RESEARCH ARTICLE

Prevalence of subclinical hypothyroidism in pregnant females of Kashmir, India

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Objectives: The objective of our study was to find the prevalence of subclinical hypothyroidism in pregnant females of Kashmir. This was done so as to assess the magnitude of the problem in the valley and to formulate a strategy based on its results.

Methods: The study was done over a period of one year from July 2009 to July 2010 in Government Medical College, Srinagar. Pregnant females attending the out-patient department of Gynecology and Obstetrics, for their routine antenatal check-ups, formed our study population. Their blood samples were taken for estimation of serum FT3, FT4 and TSH levels.

Results: Most of our patients were in the age group of 25-29 years, comprising 45.3% of the total subjects. Out of the total 902 patients, TSH was within range in 788 (87.4%) and elevated in 114(12.6%). In control group (age matched non pregnant females), 91.4% had TSH in normal range while 8.6% had elevated levels. FT4 was within range in 96.2%, low in 3.2% and raised in 0.6% in cases, while as in controls, the percentages were 92.5%, 5.4% and 2.2% respectively. Hence the prevalence of subclinical hypothyroidism (Increased TSH within normal FT4) was 12.6% in cases and 8.6% in controls.

Conclusion: A high prevalence of subclinical hypothyroidism was found in pregnant females. Therefore, thyroid screening should be made important in pregnancy and threshold for treating subclinical hypothyroidism should be kept low.

Keywords: Subclinical hypothyroidism; pregnant females; thyroid hormones

INTRODUCTION

The subclinical and clinical forms of hypothyroidism are emerging as potential contributors to morbidity from osteoporosis, cardiovascular and neuropsychiatric disease, which has resulted in routine investigation of thyroid function in almost all patients [1,2].

Hypothyroidism including subclinical hypothyroidism occurs in about 2.5% pregnancies. The etiology is usually autoimmune thyroiditis. Other causes of hypothyroidism in pregnancy include postoperative thyroid failure and non-compliance with thyroxine therapy. The effects of subclinical hypothyroidism in pregnancy include increased incidence of premature birth, placental abruption, low birth weight, low Apgar score, increased need for caesarian, hypertension in mothers, increased neonatal mortality and neuropsychiatric abnormalities in children [3,4].

METHODS

The study was conducted over a period of one year from July 2009 to July 2010 at Government Medical College, Srinagar. Pregnant females visiting the out-patient department of Gynecology and Obstetrics, Lal Ded Hospital, Srinagar (Associated hospital of Government Medical College) for their routine antenatal check-ups, formed our study population. Three months for developing protocol, Six months for data collection and the next four months for data analysis ,follow up and interpretation of results.

As per the official registration, nearly 500 pregnant women visited Lal Ded Hospital per day which means near 1,20,000 patients per year. About 10% per 1,000 of the above population was taken as sample size for the study. The selection of patients was done by simple random sampling by the technique of systematic sampling. Non-pregnant females, in age group of 25-29 years, with no previous thyroid complaints, visiting OPD formed our control group, with their total number being 10% of the study group.

The prevalence of 2.5% subclinical hypothyroidism in pregnant females was plugged in the SSCPS version 1001 software with the suggested desired precision of 0.013, yielded the sample size of 550. Keeping with the financial implications, time constraint, utility of human resource and patient intake from all across the Kashmir valley, the minimal design effect multiple of 1.5 advocated to have at least 825 pregnant women in the study. Systematic random sampling was adopted at an interval of 5 visiting pregnant women in the listed clinic that were picked at a rate of 15-21 twice a week. This accumulated to the total sample of 902 during the sample collection study period of six months.

A detailed history, especially family history of hypothyroidism was taken and general physical and systemic clinical examination was done, particularly in relation to any unnoticed symptoms related to thyroid dysfunction.

Exclusion criteria

Patients recovering from serious illness, patients receiving recombinant TSH injections and women taking any drug known to influence thyroid hormone measurement.

After obtaining their consent, blood samples were withdrawn, about 4ml of blood was drawn from the anterior cubital vein and collected in a vacutainer. The collected sample was allowed to stand undisturbed at room temperature for about 2 hours. Then the blood sample was centrifuged at 3000 revolutions/minute for about 5 minutes which helped in quick separation of serum. The separated serum was poured into sample cups which were fitted into adaptors on the 'analyzer', the adaptors were numbered, sample ordering was done and the selective keys on the 'auto analyzer' were used to feed the required information.

The serum was analyzed in "The Elecsys 2010 analyzer"; manufactured by Roche Diagnostics Gmbh, Germany, using the ECL (Electro chemi luminescent process). The electro chemiluminescence immuno assay "ECLIA" is considered to be highly sensitive method for estimation of serum FT3, FT4 and TSH levels [5-7].

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Statistical analysis

Data was expressed as mean ± S.D. and percentages. All the intergroup comparisons were made by Student's 't' test for parametric data and Mann Whitney 'U' test for non-parametric data. P value of less than 0.05 was considered significant. The software used for data analysis was SPSS 11.2, minitab and MS Excel.

RESULTS

Most of our patients were in the age group of 25-29 years, comprising 45.3% of the total studied subjects and mean age was 28.3 ± 4.2. Our control population was also in the same age group (25-29 years), comprising 46.2% with mean age being 28.5 ± 4.2 years. The pregnant females attending the outpatients department of our hospital range from 18 years to 35 years overall. But out of the total age, around 50% fall in age group 25-29 years followed by 25% falling in 30-35 years, followed by 17% falling in age group of 20-24 years.

Rural population comprised of about 83.8% in cases and 87.1% in controls, while as urban population constituted about 16.2% in cases and 12.9% in controls. The difference between study and control groups with regard to above parameters was not significant.

Out of the total studied 902 patients, 714 (79.2%) had no complaints, while 3.3% had cold intolerance, 5.8% had edema, 3.2% were hypertensive, 3.5% had hoarseness of voice and constipation was seen in 5.4% population. Amongst the controls, 88.2% had no complaints; 5.4% had cold intolerance, 3.2% had edema and 2.2% had constipation. Hypertension was seen in 1.1% while hoarseness of voice was not seen amongst control group. 79.7% of the total studied population had no relevant past history while as 7% had history of hypertension, 7.8% had menorrhagia while 5.5% had oligomenorrhoea in the past. Amongst controls, 4.3% had menorrhagia, 3.2% had oligomenorrhea, 1.1% where hypertensive in past and 91.4% had no significant past history. The difference between cases and controls with regard to above parameters was significant (Table 1).

Table 1 Presenting Characteristics of the Studied Subjects.

		Study		Control		P value
		n	%	n	%	
Relevant Table Present History	Normal	714	79.2	82	88.2	0.021 (Sig)
	Cold Intolerence	30	3.3	5	5.4	
	Edema	52	5.8	3	3.2	
	Hypertensive	29	3.2	1	1.1	
	Constipation	49	5.4	2	2.2	
	Hoarseness of Voice	32	3.5	0	0	
Relevant Past History	Normal	719	79.7	85	91.4	0.009 (Sig)
	Hypertensive	63	7	1	1.1	
	Oligomenorrhoea	50	5.5	3	3.2	
	Menorrhagia	70	7.8	4	4.3	

About 87.8% of the study population had insignificant history of previous pregnancies. Preterm delivery was seen in 6.5% and abortion in 5.7%. Amongst control group, 91.1% had no significant history while as 3.6% had abortions and 5.4% had preterm delivery. Among control population, 38.7% were nulliparas while as 61.3% were multiparas, showing difference between study and control groups to be insignificant.

Mean FT3 in study and control population was 4.7 ± 0.8. Mean FT4 in study group was 13.7 ± 1.7 and in controls, it was 13.6 ± 1.4. TSH in study group was 3.8 ± 2.9 and was similar in control group. Anti TPO antibody titres were done in few patients more so in those with highly increased TSH. It couldn't be done in all due to financial constraints (Table 2).

Table 2 Thyroid Profile and Anti-TPO antibodies.

	Study group mean ± SD	Control group mean ± SD	p value
Free T3	4.7 ± 0.8 (1.0, 6.7)	4.7 ± 0.8 (1.0, 6.7)	0.276 (NS)
Free T4	13.7 ± 1.7 (10.2, 28.1)	13.6 ± 1.4 (10.2, 20.0)	0.389 (NS)
TSH	3.8 ± 2.9 (0.4, 21.7)	3.2 ± 1.8 (0.4, 10.6)	0.071 (NS)
Anti TPO	33 (3.7%)	0 (0.0%)	0.61 (NS)

TSH was within range in 788 (87.4%) and raised in rest 114 i.e. 12.6% amongst cases. In control group, 91.4% had TSH in normal range and in 8.6%, it was found raised. FT4 was within range in 96.2%, low in 3.2% and raised in 0.6% in cases, while as in controls, the percentages were 92.5%, 5.4% and 2.2% respectively. The difference between these groups is insignificant. Hence the prevalence of subclinical hypothyroidism (TSH increased within normal FT4) in cases was 12.6% and in controls it was 8.6% (Table 3).

Table 3 Prevalence of Sub Clinical Hypothyroidism.

		Study		Control		p value
		n	%	N	%	
TSH	Raised	114	12.6	8	8.6	0.259 (NS)
	Normal	788	87.4	85	91.4	
	Low	29	3.2	5	5.4	
Free T4	Raised	5	0.6	2	2.2	0.086 (NS)
	Normal	868	96.2	86	92.5	

Out of the total cases, 30 females were having cold intolerance, 19 of which were having raised TSH i.e. 63.3% and 31.3% had hoarseness of voice. Next major symptoms was edema in 21.1% cases, constipation in 14.3%, hypertension in 10.3% while as 8% females with raised TSH had no relevant complaints. Out of 70 females having past history of menorrhagia, 23 were having raised TSH (32.9%). Amongst 62 females with hypertension in past, 9 had raised TSH (14.5%), showing a significant relation of symptoms with increased TSH (Table 4).

Table 4 TSH across Presenting Characteristics of the Cases.

		Raised		Normal		p value
		n	%	N	%	
Relevant Present History	Normal	57	8	657	92	0 (Sig)
	Cold Intolerence	19	63.3	11	42.3	
	Edema	11	21.1	41	85.4	
	Hypertensive	3	10.3	26	89.7	
	Constipation	7	14.3	42	85.7	

	Hoarseness of Voice	10	31.3	22	68.8	
	Normal	82	10.6	688	89.4	
Relevant Past History	**Hypertensive**	9	14.5	53	85.5	0 (Sig)
	Menorrhagia	23	32.9	47	67.1	

Out of total 114 cases of raised TSH, we followed 61 cases, of which 40 were put on thyroxine therapy. Out of these, 8 were lost to follow-up, and amongst the rest 31 deliveries, only 1 aborted (2.5%) (Table 5).

Table 5 Follow up among the Raised TSH Subjects.

		n	**%**
Follow Up	Yes	61	53.5
	No	53	46.5
Thyroxine Given	Yes	40	65.6
	No	21	34.4
Outcome	Delivered	42	68.9
	Aborted	3	4.9
	Lost to Follow Up	16	26.2

Out of 21 who were not on treatment, 8 were lost to follow-up, 11 delivered i.e. 52.4% and 2 aborted (9.5%) (Table 6).

Table 6 Outcome across Thyroxine Given to the Patients.

Outcome	**Yes**		**No**		**P value**
	n	**%**	**n**	**%**	
Delivered	31	77.5	11	52.4	
Aborted	1	2.5	2	9.5	0.07 (NS)
Lost to Follow Up	8	20	8	38.1	

DISCUSSION

Subclinical hypothyroidism has significant untoward consequences in pregnant females as well as on the fetus. Very little attention has been paid to this entity in pregnancy. The present study (finding the prevalence of subclinical hypothyroidism by estimating FT3, FT4 and TSH levels, in pregnant females of Kashmir India), was conducted on 902 pregnant females between age group of 15-35 years, with no previous history of thyroid dysfunction and 93 non-pregnant controls. The primary objectives of our study were to find out serum FT3, FT4 and TSH levels in pregnant females of Kashmir India in order to study the prevalence of subclinical hypothyroidism in them. This was done so as to assess the magnitude of the problem in this part of world and to formulate a strategy based on its results.

As Kashmir falls in the 'Himalaya Goitre Belt' [8] and is situated at a higher altitude with the peculiar food habits, life style and extreme climatic conditions in Kashmir, it becomes imperative to establish the levels of free thyroid hormones and TSH, especially in pregnant females as subclinical hypothyroidism has a deleterious effect on maternal and neonatal outcomes.

The age group in our study ranged from 15-35 years with females having increased TSH mostly in age group of 25-29 years. The same age group was selected for controls also.

Smith et al. [9] who interpreted TFTs in vivo during pregnancy also had their studied population of pregnant women in age group of 18-34 years.

The age group selected by Abalovich [10] was again in the range of 16-39 years, which is in concordance with our studied population. A similar age group of pregnant females between 14-40 years was taken by Andrade et al. [11] in their study. The urban population comprised 16.2% in cases amongst whom 9.6% had increased TSH, while as rural population comprised 83.8% in cases where 13.2% had increased TSH. This was mainly because most of our referrals were from Government hospitals, which is primarily being visited by the rural population. 20% of our study group and 12% of our control group showed subtle symptoms of hypothyroidism in the form of cold intolerance, edema and constipation, which is in correlation with study conducted by Glinoer et al. [12] where the prevalence of symptoms was 17%. A similar set of findings was noted by Andrade in his study [11].

There was a history of hypertension in 7% of study group and 1.1% amongst controls which falls in line with studies conducted by Leung et al. [13] with percentage of hypertension in their studied group being 7.6% and another study conducted by Davis et al. [14] where prevalence of hypertension in study group was 16%. Majority of our studied population was in second trimester. In our study 64% were multigravidas and 35.6% were primigravidas. This is in concordance with the study conducted by Smith et al. [9] where 43% were primigravidae and 57% were multigravidae. Pop et al. [15] had their study group mainly between 12-32 weeks of gestation. Mannisto et al. [16] had their study group below 20th week and Glinoer et al. [12] also had their study population mainly in second trimester being similar to our study.

Preterm deliveries were seen in 6.5% and abortions in 5.7% of the study pregnant group. Allan et al. [4] also had a rate of fetal deaths around 3.8%. Casey et al. [17] showed that preterm birth was almost 2 fold higher in women with subclinical hypothyroidism. On examination, 12.2% of study group were hypertensive, 6.3% had palpable thyroid and 1.2% had hung-up reflexes. These and other variables e.g. blood pressure, pulse, body weight and hemoglobin values of cases were almost in concordance with the study conducted by Andrade et al. [11] and many others.

The mean value of T3 in our studied pregnant females was 4.7 ± 0.8, mean FT4 was 13.7 ± 1.7 and TSH in study group was 3.8 ± 2.9. Anti TPO antibody titers were positive in 3.7% of our cases. Similar values were observed in the controls also with FT3 being 4.7 ± 0.8 FT4 13.6 ± 1.4 and TSH of 3.8 ± 2.9. But anti TPO titers were not found positive in any of the control members. Hence, according to the results of our investigation, TSH was within range in 87.4% subjects and raised in 12.6% of pregnant females. FT4 was within range in 96.2% cases, low in 3.2% and raised in 0.6% cases while in controls, percentages were 92.5%, 5.4% and 2.2% respectively. In the control group, 91.4% had TSH in normal range and in 8.6%, it was found to be raised.

Therefore, the prevalence of subclinical hypothyroidism (increased TSH and normal FT4) females of Kashmir was 12.6% and in non-pregnant controls was 8.6%.

Kamijo et al. [18] studied the incidence of transient subclinical hypothyroidism in pregnant females which came out to be 0.19%. Klein et al. [19] in California conducted a study to determine prevalence of thyroid deficiency in pregnant women and found its prevalence to be 2.5%. Vaidya et al. [20] in State of U.K. went on to assess efficacy of targeted high risk case finding approach in identifying women with thyroid dysfunction during early pregnancy and found thyroid deficiency in 2.4% cases.

Andrade et al. [11] studied prevalence of subclinical hypothyroidism with different gestational ages in Itabuna and found its 4% prevalence there with anti-TPO antibodies positive in 8% of pregnant women, while Casey [17] studied its prevalence in Parkland, which was around 2.5%.

All above results are in discordance with our findings where prevalence of subclinical hypothyroidism is very high i.e. 12.6% in pregnant females. This can be mainly because our state is situated in Himalayan goiter belt and our dietary iodine intake is less which is responsible for high

prevalence of hypothyroidism here. Besides its percentage is higher in pregnant females as compared to non-pregnant due to increased clearance of iodine in pregnancy as a result of increased GFR. Besides that increased requirements in pregnancy and various hormonal influences are also responsible for hypothyroidism in pregnancy.

Out of total 114 cases of raised TSH, we followed 61 cases, of which 40 were put on thyroxine therapy. Out of these, 8 were lost to follow-up, and amongst the rest 31 deliveries, only 1 aborted i.e. 2.5%. This is similar to study conducted by Glinoer et al where rate of spontaneous abortions was 13.3% and 3.8% in project conducted by Allan et al. [4] , indicating a much decreased rate of abortions in females put on thyroxine therapy.

Keeping in mind the high prevalence of subclinical hypothyroidism in our state and considering, as already established, that low maternal thyroxine levels increase incidence of preterm deliveries, abortions, gestational hypertension, maternal and neonatal mortality. Therefore, it becomes mandatory to make thyroid hormone estimation in pregnancy a routine investigation and start with levothyroxine therapies in pregnant females with even slightly raised TSH.

CONCLUSION

It was therefore concluded that, there is an increasing trend of the dog bite injuries in our state especially in the small children and in order to obtain the best outcome in the patients of dog bites, one need to exercise utmost care to the patients, starting from the time of their reception in the hospital, with emphasis on thorough cleansing of wound and proper antirabies shots. Primary surgical repair of dog bite lacerations after thorough wound cleansing and adequate debridement leads to best cosmetic results, with need for fewer secondary procedures.

Further, it is important to emphasize that the time has come, when the government needs to curb the growing menace of the street dogs prevalent in our state, as our study clearly reflects the fact that it is the alarming number of the dogs, rather than the dogs being rabid, which result in such severe injuries. Further a policy is made to vaccinate these animals so that the common public is safe from their bites as is being followed worldwide.

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