MMJ

Malta Medical Journal, 2025; 37(1)
http://mmsjournals.org/index.php/mmj/43

ORIGINAL ARTICLE

Pregnancy Outcomes among Patients with Inappropriate Sinus Tachycardia

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Background

About one percent of the population is affected by inappropriate sinus tachycardia. Little is known about this condition during pregnancy. Our objectives were to get a deeper understanding of the natural course of inappropriate sinus tachycardia in pregnancy and to investigate maternal and foetal outcomes.

Methods

Forty-two pregnant women with symptoms consistent with inappropriate sinus tachycardia were included in this observational cohort study and compared to 42 control pregnant women.

Results

No significant difference was found in age, twin pregnancy, diabetes, blood pressure, and hemoglobin level while the gravida of the inappropriate sinus tachycardia group was significantly lower than control (p-Value=0.002). The symptoms resolved in the majority (83%) of cases within 2 weeks of delivery. Pregnant patients with inappropriate sinus tachycardia have higher unscheduled hospital visits (38.1 vs 9.5%; p-Value=0.002) and induction of labor (45.2% vs 23.8%; p-Value=0.039)

Conclusion

Hospital visits and induction of labor were higher in pregnant patients with inappropriate sinus tachycardia which may not be necessary with more emphasis should be on empathic care and patient education.

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Approximately one percent of the population is affected by the well-known but partially understood syndrome of inappropriate sinus tachycardia.[1] Task force guidelines describe it as (1) heart rate that is more than 100 beats per minute at rest in sinus rhythm;(2) 24-hour mean heart rate of more than 90 beats per minute;(3) no secondary causes; and (4) the presence of symptoms including palpitations.[2] Exercise intolerance, shortness of breath, and palpitations may be very incapacitating despite the "benign" nature of inappropriate sinus tachycardia.[1] In the literature, however, little is known about inappropriate sinus tachycardia during pregnancy including its development and management. Similarly knowledge is scarce about how inappropriate sinus tachycardia can affect fetal and maternal health in pregnant patients.

Previous studies on inappropriate sinus tachycardia during pregnancy indicate that it is a rather common but underrecognized condition.[3,4] To present, the literature has just two further case reports.[5,6] In light of this, we attempted to investigate the fetal and maternal outcomes of patients with this syndrome through an observational cohort study.

MATERIALS AND METHODS

This prospective study was done between September 2020 and May 2022 during which 42 women with symptoms consistent with inappropriate sinus tachycardia were referred to Ibn al-Bitar Specialized Center for Cardiac Surgery (Baghdad Iraq). A comprehensive diagnostic workup was performed before delivery to firmly establish the diagnosis according to the task force expert consensus.[2] A control group of 42 pregnant patients was included. We exclude patients with a history of known inappropriate sinus tachycardia, hypertension, current use of beta-blockers or non-dihydropyridine calcium channel blockers (for the control), patient with heart failure, and renal failure or pulmonary hypertension, and any significant cardiopulmonary disease (for both groups). The research was authorized by the Local Medical Ethics Council and participants provided written informed consent.

A full medical history review and physical examination were undertaken, with an emphasis on the potential reasons for sinus tachycardia, including thyroid illness, medicines, and substances. All patients were examined for any evidence of hypovolemia (skin turgor, jugular venous pressure, and postural hypotension). A 12-lead ECG was used to detect tachycardia and establish its sinus origin to distinguish inappropriate sinus tachycardia from other supraventricular arrhythmias. Postural tachycardia syndrome (POTS) was ruled out since its symptoms are often exclusively triggered by orthostatic changes. Other potential causes like physiologic and psychological factors, panic attacks, and occult substance abuse were ruled out. Intensive investigation including thyroid function test, complete blood picture, C-reactive protein, Glomerular Filtration Rate (GFR), troponin level, plasma metanephrines, NT pro-BNP level, and echocardiography was done to exclude secondary causes.

Blood pressures were determined in both arms using a calibrated and automated blood pressure instrument (Contec ABPM50, Contec medical systems co., ltd) with the participant seated. Twenty-four hours Holter monitoring was done using Contec TLC5000 12-Channel Monitor (Contec medical systems co., Ltd).

Maternal outcomes were documented which include unscheduled hospital visits, induction of labor, cesarian section, antepartum/intrapartum bleeding, and post-partum bleeding. Fetal outcomes were documented which include preterm labor, postterm labor, fetal distress, meconium aspiration syndrome, APGAR[7] at 1 minute, and APGAR at 5 minutes.

STATISTICAL ANALYSIS

A normally distributed continuous variables were represented as mean with standard deviation as a measure of dispersion and compared across groups using the unpaired Student's t-test. The Mann–Whitney test was used to compare continuous, non-normally distributed data and represented as median and interquartile range. Categorical variables were represented as a number (with percentages) and the Chi-Square test was used to compare groups. A p-Value less than 0.05 was used as a threshold for statistical significance. Microsoft Office Excel 2019 and Statistical Package for the Social Sciences (SPSS) Version 26.0 for Windows (SPSS Inc., Chicago IL, USA) were used for conducting the analysis.

RESULTS

CLINICAL PRESENTATION

A definitive diagnosis of inappropriate sinus tachycardia during pregnancy was established in forty-two ladies and all of them have palpitations at rest or on exertion with reduced exercise capacity.

Table 1 *Baseline characteristics of the two study groups*

	IST, n=42	Control, n=42	p-value
Age, years	23.35±7.63	24.18±9.09	0.653
Gravida	2.94 [1.92-4.60]	4.52 [2.72-6.81]	*0.002*
Twin, n (%)	3 (7.1)	2 (4.8)	0.645
Diabetes, n (%)	2 (4.8)	3 (7.1)	0.645
Systolic BP, mmHg	108.38±8.71	109.82±6.71	0.397
Diastolic BP, mmHg	69.47±9.99	69.73±7.73	0.895
Hemoglobin, mg/dL	10.39±1.52	10.73±1.53	0.312
Maximum HR, bpm	119.56±11.11	85.98±15.54	*<0.001*
Holter Mean HR, bpm	101.65±5.78	78.34±8.96	*<0.001*

Abbreviations: n stands for Number; IST stands for inappropriate sinus tachycardia; BP stands for Blood Pressure; bpm stands for beats per minute; HR stands for Heart Rate

The mean age at the time of presentation was 23.35±7.63 years with gravida 2.94 [IQR 1.92-4.60] (39 singletons, 3 twins). A detailed history indicated the development of symptoms during the index pregnancy at 20.86±5.68 weeks of gestation. Comparing the inappropriate sinus tachycardia and control groups, no significant difference was found in age, twin pregnancy, diabetes, blood pressure, and hemoglobin level while the gravida of the inappropriate sinus tachycardia group was significantly lower than control as shown in Table 1.

All participants have sinus rhythm with no pathological arrhythmias detected by resting electrocardiogram and Holter monitoring. The maximal documented rest heart rate was 119.56±11.11 bpm in the inappropriate sinus tachycardia group vs 85.98±15.54 bpm in the control group with mean 24-h heart rates of 101.65±5.78 bpm in the inappropriate sinus tachycardia group vs 78.34±8.96 bpm in the control group as shown in Table 1. On Holter monitoring, diurnal heart rate fluctuation was retained, with a typical night drop with many daytime tachycardias (of variable duration).

Among the inappropriate sinus tachycardia group, 10 patients (23.8%) described prominent cardiac symptoms outside of pregnancy with inappropriate sinus tachycardia already diagnosed out of pregnancy in 4 patients (9.5%). In patients with a history of inappropriate sinus tachycardia, the presenting symptoms during the index pregnancy were unique and new; they were not a continuation or worsening of earlier symptoms. Nineteen out of 31 multigravida women (>1) had a history of symptoms in previous pregnancies (61.3%). Beta-blockers were used in 12 pregnant patients with inappropriate sinus tachycardia (28.6%). The symptoms resolved in the majority (83%) of cases within 2 weeks of delivery. Figure 1 shows these findings.

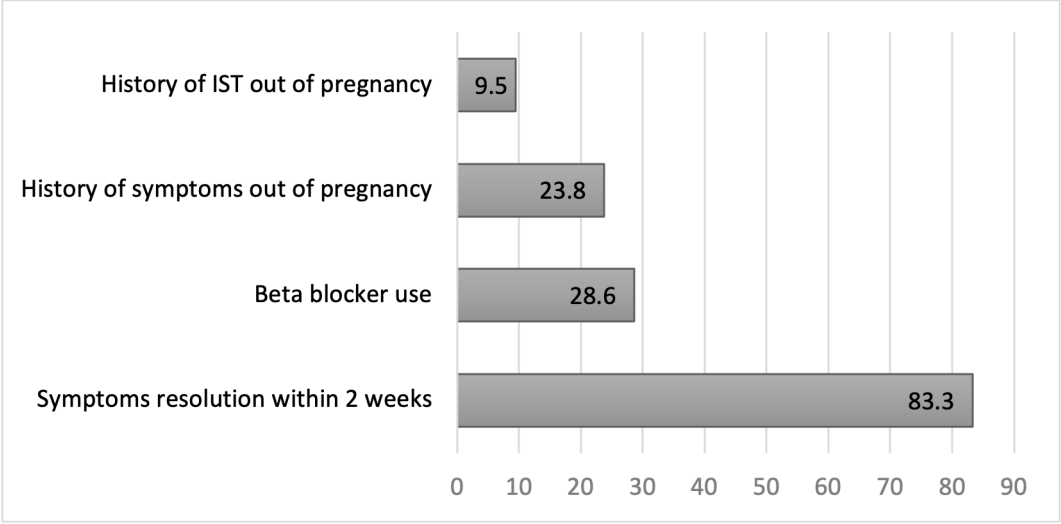

Figure 1 *Characteristics of patients with inappropriate sinus tachycardia, %*

MATERNAL AND FETAL OUTCOMES

Sixteen women (38.1%) with inappropriate sinus tachycardia had an unscheduled visit to the hospital on at least one occasion in comparison to 4 patients (9.5%) in the control group (p-Value=0.002).

No significant difference was found between the two groups regarding the rate of antepartum/ intrapartum and post-partum bleeding. During pregnancy, there were no maternal fatalities, cases of acute coronary syndrome or heart failure or thromboembolic, or hemorrhagic events.

There is a trend toward more Cesarian sections in the inappropriate sinus tachycardia group as compared to the control group which does not reach statistical significance (14 (33.3%) vs 7 (16.7%); p-Value=0.078). All cesarean sections were done for conventional obstetric reasons independent of the cardiac symptoms. The induction of labor was statistically higher (19 women; 45.2%); in comparison to the control group (10 patients; 23.8%) with a p-Value of 0.039. No significant difference was found between inappropriate sinus tachycardia and control groups regarding the rate of preterm or post-term labor, fetal distress, meconium aspiration syndrome, and APGAR at 1 and 5 minutes as shown in **Table 2**.

DISCUSSION

Our study demonstrates that pregnant women with inappropriate sinus tachycardia have lower gravida (which may be explained by a different personality traits and exaggerated response to emotional stress), more hospital admissions, and labor induction due to the poorly tolerable symptoms. An earlier study shares some of these findings but had a smaller sample size (19 patients) and lacks a control group, instead, it compares the findings to the background local and national rate.[4]

The inappropriate sinus tachycardia and control groups in this cohort generally have comparable characteristics. Given the small number of participating women, we acknowledge that care is required when assessing the relevance of the results.

The diagnosis of inappropriate sinus tachycardia based on task force guidelines [2] does not discriminate based on sex or the presence of pregnancy; thus, it may be used on pregnant women as in our cohort. Some may dispute this, arguing that the heart rate physiologic variations during pregnancy are more likely to cause sinus tachycardia at rest or exercise. Nevertheless we do not agree with that.

Hormones produced after conception cause vascular dilation and a decrease in peripheral arterial resistance. This is compensated by increasing the cardiac output to preserve an appropriate blood pressure (Cardiac output equal to stroke volume multiplied by heart rate). Stroke volume is enhanced by raising cardiac preload through fluid retention by the kidneys. Throughout pregnancy, the heart rate gradually rises by 10–20 beats per minute, from autonomic changes by baroreceptors, reaching a maximal heart rate in the last trimester.[8–10] Less than 10 percent of healthy pregnancies had heart rates greater than 100 beats per minute after 18 weeks of

Table 2 *Maternal and fetal outcomes in the study groups*

	IST, n=42	Control, n=42	p-value
Unscheduled Hospital Visit, n (%)	16 (38.1)	4 (9.5)	0.002
Induction of labor, n (%)	19 (45.2)	10 (23.8)	0.039
Cesarian Section, n (%)	14 (33.3)	7 (16.7)	0.078
Antepartum/Intrapartum Bleeding, n (%)	2 (4.8)	1 (2.4)	0.557
Post-Partum Bleeding, n (%)	3 (7.1)	4 (9.5)	0.693
Preterm Labor, n (%)	3 (7.1)	2 (4.8)	0.645
Post term Labor, n (%)	1 (2.4)	2 (4.8)	0.557
Fetal Distress, n (%)	1 (2.4)	0 (0)	0.314
Meconium aspiration syndrome, n (%)	0 (0)	1 (2.4)	0.314
APGAR at 1 minute	9.19±0.890	9.26±0.734	0.689
APGAR at 5 minutes	9.31±0.643	9.33±0.650	0.866

Abbreviations: n stands for Number; IST stands for inappropriate sinus tachycardia; APGAR stands for Appearance, Pulse, Grimace, Activity, and Respiration.

gestation and over 105 beats per minute after 28 weeks of gestation.[11–14] In the absence of an identified reason, we feel that a rest heart rate of more than 100 beats per minute during pregnancy should be regarded as abnormal. The usage of a mean heart rate higher than 90 beats per minute by 24-Hr Holter monitoring to diagnose inappropriate sinus tachycardia during pregnancy is not supported by evidence from studies that reported normal values specifically during pregnancy.

Most pregnant women in our study had symptoms only during pregnancy, with symptoms disappearance nearly immediately after delivery. In addition, around two-thirds of women had inappropriate sinus tachycardia-related symptoms during prior pregnancies with no symptoms out of pregnancy. This indicates that inappropriate sinus tachycardia during pregnancy may be a discrete condition.

Inappropriate sinus tachycardia during pregnancy may indicate an enhanced cardiac and autonomic physiological response in pregnancy, which is biologically acceptable. It is known that sympathetic tone increases and baroreceptor reflex sensitivity changes during pregnancy.[15,16] Women who developed inappropriate sinus tachycardia during pregnancy may have hormonal variations similar to those reported during the menstrual cycle, which may exacerbate these changes.[17] An increase in the HCN2 channel protein expression as reported in pregnant mice[18] may explain the raised sensitivity of the sinus node to the enhanced sympathetic tone.

The foundation of management is good communication and empathetic care. Regarding particular approaches, there is less data related to inappropriate sinus tachycardia in pregnancy; however, many of the treatments used to manage it in non-pregnant adults may be used.

Among the recommendations for a healthy lifestyle are adequate water intake and exercise.[19] These are useful in patients with postural orthostatic tachycardia and, given the number of similar physiological and clinical characteristics, may be used in women with inappropriate sinus tachycardia.[20,21]

It is possible to lower the sinus rate using pharmacological methods; however, it should be emphasized that this does not always result in symptom relief. Generally beta-blockers and non-dihydropyridine calcium channel blockers (diltiazem and verapamil) were utilized as first-choice treatments. But the use of these medications is limited by adverse effects.[22–24] Consequently ivabradine administered alone or with beta-blockers may alleviate symptoms, reduce heart rate, and improve patient tolerance.[25–30]

When prescribing during pregnancy, physicians are justifiably cautious. Labetalol has historically been the preferred beta-blocker during pregnancy, and its usage outside of the first trimester is not known to be detrimental. Bisoprolol, labetalol, metoprolol, and propranolol are classified as category C by the Food and Drug Administration (FDA). While atenolol should not be administered (category D). Breastfeeding is allowed if the mother is taking labetalol, metoprolol, or propranolol as stated by the American Academy of Pediatrics Committee on Drugs[31], while atenolol is present in breast milk at a higher level and is not included in their list.

Calcium channel blockers (diltiazem and verapamil) are considered category C by FDA The American Academy of Pediatrics Committee on Drugs states that breastfeeding is possible if the mother is taking verapamil or diltiazem.[31]

Although not specifically categorized, the FDA indicates that ivabradine may induce fetal injury during pregnancy as shown in animal research and

SUMMARY BOX

Facts known about inappropriate sinus tachycardia during pregnancy

- About one percent of the population is affected by inappropriate sinus tachycardia.
- Little is known about this condition during pregnancy
- Knowledge is scarce about how inappropriate sinus tachycardia can affect fetal and maternal health in pregnant patients

New findings from this study

- The gravida of the inappropriate sinus tachycardia group was significantly lower than control (p-Value=0.002).
- The symptoms resolved in the majority (83%) of cases within 2 weeks of delivery
- Pregnant patients with inappropriate sinus tachycardia have higher unscheduled hospital visits (38.1 vs 9.5%; p-Value=0.002) and induction of labor (45.2% vs 23.8%; p-Value=0.039)
- More emphasis should be on empathic care and patient education.

that its usage is not suggested during breastfeeding. Despite these warnings, ivabradine use during pregnancy has been reported to manage patients with inappropriate sinus tachycardia-induced cardiomyopathy.[5,6]

Sinus node ablation may be the most aggressive treatment option available. It is not always successful when applied to manage inappropriate sinus tachycardia in non-pregnant patients[32–36] and has the added harm of fetal irradiation in pregnant patients. Ablation has been reported as a therapy for severe tachyarrhythmias in pregnant women that are not caused by inappropriate sinus tachycardia.[37]

Specifically for inappropriate sinus tachycardia in pregnancy, labor often resulted in symptom alleviation. Numerous studies in different populations have shown that labor induction at term is safe for both mother and child[38–40], despite the fact that it is an intervention that not all women would prefer. All labor inductions were performed at term in our study. Given the "benign" prognosis of inappropriate sinus tachycardia, we emphasize the need for a conservative approach wherever feasible.

CONCLUSIONS

The pregnancies of women in this study were disrupted by many intolerable symptoms of exercise intolerance and palpitations with a higher incidence of labor induction and more unscheduled hospital visits. Inappropriate sinus tachycardia during pregnancy may constitute a unique arrhythmia, perhaps induced by an increased cardioautonomic reaction to pregnancy-related physiological changes. The emphasis of treatment should be on compassionate care, lifestyle modifications such as exercise and enough water intake, and patient education. Consider pharmacological treatments only for symptoms that are frequent and bothersome. We feel that this issue needs additional research with a higher sample number and longer follow-up; and investigation of therapeutic modalities. We anticipate that this publication will raise awareness of inappropriate sinus tachycardia during pregnancy.

ACKNOWLEDGMENTS

We gratefully thank the staff in Ibn al-Bitar Specialized Center for Cardiac Surgery for their support.

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