Pregnancy Outcome and Health Status of The Offspring of Differentiated Thyroid Cancer Patients, Who Accidentally Conceived within two years of Radioiodine Ablation Therapy

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ABSTRACT

Objectives: To assess the pregnancy outcome and health status of the offspring of women conceived within 2 years of RAI therapy.

Study design: A case control study of 27 pregnant women, where evaluation of pregnancies and health status of offspring in further follow-up were done of 17 cases who got pregnant within 2 years of receiving radioiodine therapy for differentiated thyroid cancer, and the control group consisted of 10 healthy pregnant women of the same age group without any thyroid disorder.

Results: Among 17 cases, 8 (47.0%) were conceived within one year of the administration of I-131. One (5.9%) of 17 patients had hypertensive crisis (pre-eclampsia), and two (11.7%) showed preterm labor, which was not significant and not dependent on the therapeutic dose of ^{131}-I or time interval. The mean birth weight (2972.4 ± 376.7 gm) and birth length (46.1±2.6 cm) of children in the study cases were significantly lower compared to children in the control group (3230 ± 179.5 gm; 49.2 ± 1.1 cm). No congenital anomaly, abnormal thyroid hormone level, or sonographically detectable thyroid gland abnormality were found. The normal neuropsychomotor development of their children and good school performances were assured. There was no case of miscarriage, stillbirth, or neonatal death. All the children are healthy now.

Conclusion: Although the study showed that radioiodine therapy has no significant effect on pregnancy outcomes or the health status of offspring, precautions should be taken to avoid risky pregnancies, and patients should be encouraged to conceive after an adequate time interval after therapy.

Keywords: Pregnancy outcome, Health status of offspring, Radioiodine therapy

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INTRODUCTION

Radioactive iodine (^{131}I) therapy (RAI therapy) is worldwide accepted as a treatment for differentiated thyroid carcinoma (DTC) due to its effectiveness in preventing relapse and treating metastases. It has been used for more than 80 years in treating DTC patients (1-4). Since young females of reproductive age compose the majority of DTC (4–8), pregnancy is common after the radioiodine ablation for thyroid carcinoma.

Radiation has a mutagenic effect on germ cells, which may result in abortion, premature birth, stillbirth, and genetic damage to offspring, including congenital anomalies or even malignancy (9, 10). To avoid such effects, at least a one-year interval between therapeutic administration of radioiodine and conception has been recommended (11).

In different nuclear medicine institutes in Bangladesh, we recommend female patients of childbearing age not to conceive within 2 years following RAI ablation to assure a safe pregnancy outcome and healthy offspring. But, due to illiteracy, ignorance, irregularity of the menstrual cycle after therapy, or unwillingness to use any contraceptive method, especially for patients with low socio-economic conditions, they often conceive accidentally within the interval period. Being informed of the adverse effects of radiation during pregnancy and on offspring, many patients plan induced abortions. However, few of them want to continue pregnancy because of socio-religious issues, valuable

pregnancy, familial issues (like a husband staying abroad for a long period), etc.

The objective of the study was to assess the pregnancy outcome and health status of the offspring of women who accidentally conceived within 2 years of RAI therapy and wanted to continue pregnancy. We also compared the single-fetus pregnancy outcome and health status of offspring to another group of 10 healthy women with no thyroid disease.

PATIENTS AND METHODS

A total of 17 young registered DTC patients attending the National Institute of Nuclear Medicine and Allied Sciences (NINMAS) and the Institute of Nuclear Medicine and Allied Sciences (INMAS), Bogura, between the periods of 2009 and 2018, reported pregnancy during the risk period of post ablation. Among the 17 study patients, 9 had a previous (before diagnosed as DTC) singleton pregnancy with healthy children, 2 had a previous history of induced abortion, and 6 had no history of pregnancy or abortion. Eight patients received 75 mCi, 5 patients received 100 mCi, and 4 patients received 150 mCi of ^{131}-I as ablation therapy. They have been treated with an optimal suppressive and replacement dose of levothyroxine and followed up systematically at regular intervals after RAI therapy. According to protocol and follow-up after 1 year of therapy, whole-body diagnostic scintigraphy was performed 72 hours after administration of 5 mCi of I-131 in 6 patients. Eight (08) of them got pregnant by that time (1 year), and three patients did not come for a diagnostic whole-body scan on routine follow-up after 1 year of therapy.

During the first trimester of pregnancy, levothyroxine dosage and TSH level were carefully monitored, and the mothers were asked to monitor pregnancy events. Between 18 and 21 weeks of pregnancy, they are requesting an ultrasonographic anomaly scan. Mothers in their last trimester were requested for the following data about the newborn baby: birth weight, birth length, gender, congenital anomaly, and thyroid stimulating hormone (TSH) level of the newborn baby's blood at the 1st and 2nd weeks of birth. After birth, the mother was requested to check on the baby's developmental milestones, mental status, and school performances. The thyroid ultrasonography was performed to check the thyroid gland, and the complete blood count (CBC) and thyroid hormonal status of the children were monitored annually.

The control group consisted of 10 healthy single-fetus consecutive pregnant women with no thyroid disease (normal thyroid hormones, TSH hormone, and negative thyroid peroxidase antibodies level) who attended the Gynaecology and Obstetrics outdoor of Mohammad Ali Sadar Hospital, Bogura, from 2016 to 2019 with an age range of 19 to 32 years (mean 24 ± 3.8 years).

Standard descriptive statistical analyses were performed, including distribution rates for categorical data and the calculation of means and standard deviations for continuous variables. Statistical analysis was evaluated using the software tool Statistical Package for Social Sciences (SPSS 16.0). The chi-square test was used for differences of proportions and the student's t-test for differences between the means. The adopted level of significance was $\alpha = 0.05$ ($p \leq 0.05$).

RESULT

Table 1 shows the demographic distribution of the study population. The mean age of the study population at the time of conception varied from 19 to 36 years (mean 27 ± 4.2 years). The control group consisted of 10 healthy single-fetus pregnant women with a range of 19 to 32 years (mean 24 ± 3.8 years). The student's t-test showed no significant difference between the studied and control groups.

Among 17 pregnant women, 8 (47.0%) conceived within one year of the administration of ^{131}-I. Table 2 shows the pregnancy events in the study population. One (5.9%) of 17 patients had a hypertensive crisis (pre-eclampsia), and two (11.7%) showed preterm labor, which was not significant. Table 3 shows detailed medical records of study populations and we observed that preterm labor was not dependent on the therapeutic dose of ^{131}-I or time interval.

Table 1: Demographic distribution of study population (n=17)

Variables	Number of patients	Range or %
Age (year) mean ± SD	27 ± 4.2	19-36
Type of carcinoma		
Papillary thyroid carcinoma	9	52.9
Follicular variant of papillary carcinoma	4	23.5
Papillary thyroid carcinoma with LN metastasis	4	23.5
Ablation dose		
≤100	13	76.5
>100	4	23.5
Interval (months) I-131/pregnancy		
6-9	4	23.5
10-12	4	23.5
13-15	5	29.4
16-19	4	23.5
Previous obstetric history before therapy		
Healthy child	9	52.9
Abortion	2	11.7
No previous history of pregnancy	6	35.3

Table 2: Pregnancy status of study population (n=17)

Variable	Number of patients	Range or %
Pregnancy events		
Risk of miscarriage	0	0
Placental insufficiency	0	0
Eclampsia/Pre-eclampsia	0/1	0/5.9
Placental detachment	0	0
Preterm labour	2	11.7
Sonographically detectable anomaly		
Present	0	0
Absent	17	100

Table 3: Birth status and present state of health of offspring (of study population) with administrative dose and time interval therapy/conception

Case	F/U period (years)	I-131 dose	Time interval Therapy & Conception (months)	Birth status						Further health status of offspring				
				Birth health	Sex M/F	Weight (gm)	Length (cm)	Congenital anomaly (yes/no)	TSH level at birth (normal / abnormal)	Developmental delay (yes/no)	Mental retardation	School performance	Last thyroid hormone & CBC status (normal/ abnormal)	Thyroid ultrasound
1	13	100	10	Term	M	3100	47	No	Normal	No	No	Good	Normal	Normal
2	11	100	8	Term	F	2940	44	No	Normal	No	No	Good	Normal	Normal
3	10	150	17	Term	F	3050	46	No	Normal	No	No	Good	Normal	Normal
4	9	100	13	Term	F	2820	46	No	Normal	No	No	Good	Normal	Normal
5	9	100	16	Term	M	3000	48	No	Normal	No	No	Good	Normal	Normal
6	8	150	11	Term	F	3140	49	No	Normal	No	No	Good	Normal	Normal
7	8	75	9	Term	M	3050	46	No	Normal	No	No	Good	Normal	Normal
8	7	100	14	Term	M	3520	51	No	Normal	No	No	Good	Normal	Normal
9	6	75	10	Term	F	3070	46	No	Normal	No	No	Good	Normal	Normal
10	6	75	18	Preterm	M	2120	41	No	Normal	No	No	Good	Normal	Normal
11	6	75	13	Term	F	3200	48	No	Normal	No	No	Good	Normal	Normal
12	6	150	11	Preterm	F	2060	41	No	Normal	No	No	Good	Normal	Normal
13	5	75	14	Term	M	3140	47	No	Normal	No	No	Good	Normal	Normal
14	5	75	15	Term	F	3410	49	No	Normal	No	No	-	Normal	Normal
15	5	75	7	Term	F	2900	45	No	Normal	No	No	Good	Normal	Normal
16	5	150	19	Term	M	3150	46	No	Normal	No	No	-	Normal	Normal
17	4	75	8	Term	M	2860	44	No	Normal	No	No	-	Normal	Normal

Table 4: Birth status and present state of health of offspring of control group (N=10)

Case	Birth health	Sex M/F	Weight (gm)	Length (cm)	Congenital anomaly (yes/no)	TSH level (normal/ abnormal)	Developmental delay (yes/no)	Mental retardation	School performance	Last thyroid hormone & CBC status (normal/ abnormal)	USG of thyroid gland
1	Term	F	3400	50	No	Normal	No	No	Good	Normal	Normal
2	Term	F	3140	49	No	Normal	No	No	Good	Normal	Normal
3	Term	M	3260	49	No	Normal	No	No	-	Normal	Normal
4	Term	F	3100	49	No	Normal	No	No	Good	Normal	Normal
5	Term	M	3500	51	No	Normal	No	No	-	Normal	Normal
6	Term	F	3140	49	No	Normal	No	No	-	Normal	Normal
7	Term	M	3050	48	No	Normal	No	No	Good	Normal	Normal
8	Term	M	3520	51	No	Normal	No	No	-	Normal	Normal
9	Term	F	3070	48	No	Normal	No	No	-	Normal	Normal
10	Term	F	3120	48	No	Normal	No	No	-	Normal	Normal

Tables 3 and 4 also show the birth status and present health status of the offspring of the study populations and the control group in detail. All the children are healthy now. The mean birth weights of children in our cases are significantly lower compared to children in the control group (Table 5). We also found a statistically significant difference in the birth length of the offspring of the studied group (46.1 ± 2.6 cm) and that of the control group (49.2 ± 1.1 cm), p = 0.0015 (Table 5)

Table 5: Birth status and present state of health of offspring according to group

Variable	Case (n=17)	Control (n=10)	p-value
Term birth	15	10	0.1697
Mean birth weight (gm ± SD)	2972.4 ± 376.7	3230 ± 179.5	0.0542
Birth length (cm ± SD)	46.1±2.6	49.2 ± 1.1	0.0015
Congenital anomaly	0	0	
Abnormal TSH level	0	0	
Developmental delay	0	0	
Mental retardation	0	0	
Abnormal thyroid hormone level	0	0	
Abnormal complete blood count	0	0	
Sonographic abnormality of thyroid gland	0	0	

No congenital anomaly, abnormal thyroid hormone level, or any sonographically detectable thyroid gland abnormality was found in any of the children in the study population. All the mothers spoke about the normal neuropsychomotor development of their children and their good school performances so far. There was no case of miscarriage, stillbirth, or neonatal death.

DISCUSSION

Temporary gonadal damage (depression of spermatogenesis) in male or ovarian failure (amenorrhea or irregular menses) in female patients has been reported in a few previous studies, for which patients may experience difficulty conceiving for a short period after radioiodine therapy. But when a patient gets pregnant, questions arise about the effect of radiation during pregnancy, the pregnancy outcome, or the further health status of the offspring. Data on the genetic effects of I-131 therapy in thyroid disorders are scant. Studies on pregnancy in patients treated with radioiodine for thyrotoxicosis (12–14) or thyroid cancer have not revealed any significant effects (15–17), except for a few cases of miscarriage and stillbirth. Hence, few authors recommended that an interval between administration of radioiodine and conception reduce the risk of pregnancy complications and help in a good pregnancy outcome (11). Additionally, a well-controlled thyroid hormone level has been recommended to avoid pregnancy complications associated with iatrogenic hypothyroidism or hyperthyroidism (18).

Study patients were followed up closely with the aim of controlling serum TSH levels and being scanned for fetal anomalies within 18–21 weeks. Pregnancy was continued when a sonographically detectable fetal anomaly was not found. Uneventful pregnancies were observed in all the patients except for two preterm labors. This observation differs from Schlumberger et al. (19), who reported a high incidence of miscarriage in pregnancies occurring within one year of radioiodine ablation.

A group of researchers observed three cases of congenital anomalies (Trisomy 18, aplastic anemia, and congenital hip dysplasia) in children who were conceived within one year of I-131 administration (1). But the present study showed no evidence of such genetic damage in the offspring, even in cases of just 7 months of 75 mCi (lowest interval time) or 11 months of 150 mCi (lowest interval time with highest dose) radioiodine therapy.

We only observed significant differences in the mean birth weight and mean birth length of the fetuses of our cases and healthy control mothers. But all of the cases underwent a caesarean section for risk-free delivery at least one or two weeks before the expected date, which may cause a reduction in the mean birth weight and length. Otherwise, the offspring, including the preterm babies, are in good health so far, with normal thyroid functional status, a normal complete blood count, and developmental milestones like normal healthy children.

Although our study with a handful of data showed no significant complicating effect of radioiodine therapy on pregnancy period and radiation-related genetic damage to offspring, we cannot conclude that conception within a short period of RAI therapy is safe. Rather, precautions should be taken for women of childbearing age. They should be properly informed about the radiation effect, advised to avoid risky pregnancies, and encouraged to conceive after an adequate time interval after therapy.

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