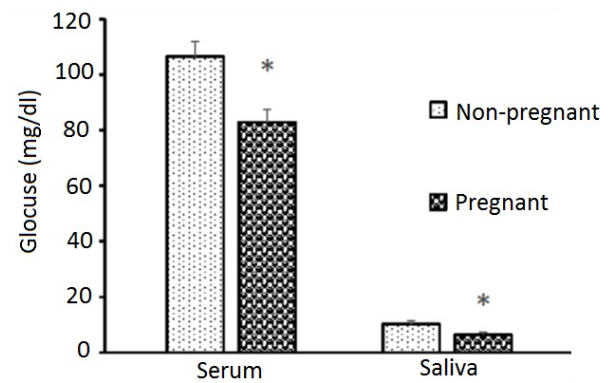**Figure 1.** Mean Serum and Salivary Glucose Concentrations in Pregnant and Non-pregnant Women. *Note.* *: A significant difference at $P < 0.05$.
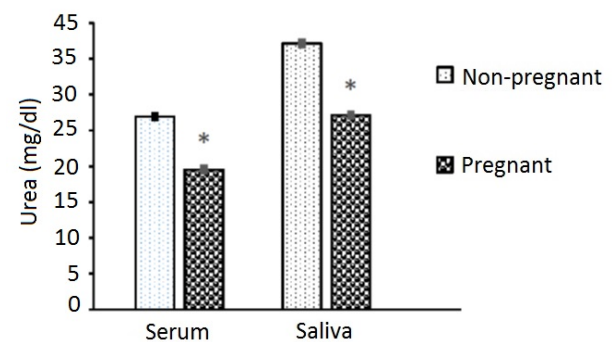

Figure 2. Mean Serum and Salivary Urea Concentrations in Pregnant and Non-pregnant Women. *Note.* *: A significant difference at $P < 0.05$.

the findings obtained in the present study in which we compared two salivary markers (i.e., glucose and urea) in pregnant and non-pregnant women. The reason for this consistency can be attributed to the type of statistical population tested in our study and these two researchers' study. In addition, all three studies examined salivary markers in pregnant women using photometry as the method of measuring markers. Furthermore, the sample size was close to each other; for example, Shimada et al studied 58 pregnant women with glucose metabolism disorders or hypertension and 40 healthy pregnant women, and we examined 30 pregnant women and 30 non-pregnant women. In the present study, we sought to investigate the effect of pregnancy on two serum markers, namely, glucose and urea. The results of the measurements indicated a reduction in the serum levels of these two markers during pregnancy, which is in line with the findings of Kalhan et al. The reason for this agreement could be the condition of the subjects so that the participants in both studies went for sampling on an empty stomach with no underlying diseases. In addition, the venipuncture method for serum preparation and the measuring method for glucose and urea in serum samples were the same in both studies. In other words, the venipuncture was performed from superficial veins in the cubital area, and the samples were immediately centrifuged. The serum glucose and urea levels were also determined using glucose and urea diagnostic kits (5).

Naseri et al and Bilancio et al reported a correlation

Table 1. Mean Saliva and Serum Glucose and Urea Levels in Pregnant and Non-pregnant Women

	Pregnant	Non-pregnant
Salivary glucose (mg/dL)	6.4±0.9	10.2±1.4
Serum glucose (mg/dL)	82.9±4.5	106.5±5.3
Salivary urea (mg/dL)	27.1±1.9	37.1±3.3
Serum urea (mg/dL)	19.5±2.3	26.9±1.9

between serum and salivary glucose levels and a correlation between serum and salivary urea levels, respectively (13, 18). Naseri et al, in a review of more than 373 studies, concluded that there was a correlation between serum and salivary glucose levels (13). Bilancio et al collected saliva and serum samples three hours after breakfast then froze them immediately, and measured the serum and salivary levels of urea by commercial urea kits. They found a correlation between serum and salivary urea levels. In the present study, we examined 30 pregnant women and 30 non-pregnant women, the results of which were consistent with the above-mentioned studies. The reason for this consistency of the results, despite the differences between the study groups, can be attributed to the methods of collecting samples and measuring serum and salivary markers (13, 18). Furthermore, Soares et al measured and compared the blood and salivary levels of glucose and finally found no correlation between the blood and salivary glucose concentrations. In addition, the methods of collecting samples and measuring serum and salivary glucose levels by Soares et al were similar to our study. However, their findings were inconsistent with our results probably due to the difference in the type of statistical population and sample size because Soares et al examined the patients with type 2 diabetes, but we studied pregnant and non-pregnant women (4). Likewise, Vasconcelos et al conducted a study to establish a correlation between serum and salivary levels of glucose, the results of which suggested that this correlation was inconsistent with the results of our study. The reason for this discrepancy could be the difference in the method of measuring serum glucose in the two studies, namely, Vasconcelos et al determined serum glucose using a glucometer, while we determined the serum glucose level using laboratory blood testing that is more accurate and reliable than the method used by Vasconcelos et al (12).

Conclusion
The results obtained from the present study demonstrated that the serum and salivary levels of glucose and urea in pregnant women were lower than those in non-pregnant women. Furthermore, there was a positive correlation between their serum and salivary levels; therefore, it seems that saliva can replace serum concerning the measurement of glucose and urea concentrations.

Ethical Statement
The present study was conducted after obtaining informed consent from all participants, and all records were anonymized and deidentified prior to the analysis. This study was approved by the ethics committee of Aja University of Medical Sciences (IR. AJAUMS.REC.1399.071).

Authors' Contribution
MSA contributed to the study design, concept, and editing of the manuscript. AD wrote the manuscript and performed the data collection. MSSA and SAKM contributed to the study design, concept, and editing of the manuscript.

Informed Consent
The present study was conducted after obtaining informed consent from all participants.

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