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Prevalence of Hypothyroidism in Prgnancy And Pregnancy Outcome

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Abstract: *The second most common endocrinological disorder in pregnancy is thyroid dysfunction. The most common cause of hypothyroidism is primary abnormality in thyroid. Thyroid hormone is essential for the normal development of the placenta. There is evidence that preeclampsia, placental abruption and preterm labor are all causatively linked to faulty early placentation. Thyroid hormone is important for normal neuronal migration, synaptic transmission and myelination during the early stages of neurodevelopment and hence healthy development of foetus.*

Aim Of The Study: *To study the prevalence of hypothyroidism in pregnancy and the pregnancy outcome in those pregnancies. This study involves screening 1000 consenting eligible women during first trimester. They will be subjected to TSH screening and if the values are deranged then they will undergo FT4. Based on the reports they will be classified as euthyroid, hypothyroid, subclinical hypothyroid and hyperthyroid. For the purpose of this study the patients who are hypothyroid and subclinical hypothyroid will be followed till the termination of pregnancy. All the patients will be treated based on the thyroid profile. Thyroid profile will be repeated every 4 weeks up to 20 weeks and at 32 weeks of gestation and doses titrated accordingly. The normal patients will serve as controls. In our study, there is an increase in the number of spontaneous abortion, GDM, Pre-eclampsia, oligohydramnios, preterm labor, IUGR and low birth weight in inadequately treated group.*

Hence early diagnosis and adequate treatment of maternal hypothyroidism in pregnancy is essential in decreasing the incidence of complications like abortion, pre eclampsia, IUGR, placental abruption, oligohydramnios and low birth weight which are associated with hypothyroidism.

Keywords: *Thyroid hormone, thyroxin, abortion, pre eclampsia, IUGR, placental abruption, oligohydramnios, low birth weight*

Aim of the study*: To study the prevalence of hypothyroidism in pregnancy and the pregnancy outcome in those pregnancies.*

I. Introduction

The second most common endocrinological disorder in pregnancy is thyroid dysfunction. The most common cause of hypothyroidism is primary abnormality in thyroid.Thyroid hormone is essential for the normal development of the placenta. There is evidence that preeclampsia, placental abruption and preterm labor are all causatively linked to faulty early placentation. Thyroid hormone is important for normal neuronal migration, synaptic transmission and myelination during the early stages of neurodevelopment.Not much studies available to see if early thyroxine supplementation and adequate treatment reduces the incidence of complications in pregnant woman with hypothyroidism .This study is to see if diagnosed early and adequately treated hypothyroid women are able to alleviate the complications. Overt hypothyroidism is characterized by increased TSH and low T4levels. The incidence is 0.3 -0.5%. Overt hypothyroidism is associated with anaemia, miscarriage, preeclampsia, placental abruption, preterm labour, postpartum haemorrhage, neonatal respiratory syndrome. Leung AS et al[1] in 1993 did a study in 1993 and found that overt hypothyroidism is associated with an increased incidence of preeclampsia and low birth weight babies. ACOG[2] practice bulletin on thyroid disease in pregnancy in 2001 states that untreated hypothyroid women are more prone for pre eclampsia and inadequate treatment results in low birth weight babies.Ohara N et al[3] in 2004 reviewed the literature on the role of thyroid hormone in trophoblast function and fetal neurodevelopement. They concluded that close scrutiny of maternal thyroid hormones to ensure adequate hormone levels in early pregnancy are of prime importance in preventing miscarriage and neurodevelopment deficits in infants. A study by Evelyn Man and colleagues(4) in 1969 compared the outcomes of 1252 normothyroxinemic pregnancies with 168 hypothyroxinemic pregnancies. 30 out of the 168 hypothyroid women ended up having preterm deliveries or fetal death(19.6%) compared only12.6 % in the euthyroid group. These data show that adequate thyroxine replacement greatly improves but does not totally suppress thefrequency of obstetric complications.

Subclinical Hypothyroidism is a condition in which TSH is elevated ,but FT4 is normal. Incidence of subclinical hypothyroidism is at least 2.5% .Usually it is symptomatic, but there is evidence autoimmune thyroid disease (positive TPOAbs and or TG antibodies)in 50-60%. Subclinical hypothyroidism was found to be more common in women delivering before 32 weeks(5). Pregnancies complicated by subclinical

hypothyroidism had a 3 fold increased risk of developing placental abruption and 2 fold increased risk of preterm labor compared to euthyroid women (6). Gestational hypertension also occurred more commonly in these women (7). Even raised maternal TSH (high level of normal) is associated with neonatal respiratory distress, miscarriage and preterm delivery. The likelihood of patients diagnosed as hypothyroids during pregnancy to continue to be hypothyroid even after pregnancy depends on the initial TSH value. The United States Preventive Services Task force reported that nearly almost all patients with an initial TSH >10 mIU/ml developed overt hypothyroidism within 5 years(8). Isolated hypothyroxinaemia is defined as a condition with normal TSH and low fT4. Cleary Goldman and colleagues in 2008 screened 10,990 patients for thyroid dysfunction . They noted that the presence of this isolated hypothyroxinemia in 1st trimester was associated with an increased occurrence of preterm delivery and macrosomia.Its occurrence in 2ndtrimester was associated with gestational diabetes(9).

Clinical features of hypothyroidism:

Hypothyroidism developing in childhood results in delayed development and may even cause abdominal distension, umbilical hernia and rectal prolapse. Mental performance is diminished but severe retardation is uncommon. In adults mostly symptoms are non specific. They include weight gain, fatigue, intolerance to cold, constipation and menstrual irregularities like menorrhagia. Patients with myxedema have typical facial features. Skin is yellowish due to reduced conversion of carotene to vitamin A. Hair becomes brittle and there is also a characteristic loss of the outer two third of eye brow. Untreated patients can develop dementia which is called myxedema madness. There is decreased libido and fertility in both sexes. Cardio vascular changes include bradycardia, pericardial or pulmonary effusion.

Complications of hypothyroidism in pregnancy are Spontaneous abortion, Pregnancy induced hypertension (pre eclampsia, eclampsia), Placental abruption, IUGR, Oligohydramnios, Preterm delivery, Fetal distress and Low birth weight There is clinical and scientific evidence that hypothyroxinemia causes poor neurodevelopment outcome in the children of mothers with low thyroxine levels. In a study by Morreale de Escobar et al in2004, it was noted that thyroid hormone accumulates in the cerebral cortex before 20 weeks(10). Early and aggressive treatment with thyroxine is crucial for infants with congenital hypothyroidism. Postpartum thyroiditis is a characterized by a lymphocytic infiltration of the thyroid gland .It's reported incidence is in about 5% of pregnancies(11). Pop et al revealed decrease in the intelligent quotient of children aged 5 years whose mothers were TPO antibody positive at 32 weeks of gestation even though they were actually euthyroid(12). Brown and co-workers in 1996 did a study on over one million babies and found that only 1 in 180,000 neonates born to mothers with Hashimotos thyroiditis had thyroid dysfunction (13).

In mild degrees of hypothyroidism, ovulation and conception can occur, but the pregnancies that result are complicated by abortions, stillbirth or prematurity(14). On the other hand, severe hypothyroidism is commonly associated with ovulatory dysfunction and, thus, infertility. Hypothyroid women can present with menstrual irregularities, especially oligomenorrhoea. Treatment of thyroid under-function with L-thyroxine (L-T4) usually restores a normal menstrual pattern and alleviates these pathological mechanisms (15). Normal thyroid function is critical for normal functioning of the gonadal axis, thus important in maintaining normal reproduction. Gonadal steroid synthesis by oocytes depends on an adequate level of thyroid hormones. T3 modulates the regulating action of LH and FSH on steroid biosynthesis, thyroid hormones increase and enhance estrogenic responses(16). Dysthyroidism is associated with anovulatory cycles, sub fertility or infertility Abortion rate as high as 60% in inadequately treated overt hypothyroids and 70% in subclinical hypothyroids (17). Matsua et al showed that Free T3 and Free T4 values were significantly lwer in women whose pregnancies terminated in abortions (18).

There are theories that consider autoimmune thyroiditis a consequence of increased lymphocytes T activation. Patients with antecedents of habitual abortions show an increased number of endometrial T lymphocytes. Expression of the antithyroid antibodies may be an epiphenomenon that reflects an autoimmune imbalance, causing the rejection of the product of conception. This hypothesis is supported by the existence of an increased CD5/20 lymphocyte positivity in women with recurrent miscarriage(19).

In 1990 Stagnaro- Green et al showed that among 552 women who were screened for thyroid antibodies , abortion rate of 17% was observed in antibody positive group as compared to 8.4% in antibody negative group(20). Bussen Steck et al in 1995 screened 22 non pregnant women with bad obstetric history for thyroid antibodies and detected a higher prevalence of thyroid antibodies in 36% compared to 9% in multiparous controls and 5% in nulliparous controls(21). Matalon ST et al in 2001showed that elevated levels of thyroid auto antibodies are associated with increased rate of abortions in euthyroid women(22). Thyroid replacement therapy with intra-venous immunoglobulins (IVIG) was helpful in preventing a new miscarriage (23). The journal of clinical endocrinology and metabolism Adopted a clinical practice guideline in 2007 which recommended screening among the following high risk women(24).

a) Women with a previous history of hyper /hypo thyroid disease / thyroidectomy/goitre.
b) Women with family history of thyroid dysfunction
c) Women with symptoms/signs suggestive of thyroid dysfunction
d) Women with autoimmune diseases like Type 1 DM
e) Women with a history of infertility
f) Women with history of head and neck irradiation
g) Women with history of recurrent miscarriages or preterm deliveries.

Treatment of hypothyroidism with Levothyroxine or T4, is a synthetic form of normally secreted by the thyroid chiral L-form.In patients with overt hypothyroidism the dose of thyroxine should be adjusted to reach a TSH not more than 2.8 IU/ml periconceptionally. The Thyroxin dosage usually needs to be increased by 4-6 wks of gestational age and may require a 30-50% increase. If a patient is diagnosed to have overt hypothyroidism during pregnancy, titrate the dose rapidly to keep the TSH at a level less than 2.5 IU/ml in the first trimester and less than 3 IU/ml in second and third trimesters. The panel recommends also thyroxin replacement in women with subclinical hypothyroidism.

Materials and methods
This study was conducted in Chengalpattu Medical College, Chengalpattu, from January 2015, after approval from institutional ethics committee.
Design Of Study: A Prospective study.
Period Ofstudy: 1 Year.

This study involves screening 1000 consenting eligible women during first trimester. They will be subjected to TSH screening and if the values are deranged then they will undergo FT4. Based on the reports they will be classified as euthyroid, hypothyroid, subclinical hypothyroid and hyperthyroid. For the purpose of this study the patients who are hypothyroid and subclinical hypothyroid will be followed till the termination of pregnancy. All the patients will be treated based on the thyroid profile. Thyroid profile will be repeated every 4 weeks upto 20 weeks and at 32 weeks of gestation and doses titrated accordingly. The normal patients will serve as controls.

Inclusion criteria:
1. Less than 13 weeks gestation.
2. Singleton pregnancy.
3. Primigravida or multigravida.
4. Known hypothyroid patients.

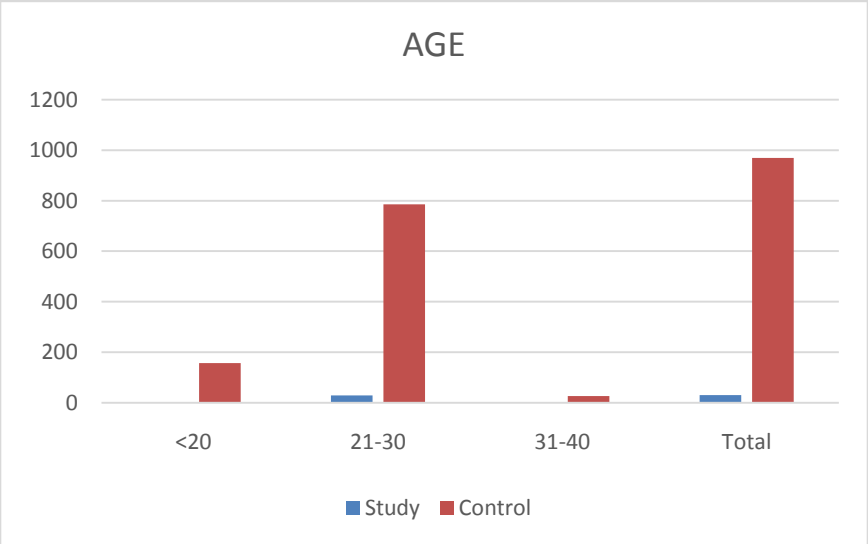
Exclusion criteria:
1. Multifetal gestation.
2. Known chronic disorders like diabetes and hypertension.
3. Previous bad obstetric history with known cause.
4. Those who plan to deliver in other hospital.

Methodology: Patients satisfying the inclusion criteria and who consent for the study are included.Clinical history and relevant investigations are collected as mentioned in the proforma enclosed. All the eligible patients will be screened and their thyroid status defined. Patients who are hypothyroid and subclinical hypothyroid will be followed till termination of pregnancy. The clinical progression with the treatment given will be noted. The results from the study will be analyzed statistically.

II. Results

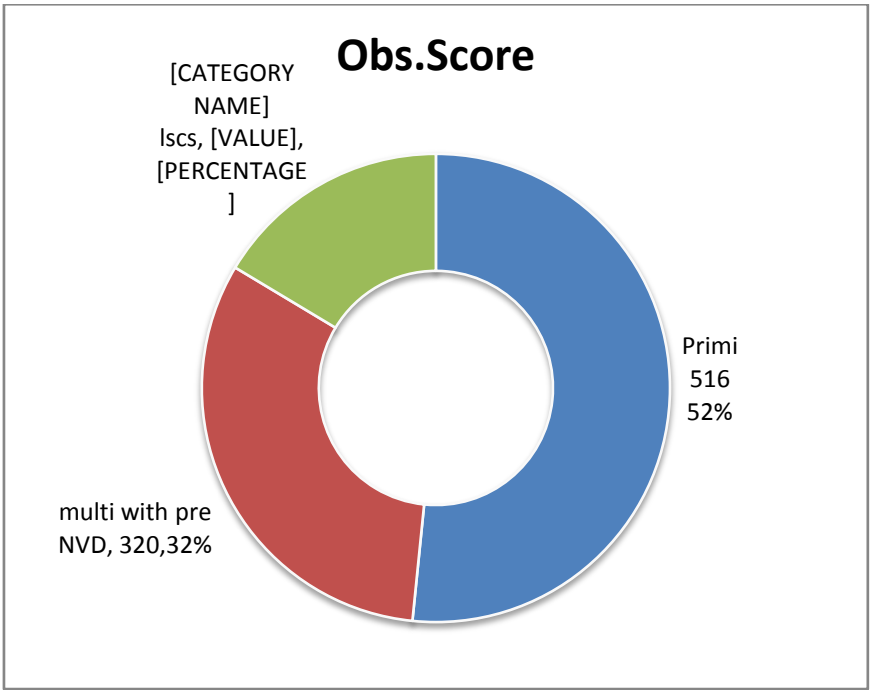
The data collected from the study will be analyzed statistically and submitted.

Age:



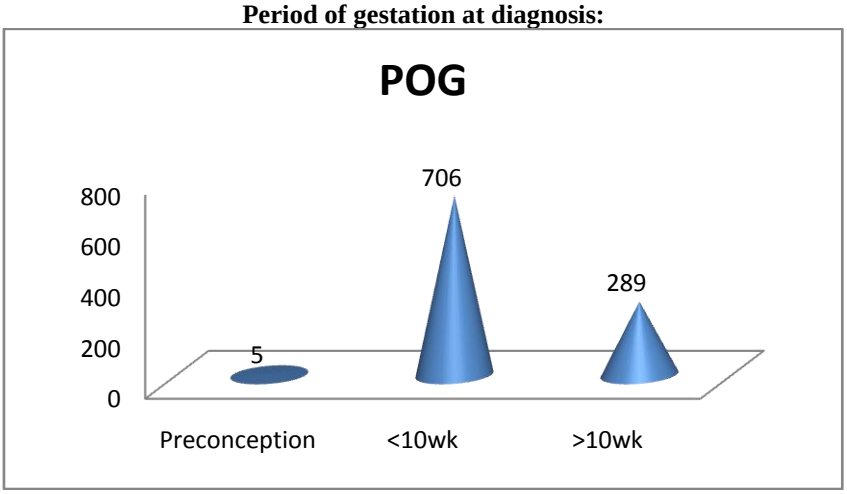
Age	Study	Control
<20 yrs	2	157
21-30 yrs	29	786
31-40 yrs		26
Total	31	969

Obstetric score:



OBS.SCORE	Study	Control
Primi	15	501
Multi with prev normal delivery	9	311
Multi with pre lscs	7	157
Total	31	969

Period of gestation at diagnosis:

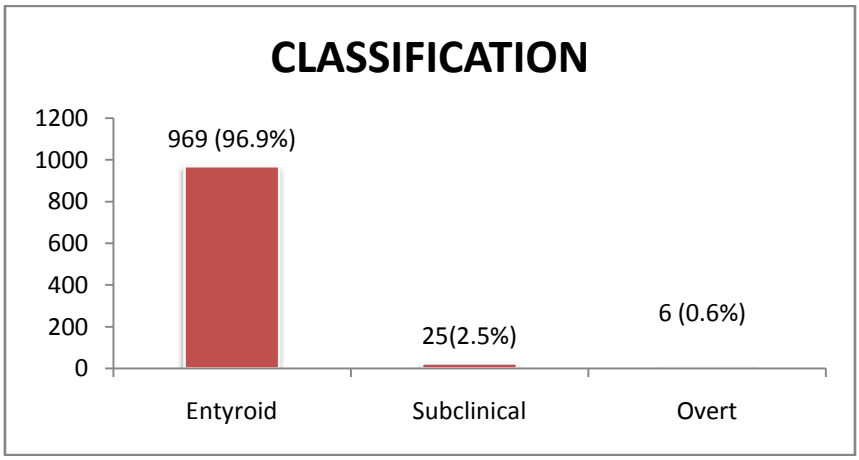


POG	Study	Control
Preconceptional	5(16.12%)	
<10wk	13(41.9%)	693(71.51%)
>10wk	13(41.9%)	276(28.48%)
Total	31(100%)	969(100%)

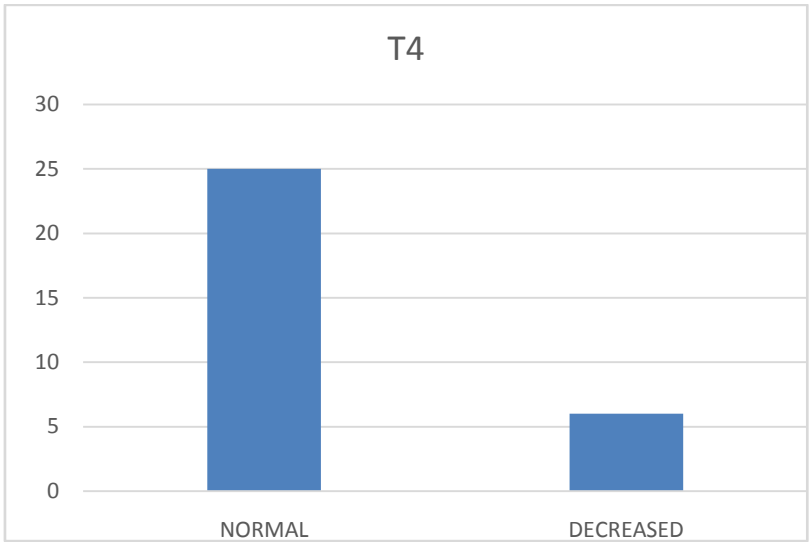
Classification:

CLASSIFICATION	Frequency
Euthyroid	969 (96.9)
Subclinical hypothyroid	25 (2.5%)
Overt hypothyroid	6 (0.6%)
Total	1000

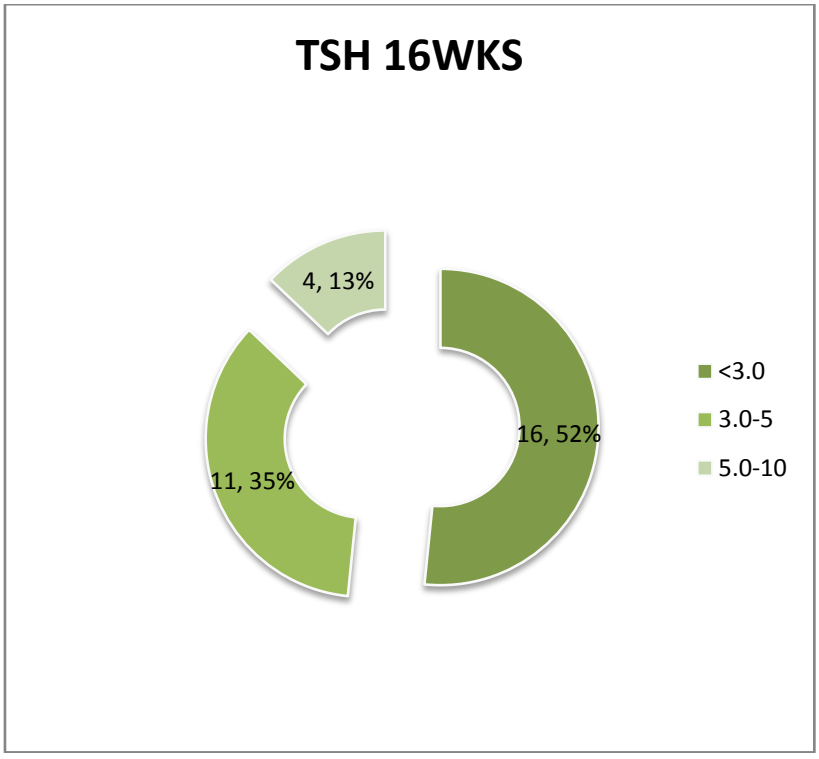
Classification	Study	Control	Total	Chi Sq	P
Euthyroid	0	969	969 (96.9%)	1000	**0.0001**
Subclinical Hypothyroid	25	0	25 (2.5%)		
Overt Hypothyroid	6	0	6 (0.6%)		
Total	31	969	1000 (100%)		



This table shows the prevalence of hypothyroidism in my study group that is 3.1% of the totally screened patients 2.5% of them are sub clinically hypothyroid, 0.6% of them are overt hypothyroid. Chi sq. & p value 0.0001 which is significant.

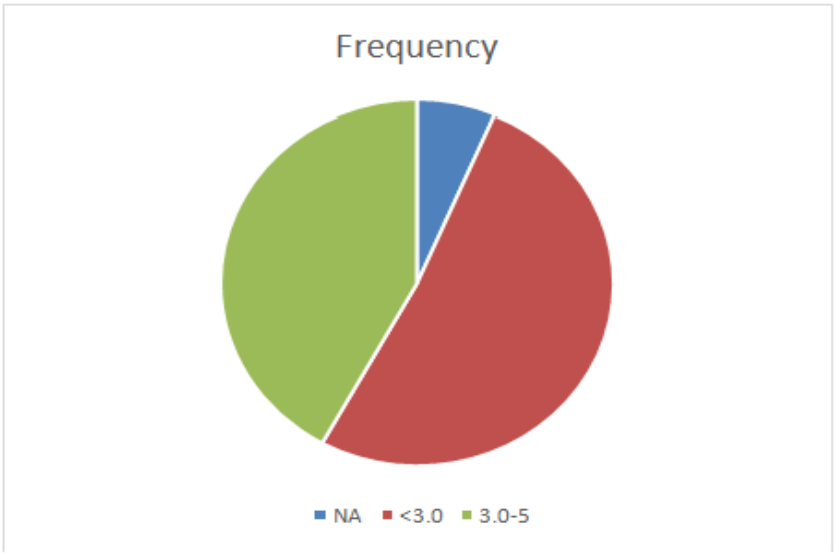


Tsh at 16 weeks:



TSH16	Frequency
<3	16
3-5	11
5-10	4
Total	31

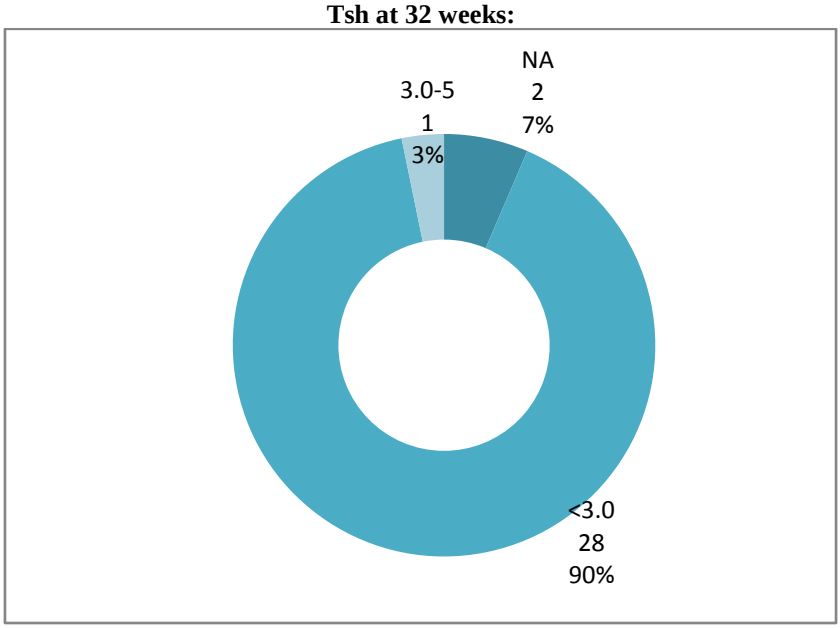
Tsh at 20 weeks:



TSH at 20 wks	Frequency
Spontaneous abortion before 20 wks (NA)	2
<3.0	16
3-5	13
Total	31

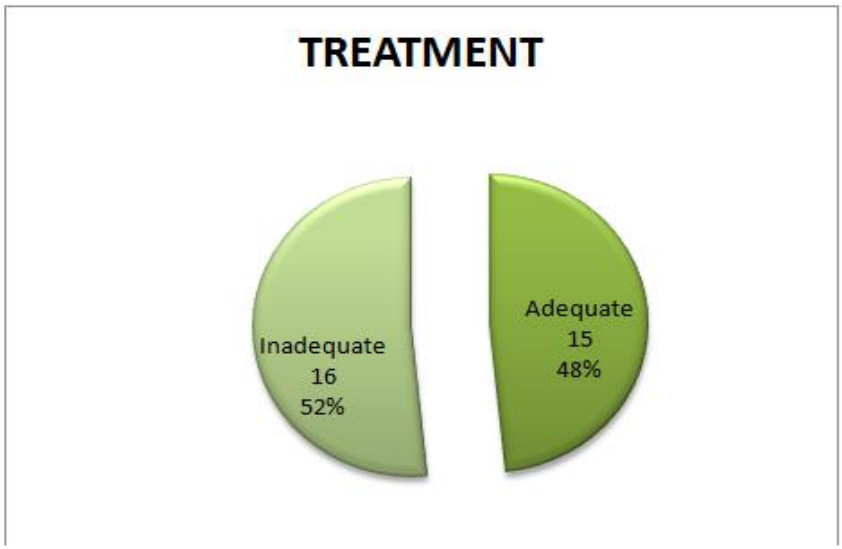
In this table NA denotes those who abort spontaneously before 20 wks of gestation.

Tsh at 32 weeks:



TSH at 32 wks	Frequency
Spontaneous abortion before 20 wks (NA)	2
<3	28
3-5	1
Total	31

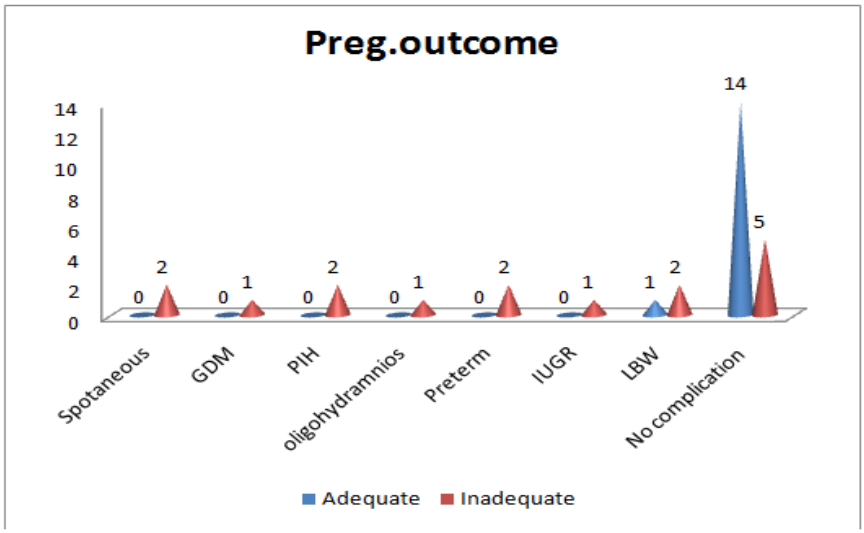
Treatment:



TREATMENT	Frequency
Adequately treated	15(48%)
Inadequately treated	16(52%)
Total	31(100%)

Those who have been diagnosed before 10 weeks and on treatment,if their repeat TSH values become normal theywere grouped under adequately treated group.Those who have been diagnosed after 10 weeks of gestation and treated of those who fail to reach normal levels of TSH despite aggressive treatment were classified as inadequately treated. In our study group 48% patients are adequately treated and 52% of the patients are inadequately treated .

Pregnancy outcome:

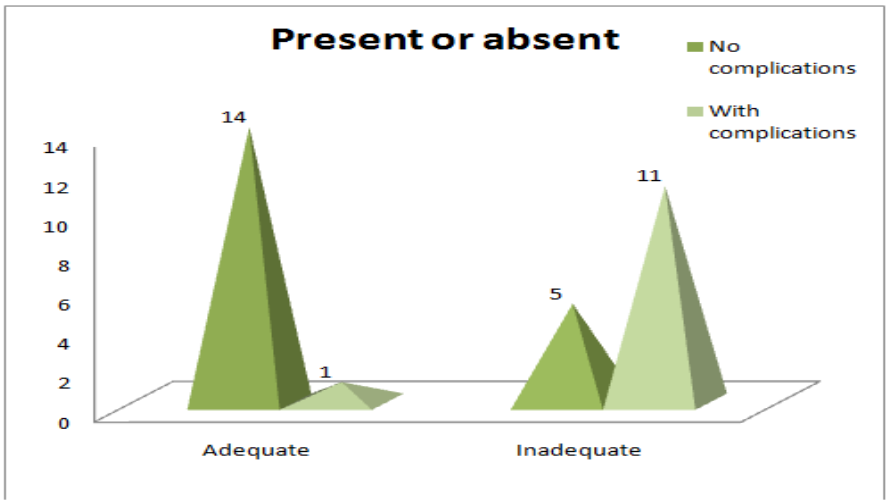


PREG.OUTCOME	Adequately treated	Inadequately treated	Total
Spontaneous abortion	0	2 (12.5%)	2
GDM	0	1 (6.2%)	1
PIH	0	2 (12.5%)	2
oligohydramnios	0	1 (6.2%)	1
Preterm	0	2 (12.5%)	2

			2
IUGR	0	1 (6.2%)	1
LBW	1 (6.66%)	2 (12.5%)	3
Total complications	1(6.6%)	11(68.75%)	12
No complication	14(93.33%)	5 (31.25%)	19
Total	15	16	31

This table shows only 6.66% of the patients of adequately treated patients developed complication that is low birth weight, whereas 68.75% of the inadequately treated patients developed complications. Overall Chi square value for complications:12.57. P value for complications is:0.00039.

Complications:



Outcome	Adequately Treated	Inadequately Treated	Chi sq	P
No complications	14(93.33%)	5(31.25%)	12.57	0.00039
With complications	1(6.66%)	11(68.75%)		
Total	15(100%)	16(100%)		

This table shows that 11 (68.75%) out of the16 inadequately treated hypothyroid mothers developed complications whereas only 1 (6.66%) out of 15 adequately treated patients developed complications.Chi square value:12.57.

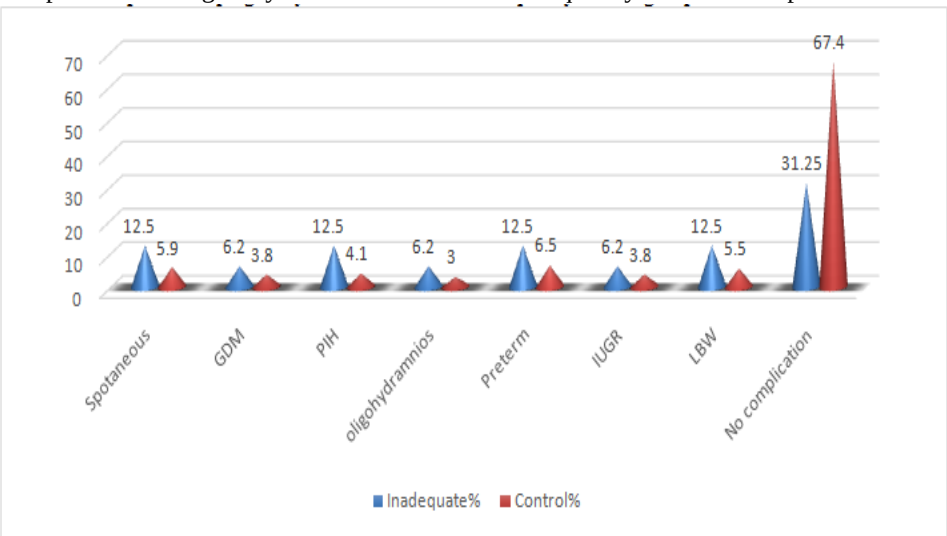
P value: .00039which is significant.

Low birth weight:

LBW	Adequate	Inadequate
No	14(93.33%)	14(87.5%)
YES	1(6.66%)	2(12.5%)

This table shows that 12.5% of the inadequately treated hypothyroid woman delivered low birth weight babies and only 6.66% of the adequately treated patients delivered low birth weight babies.

Comparison Of Pregnancy Outcomes Between Inadequately Treated Group And Control:



Preg.Outcome	Inadequate	Inadequate%	Control	Control%	Chi Sq	P
Spotaneous Abortion	2	12.5%	57	5.9%	9.26	0.00233
Gdm	1	6.25%	37	3.8%		
Pih	2	12.5%	40	4.1%		
Oligohydramnios	1	6.25%	29	3%		
Preterm	2	12.5%	63	6.5%		
Iugr	1	6.25%	37	3.8%		
Lbw	2	12.5%	53	5.5%		
Total Complications	11	68.75%	316	32.6%		
No Complications	5	31.25%	653	67.4%		
Total	16	100%	969	100		

This table compares the outcome of inadequately treated hypothyroid pregnant mothers with normal control group. In our study group 12.5% the inadequately treated hypothyroid mothers had spontaneous miscarriages whereas only 5.9% of the control population had spontaneous miscarriages. Again 12.5% of the inadequately treated hypothyroid mothers developed preeclampsia whereas only 4.1% of the control population developed preeclampsia. In our study group 6.25% of the inadequately treated hypothyroid patients developed oligohydramnios whereas only 3.5% of the control group developed oligohydramnios. Around 12.5% of the inadequately treated hypothyroid patients delivered preterm babies against the control group where only 6.5%. patients delivered preterm babies. Around 6.25% of the inadequately treated patients delivered IUGR babies,whereas only 3.8% of the patients in the control group delivered IUGR babies.

In our study group 12.5% of the inadequately treated hypothyroid mothers delivered low birth weight babies , whereas in the control group only 5.5% patients delivered low birth weight babies.From the above table we came to know that 68.75% of the inadequately treated patients developed complications like GDM, preeclampsia,IUGR,oligohydramnios, preterm deliveries and low birth weight. Whereas only 32.6% of the control group developed these complications ,this implies a significant association between inadequately treated hypothyroidism and poor pregnancy outcomes as evidenced by the p value of 0.002 which is very significant.
The overall chi sq.
value: 9.26
P value: 0.00233
It is statistically significant.(0.05%)

III. Discussion

This study was conducted in Chengalpattu Medical College & Hospital.The purpose of the study was to follow the pregnancy outcomes in pregnant women with hypothyroidism to see whether they developed complications if left untreated and if adequate treatment altered the occurrence of complications. The total number of pregnant women included in this study were 1000.All women who have been diagnosed as hypothyroid started on treatment over a period of 1 year were taken consecutively. All antenatal women were screened using TSH at their first booking visit during first trimester.

Those who had an elevated TSH levels, were further tested with FT4 and started on treatment with levothyroxine irrespective of whether FT4 was elevated or not. The cut-off level for TSH was taken as 2.5 mIU/ml. Serum thyrotropin (TSH) level in early pregnancy is decreased because of thyroid stimulation from the weak TSH effects of HCG. In a study by Green WL in 2005, truly normal range of TSH is defined as 0.5-2.5mIU/ml(6). So adequate replacement therapy should be given when TSH is above 2.5mIU/ml and/or with low T4, FT4 in pregnancy. Patients with TSH values between 2.5-5mIU/ml were started on a dose of 25microgram and those with levels from 5-10mIU/ml were given 50microgram.Those with levels above 10mIU/ml were started on higher doses after consulting with the endocrinologist. It was not possible for all patients with an elevated TSH to undergo further testing with FT4 for many reasons like some being already started on treatment if they had already been diagnosed preconceptionally or if they had been started on treatment even before FT4 levels were available. TSH levels were repeated for these patients 4-6 weeks after initiating the treatment upto 20 wks, then at 32 wks and thyroxine dosage titrated accordingly. Based on whether they were started on treatment before 10 weeks and given prompt dosage titration, or after 10 wks they were grouped as those receiving adequate treatment and inadequate treatment. A patient was considered to have received adequate treatment if the repeat TSH values were less than 3 mIU/ml Both the groups were followed till delivery and closely observed for the development of complications.

Out of 1000 pregnant woman screened in the first trimester 0.6% (6) patients were overt hypothyroid and 2.5% (.25) of the patients were subclinical hypothyroid. Hence prevalence of hypothyroidism in our study group is 2.5% subclinical hypothyroidism and 0.6% overt hypothyroidism. Out of the 1000 patients screened, 31 patients werefound to be hypothyroid out of them 15 adequately treated, while 16 patients received inadequate treatment. Out of the 15 adequately treated patients only 1 developed complications (6.7%). But 11 out of the 16 patients receiving inadequate treatment developed complications(68.75%). The results of our study revealed that gestational diabetes .(GDM)was found in 1 out of the 16 inadequetely treated hypothyroid patients (6.2%) showing a possible relationship between hypothyroidism and glucose intolerance. on the other side 37 (3.8%)out of 969 patients in the control gestational diabetes . Approximately 12.5% of inadequately treated patients end in spontaneous miscarriage (24) against 5.9% in the control group. It was also noted that in our study group , the women who had miscarriages had higher TSH values at diagnosis (>5mU/L). Preeclampsia is identified in 2(12.5%) out of the 16 inadequately treated hypothyroid patients(48) against 40 out of 969 that is 4.1% of control group patients. Davis et al 1988 followed 25 hypothyroid women through 28 pregnancies who were divided into two groups, of which 16 were clinically hypothyroid and 12 had subclinical hypothyroidism. This study showed that mothers with overt hypothyroidism are more at risk for preeclampsia. Inadequately treated hypothyroid women in our study had 6.2% pregnancies complicated by Oligohydramnios which was higher than control group which is only 3% .In our study population 12.5% of inadequately treated hypothyroid pregnancies ended up in preterm delivery (delivery before 37 weeks of gestation) which was higher than the control group which is 6.5%. This is similar to the outcome of a study done by Jones WS et al in the American Journal of Obstetrics and Gynaecology in 1969 who concluded that premature deliveries were more frequent in pregnant women who had low thyroxine levels.

In our study 6.2% of the foetuses of inadequately treated mothers had intrauterine growth restriction which was higher than its occurrence in the control population which is only 3.8%. Out of the 16 inadequately treated patients in our study, 2 women delivered babies with low birth weight (12.5%), whereas, only 1 women in the adequately treated group had low birth weight babies (6.7%) and in the control population only 5.5% of the woman delivered low birth weight babies. But, Low birth weight among these babies was mainly attributed to prematurity.

There was no case of placental abruption in the inadequately treated patients in our study although Casey Brian et al in 2005 in their study concluded that pregnancies complicated by subclinical hypothyroidism had a 3 fold increased risk of developing placental abruption and 2 fold increased risk of preterm labour compared to euthyroid women .

IV. Conclusion

Thyroid hormone is essential for early placental development in pregnancy. Especially during the first twelve weeks of pregnancy the fetus entirely depends upon the the maternal thyroid hormone for the normal neural and skeletal development. Hence early diagnosis and adequate treatment of maternal hypothyroidism in

pregnancy is essential in decreasing the incidence of complications like abortion, pre eclampsia, IUGR, placental abruption, oligohydramnios and low birth weight which are associated with hypothyroidism. Inadequately treated hypothyroid women in my study group had increased risk of developing preeclampsia.There was a significant increase in the incidence of abortion or fetal growth restriction in the inadequately treated group.Adequate treatment significantly reduced certain complications like pre eclampsia.

Bibliography

[1]. Leung AS, Millar LK, Koonings PP. Perinatal outcome in hypothyroid pregnancies. Obstet Gynecol 1993; 81: 349-53.
[2]. ACOG practice bulletin on thyroid disease in pregnancy. No :32 Nov 2001 issue. Am Fam Physicians 2001 May 15; 65(10) :2158 - 2162
[3]. Ohara N, Tsujino T, Mauro T. The role of thyroid hormone in trophoblast function, early pregnancy maintainence and fetal neurodevelopment. J Obstet Gynaecol Can, 2004; 26: 982-90.
[4]. Montoro, M.M., Collea, J.V., Frasier, S.D. and Mestman, J.H. (1981) Successful outcome of pregnancy in women with hypothyroidism. Ann. Intern. Med., 94, 31±34
[5]. Journal of thyroid research. Volume: 2011, article ID 397012, 4 pages. DOI: 10.4061/2011/397012. John .H.Lazaws
[6]. Casey,Brian.M;Dashe,Jodi.S;Wells,C.Edward;McIntire,Donald D;Byrd,William;Leveno Kenneth J. et al,Green Journal,Feb2005.105(2):239-245.
[7]. D.K.James,P.J.Steer,C.P.Weiner,B.Gonik,High risk pregnancy management options,Third edition,Elsevier,Philadelphia,pg:1005
[8]. Helfand M.Screening for subclinical thyroid dysfunction in nonpregnant adults:a summary of the evidence for The US Preventive Services Task Force.Ann Intern Med.2004;140:128-141.
[9]. Cleary-Goldman J,Malone FD,Lambert-Messerlian G,Sullivan L,Canick J et al,Maternal thyroid hypofunction and pregnancy outcome.Obstet Gynecol.2008 Jul;112(1):85-92.
[10]. Morreale de Escobar G,Obregon MJ,Escobar del Rey F.Role of thyroid hormone during early brain development.Eur J Endocrinol.2004;151(suppl 3):U25-37.
[11]. Prummel MF,Wiersinga WM.Thyroid peroxidase autoantibodies in euthyroid subjects.Best Pract Res Clin Endocrinol Metab.2005;19:1-15
[12]. Pop VJ,Jl Kuijpens,van Baar AL,et al.Low maternal free thyroxine concentrations during early pregnancy are associated with impaired psychomotor development in infancy.Clin Endocrinol.1999;50:147-148.
[13]. Brown RS,Bellisario RL,Botero D et al; Incidence of transient congenital hypothyroidism due to maternal thyrotropin receptor-blocking antibodies in over one million babies..J Clin Endocrinol Metab81:1147,1996.
[14]. Davis, L.E., Leveno, K.J. and Cunningham, F.G. (1988) Hypothyroidism complicating pregnancy. Obstet. Gynecol., 72, 108±112.
[15]. Krassas, G.E. (2000) Thyroid disease and female reproduction. Fertil. Steril., 74, 1063±1070
[16]. Cecconi S, Rucii N, Scadaferri ML, et al. Thyroid hormones effects on mouse oocyte maturation and granulose cell aromatase activity. Endocrinology 1999;140:1783-8.
[17]. Abalovich M, Gutierrez S, Alcaraz G, Maccallini G, Garcia A, Levalle Oovert and subclinical hypothyroidism complicating pregnancy.2002 Jan;12(1):63-8.
[18]. Matsua K, Kaberlein G, Burrow G. Spontaneous pregnancy termination and thyroid abnormalities. Hum Reprod 2000; 15: 163-79
[19]. Roberts J, Jenkins C, Wilson R, et al. Recurrent miscarriage is associated with increased numbers of CD5/20 positive lymphocytes and an increased incidence of thyroid antibodies. Eur J Endocrinol 1996;134:84-6
[20]. Stagnaro-Green A,Roman SH,Cobin RH,et al.Detection of at risk pregnancy by means of highly sensitive assays for thyroid autoantibodies.JAMA.1990;264:1422-1425.
[21]. Bussen S,Steck T.Thyroid autoantibodies in euthyroid non-pregnant women with recurrent spontaneous abortions.Hum Reprod.1995;10:2938-2940.
[22]. Matalon ST,Blank M ,Ornoy A,et al.The association between anti-thyroid antibodies and pregnancy loss. Am J Reprod Immunol.2001;45:72-77.
[23]. Vaquero E, Lazzarin N, De Carolis H. Mild thyroid abnormalities and recurrent spontaneous abortion: diagnostic and therapeutic approach. Am J Reprod Immunol. 2000; 43: 204-8.
[24]. The journal of clinical endocrinology and metabolism. J. Clin Endocrinol Metab : 92/8 (supplement) S1-S47, 2007. Management of thyroid dysfunction during pregnancy and post partum: An endocrine society clinical practise guidelines.