INTRODUCTION

Hypothyroidism is very well known to lead to abortions.\[1\] The reverse association of parity and abortions with future risk of hypothyroidism has also been recently shown to exist.\[2,3\] Fetal microchimerism that occurs after pregnancy and abortions has been shown to be responsible for this.\[4\] Fetal microchimerism is defined as the presence of fetal cells in maternal tissues.\[5\] Although fetal cells enter maternal circulation in most pregnancies, the fetal loss (abortion) is more likely to induce fetal microchimerism.\[6\] Some investigators, however, believe that microchimeric cells are the innocent bystanders and are not responsible for hypothyroidism in females.\[7\] We conducted a case–control study to investigate the odds of “abortion in the past” in the newly diagnosed hypothyroid females compared to their age-matched euthyroid controls.

METHODOLOGY

Type of study
Case–control study; duration: 1 year (January–December 2016); setting: Department of Medicine, Tertiary care 785 bedded teaching hospital in the Sub-Himalayan Region of North India

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Null hypothesis
The odds of a past abortion in newly diagnosed hypothyroid females are not significantly higher than that in their age-matched euthyroid females.

Alternative hypothesis
The odds of a past abortion in newly diagnosed hypothyroid females are significantly higher than that in their age-matched euthyroid females.

Definitions
Newly diagnosed hypothyroidism
It was defined as the signs and symptoms suggestive of hypothyroidism along with the biochemical values of serum thyroid stimulating hormone (TSH) levels of ≥5 mIU/L in the presence of low free T3 or free T4. Clinical features were noted for all hypothyroid females.

Autoimmunity
It was defined positive when thyroid peroxidase (TPO) antibody level was ≥30 U/ml.

Exclusion criteria
In the absence of signs and symptoms suggestive of hypothyroidism, patients with serum TSH level of <10 mIU/L and normal free T3/free T4 were excluded from the study.

Cases
We enrolled all consecutive newly diagnosed married hypothyroid females presenting in the Department of Medicine over 1 year as the cases.

Controls
Age-matched controls were selected by a convenient random sampling from the females attending the outpatient Department of Medicine for minor unrelated complaints. Hypothyroidism (TSH level >5 mIU/L) was ruled out in controls. Controls belonged to the same geographic area as the cases.

Exposure variable
We checked the exposure variable, i.e., past abortion (elective or therapeutic) in the cases and controls.

Statistical analysis
The data were analyzed using SPSS software (version 23, SPSS, Inc., Chicago, IL, USA). The continuous variables were expressed as means and standard deviations, and categorical variables were expressed as proportions. The comparison of continuous variables was done using t-test, and categorical variables were compared using Fisher’s exact. An alpha error of 95% was considered statistically significant (P < 0.05).

Approval from ethics committee was obtained for this study, and informed consent was obtained from the participants before enrollment.

RESULTS

Newly diagnosed hypothyroid females
We enrolled 120 married females with newly diagnosed hypothyroidism as the cases, and 176 age-matched euthyroid married females as the controls. Cases and controls had a mean age 42.2 ± 9.8 years and 41.1 ± 12.4 years, respectively, they shared a similar socioeconomic and cultural background.

Mean TSH of the cases and controls was 31.7 ± 26.6 mIU/L (range 8–100 mIU/L) and 2.28 ± 0.87 (range 0.5–4.5 mIU/L) (P < 0.0001).

The exposure variable, i.e. the history of abortion (elective or therapeutic) was present in 71 (59%) cases and 10 (6%) controls. Odds ratio (OR): 23.5 (12.2–48.9) P < 0.0001 [Table 1].

TPO positivity and negativity among the cases were documented in 92/120 (77%) and 29/120 (33%), respectively. A history of past abortion among TPO positive and negative hypothyroid cases was 57/92 (62%) and 14/28 (50%), respectively (P = 0.28).

Other important signs among the hypothyroid cases were loss of lateral third of eyebrows in 14 (11.5%), goiter in 4 (3.3%), slowness of speech in 31 (25.8%), and delayed relaxation of Achilles tendon reflex in 27 (22.5%) females.

DISCUSSION
Hypothyroidism leads to abortions and stillbirths; this is known for long. The reverse phenomenon that abortion leads to hypothyroidism in later life is a relatively new finding in biology. Studies show that abortions and parity are both associated with future autoimmune diseases in females. This association was strongest for the autoimmune hypothyroidism.

The available evidence is contradictory; some show a positive association of parity with future hypothyroidism; others show no association.
Our case–control study showed a significant association between newly diagnosed hypothyroidism and past abortions in females living in the Sub-Himalayan Region of North India. OR of 23.5 and \( P < 0.0001 \).

Fetal microchimerism has been held responsible for the development of autoimmunity in females. It becomes established during pregnancy and is aided by the maternal immune suppression in pregnancy by the placenta.\(^5\) Fetal microchimerism may persist in the postpartum period for decades after the last pregnancy or abortion.\(^5\) High OR (23.5; \( P < 0.001 \)) for past abortion in the cases aged 42.2 ± 9.8 years, in our study, shows that the risk for hypothyroidism persists for a lifetime after an abortion.

The identification of fetal cells that persist preferentially in maternal tissues subject to autoimmunity, such as skin and thyroid, has also suggested the possible immune modulation of the autoimmune response at the target tissue by fetal cells.\(^5,\,8\) The exact mechanism of fetal microchimerism leading to autoimmune hypothyroidism is yet unclear. There are 4 possible hypotheses related to microchimerism with sufficient supporting evidence for each one of them:\(^11\) (1) microchimerism-induced graft versus host reaction; (2) microchimerism Induced host versus graft reaction; (3) microchimeric cells repair injured tissues resulting in their concentration in injured tissues; and (4) microchimeric cells are innocent bystanders.

TPO positive and negative females had a history of past abortion 62% and 50%, respectively \( (P = 0.28) \); thus, abortion is equally associated with TPO positive and negative forms of hypothyroidism. This is a new finding and needs corroboration in a larger sample size study.

**Limitations**

This is a clinical study done in a single center. Controls were selected as a convenient random sample from the outpatient department. The controls were matched only for age but not for other variables such as hypertension, diabetes, and dyslipidemia.

**Strengths**

A total of 120 newly diagnosed females were studied over 1 year as cases, which is a large enough sample to conduct a case–control study. The controls were age-matched and belonged to the same geographic region as controls.

**CONCLUSION**

Our study suggests that abortion (elective or therapeutic) in the past is strongly associated with newly diagnosed hypothyroidism in females aged 42.2 ± 9.8 years. OR: 23.5 \( (P < 0.0001) \). Interestingly, abortion was associated with both, TPO positive and negative hypothyroidism.

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**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES**

1. Zhang Y, Wang H, Pan X, Teng W, Shan Z. Patients with subclinical hypothyroidism before 20 weeks of pregnancy have a higher risk of miscarriage: A systematic review and meta-analysis. PLoS One 2017;12:e0175708.
2. Friedrich N, Schwarz S, Thonack J, John U, Wallaschofski H, Voelke H. Association between parity and autoimmune thyroiditis in a general female population. Autoimmunity 2008;41:174-80.
3. Carlé A, Pedersen IB, Knudsen N, Perrild H, Ovesen L, Rasmussen LB, et al. Development of autoimmune overt hypothyroidism is highly associated with live births and induced abortions but only in premenopausal women. J Clin Endocrinol Metab 2014;99:2241-9.
4. The Role of Fetal Microchimerism in Autoimmune Disease. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2894651/. [Last accessed on 2017 May 13].
5. Ando T, Davies TE. Clinical review 160: Postpartum autoimmune thyroid disease: The potential role of fetal microchimerism. J Clin Endocrinol Metab 2003;88:2965-71.
6. Khosrotehrani K, Johnson KL, Dupuy A, Cha DH, Bianchi DW. The influence of fetal loss on the presence of fetal cell microchimerism: A systematic review. Arthritis Rheum 2003;48:3237-41.
7. O’Donoghue K. Pregnancy and the risk of autoimmune disease: An exploration. Chimerism 2011;2:84-5.
8. Klintschar M, Immel UD, Kehlen A, Schwaiger P, Mustafa T, Mannweiler S, et al. Fetal microchimerism in Hashimoto’s thyroiditis: A quantitative approach. Eur J Endocrinol 2006;154:237-41.
9. Walsh JP, Bremner AP, Bulsara MK, O’Leary P, Leedman PJ, Feddema P, et al. Parity and the risk of autoimmune thyroid disease: A community-based study. J Clin Endocrinol Metab 2005;90:5309-12.
10. Sgarbi JA, Kasamatsu TS, Matsumura LK, Maciel RM. Parity is not related to autoimmune thyroid disease in a population-based study of Japanese-Brazilians. Thyroid 2010;20:1151-6.
11. Lepez T, Vandelooestyn M, Deforce D. Fetal microchimeric cells in autoimmune thyroid diseases: Harmful, beneficial or innocent for the thyroid gland? Chimerism 2013;4:111-8.