Research Paper Agricultural Science

Effect Of Cropping Pattern on Growth, Yield Attributes and System Productivity of Citronella (*Citronella Winterianus*) Intercropping with Mustard in Central U. P.

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ABSTRACT

Aims: To study the effect of Autoimmune Thyroid Disorders on pregnancy outcome. Subjects and methods: The study cohort comprised of 100 pregnant women attending the antenatal clinic of SSH, BHU. Thyroid hormone level and thyroid peroxidase antibody were estimated. Patient with thyroid dysfunction were assessed periodically or treated depending on the severity. Subjects were followed until delivery. Results: Hypothyroid and TAI were associated with miscarriage. Conclusions: TAI and hypothyroid were significantly associated with miscarriage.

KEYWORDS Thyroid dysfunction, miscarriage, thyroid peroxidase antibody

INTRODUCTION:-

Pregnancy can be viewed as a state in which a combination of events concurs to modify the thyroidal economy. There is change in the level of thyroxine –binding globulin, total thyroid hormone level and change in the level of thyroid stimulating hormone (TSH) during normal pregnancy. Thyroid dysfunction may be overlooked in pregnancy because of the nonspecific symptoms and hypermetabolic state of normal pregnancy.

Thyroid dysfunction has varied impact on pregnancy outcome. The risk of miscarriage is increased in autoimmune throid disease. Severe maternal hypothyroidism can result in irreversible neurological deficit in the offspring.

MATERIALS AND METHODS:-

The present work entitled "**effect of Autoimmune Thyroid Disorders on pregnancy outcome"** was carried out on patients attending the outpatient Department of Obstetrics and Gynecology in collaboration with the department of Endocrinology,Sir Sunderlal Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi. Quantitative measurement of T3, T4, TSH, Anti-TPO in serum using solid-phase, competitive chemiluminescent enzyme immunoassay was carried out in the Department of Endocrinology, Institute of Medical Sciences, B.H.U, Varanasi. The study was Randomised Case Study. Two years, from 1st JULY 2012 to 30th June 2014. All the pregnant women attending the outpatient Department of Obstetrics and Gynaecology were screened for thyroid disorders.

Fifty hypothyroid and fifty euthyroid pregnant women which were singleton pregnancy were included in the present study.

All women were subjected to the following protocol:

a) Detailed history. b) Clinical examination. c) Routine antenatal investigations(blood group, blood sugar, CBC....) d) USG-Gestational d) Thyroid function tests e) Anti-TPO-Antibod f) Neonatal thyroid profile.

A detailed history was taken in each case and recorded in predesigned proforma.

Study cohort was selected from consecutive pregnant females who attended the antenatal clinic. The females were included irrespective of their gravida status (primigravida/multigravida). Institutional ethics committee permission was obtained, and subjects were recruited for the study after obtaining written informed consent. They were subjected to clinical evaluation with emphasis on the family history of thyroid disorder and the obstetric history.

Serum T3, T4,TSH and thyroid peroxidase antibody (TPOAb) were done as initial hormonal investigations, and the subjects were grouped based on the thyroid autoimmunity. Those with raised thyroid peroxidise were included in group 1 as cases and those were euthyroid with normal thyroid peroxidise were included in group 2 as controls. Those hypothyroid were given levothyroxine and dose varied according to TFT.

Maternal serum thyroid function tests including anti-TPO antibody and dose of LT4 was monitored throughout pregnancy. Maternal complications were noted which include miscarriage, infection, preeclampsia, preterm delivery, post partum haemorrhage, congestive heart failure(CHF), thyroid storm and placental abruption in their follow up in antenatal clinic.

According to maternal complications, admissions were done. They were followed till delivery.

Fetal and neonatal complications were recorded from NICU including prematurity, low birth weight, small size for gestational age, intrauterine fetal death, congenital anomaly, still birth and fetal and neonatal goitre and/or thyrotoxicosis were noted.

Mothers were followed in postpartum period for subsequent thyroid disorders with thyroid function tests and detailed clinical history and examination.

RESULTS:-

The results of present study are summarised as follows:

Total 100 patients were included with age range 20-36 years. Out of 100 subjects, 32 were primigravidae, in which 13 were in case group and 19 in control group. Seventeen subjects (15 in case group and 2 in control group) had history of spontaneous abortion in previous pregnancy and 6 patients had history of still birth in previous pregnancy which was statistically significant.

Six patients had history of Gestational Diabetes Mellitus (5 in case group and 1 in control group) in previous pregnancy. Out of 100 subjects 10 had history of infertility treatment and 9 had history of pregnancy induced hypertension. Eight patients had pre-eclampsia, 7 subjects had Gestational Diabetes Mellitus in present pregnancy. Five patients in case group ended with spontaneous abortion and one in control group. Out of 100 subjects, 9 had preterm delivery and 18 had low birth weight babies (14 in case group and 4 in control group) which was statistically significant.

In neonatal outcome one case had congenital anomaly in baby and 3 had neonatal hypothyroidism and one had neurological deficit in neonate. Six patient had post partum haemorrhage (4 in case and 2 in control group). Neonatal morbidity was significantly high (15 babies were admitted in NICU) in the case group. Pre-eclampsia, Gestational Diabetes Mellitus, miscarriage, PPH and neonatal mortality were high in the case group than in controls. Out of 100, 28 had caesarean section in case group and 21 in controls.

In follow up of 100 subjects till 3 months post partum, 3 patients in case group develop subsequent thyroid disease.

DISCUSSION:-

Hypothyroidism, both overt and subclinical, is common in women of reproductive age and during pregnancy, with frequencies ranging from 0.3% to 2.5%. More recently, the potential adverse impact of maternal hypothyroidism and hypothyroxinemia, even when subclinical, on neurodevelopmental outcomes in the offspring has been recognized. Congenital hypothyroidism is the most frequent cause of preventable mental retardation. Neonatal hypothyroidism has an incidence of one in 3.000–4.000 births and includes both permanent and transient types. Thus, early diagnosis and treatment is recommended.

SPONTANEOUS ABORTION

Mothers with overt or subclinical hypothyroidism, even those with mild subclinical disease, might have an increased risk of miscarriages, at least in hospital setting (Abalovich *et al.* 2002, Negro *et al.*2010a).

Hypothyroidism is significantly associated with miscarriage (Vimal *et al.* 2011, Lila *et al.* 2011).

In the present study, 15 (40.54%) patients with thyroid autoimmunity and two patient (6.45%) in euthyroid group had spontaneous abortion in previous pregnancy which was statistically significant(p=0.02).(Table 6).

In the present study, out of 50 cases who had thyroid autoimmunity 5(10%) and out of 50 controls, 1(2%) ended their pregnancy with spontaneous abortion.(Table 12).

PRE-ECLAMPSIA

We found no association between thyroid dysfunction and preeclampsia, a finding which has been established in other studies (Allan *et al.* 2000, Casey *et al.* 2005), but this has been questioned recently regarding late-onset preeclampsia (Ashoor *et al.* 2010).

In the present study, 16% (vs. 6%) with thyroid autoimmunity had preeclampsia which was not significant(Table 10), whereas 18.91 (vs. 6.45%) mothers had pregnancy induced hypertension in previous pregnancies.(Table 8)

GESTATIONAL DIABETES MELLITUS

About 10% of pregnancies are complicated by previously unknown impairment of glucose metabolism.

The present study shows that in subjects with thyroid autoimmunity 13.3% (vs. 2.04%) had gestational diabetes in present pregnancy which was statistically significant.(Table 11).

On investigating 100 subjects, five (13.5%) in group with thyroid autoimmunity and one (3.22%) in euthyroid group had GDM in their previous pregnancy (Table 7) which was not significant.

Hypothyroidism has been associated with insulin resistence(Maratou *et al*. 2009). In addition autoimmune thyroiditis and thyroid dysfunction have been found to be more prevalent among patients with both type I and type II diabetes compared with non diabetic subjects(McCanlies *et al*. 1998 Akbar *et al*. 2006, Schroner *et al*. 2008).

Thyroid antibodies have been associated with increased risk of gestational diabetes (olivieri *et al.* 2000) but with conflicting results (Montaner *et al.* 2008).

INFERTILITY

Thyroid autoimmunity is the most prevalent autoimmune state that affects up to 4% of women during the age of fertility.

A MEDLINE search done from 1965 to 1996. More than 300 original and review articles were evaluated, from which the most relevant were selected. Result(s): Autoimmune processes now are accepted widely as one of the possible mechanisms of many human diseases. The presence of autoimmune disorders has been associated repeatedly with reproductive failure. On the other hand, reproductive failure may be the first manifestation of autoimmune disorders.

In the present study, 8(16%) in group of thyroid autoimmunity and 2(4%) in euthyroid group had history of infertility treatment.(Table 5).

SUBSEQUENT THYROID DISORDERS

Our results are not in accordance with those of previous studies and show that thyroid dysfunction and/or antibodies detected during pregnancy are not good predictors of subsequent thyroid disease. In our study only 6% with thyroid autoimmunity had subsequent thyroid disease in subjects 3 months following delivery.(Table 22).

ROUTE OF DELIVERY (Cesarean section vs. Vaginal delivery)

Caesarean sections (Matalon *et al.* 2006, Wikner *et al*. 2008) and induction of labour (Wikner *et al.* 2008) are also more prevalent among those with hypothyroidism .

In the present study, 62.2% (vs. 42.85%) hypothyroid mothers had caesarean section in present pregnancy which was contrary to findings of other studies(Table 13).

INFERTILITY AND RECURRENT PREGNANCY LOSS IN THYROID AUTOIMMUNITY

Thyroid autoimmunity predisposes to infertility and pregnancy complications (Gilad *et al.* 2011, Avi *et al.* 2011).

In the present study, 40% hypothyroid women had bad obstetric history in which 30%(vs. 4%) had spontaneous abortion and 10%(vs. 2%) had still birth in their previous pregnancies. This was in accordance with other studies(p=0.001). (Table 9).

FETAL AND NEONATAL COMPLICATIONS

Subclinical hyperthyroidism and hypothyroxinemia were not associated with any adverse peri- and neonatal outcome in our study. Subclinical hyperthyroidism is considered to be a somewhat physiological condition during pregnancy.

In line with this, adverse outcomes have not been associated with subclinical hypothyroidism previously (Casey *et al.* 2006) our results are in accordance with this.

One study reported a doubled rate of preterm deliveries in connection with autoimmune thyroiditis and declining thyroid function during pregnancy (Glinoer *et al*. 1994).

Hypothyroxinemia, on the other hand, has been considered to be a risk factor for preterm births: they have been observed in 8.4% of hypothyroxinemic mothers compared with 6.1% euthyroid mothers (Cleary-Golman *et al.* 2008).

Both overt and subclinical hypothyroidism have been associated with an increased risk of preterm birth (Abalovich *et al*. 2002, Casey *et al.* 2005, Stagnaro-Green *et al*. 2005, Antolic *et al*. 2006, Wikner *et al*. 2008). The retrospective study carried out by Abalovich *et al*. showed a very high incidence of preterm births in a small population based on hospital patients: 20%, 7.2% and 11.1% among mothers with overt hypothyroidism, subclinical hypothyroidism, euthyroidism under levothyroxine treatment, respectively (Abalovich *et al.*2002).

In the present study, 20% of hypothyroxinemic mothers experienced preterm birth, a result differing significantly from that in the control group(p=0.003).(Table 15)

Infants of hypothyroxinemic mothers have poorer neuropsychological outcomes(Pop *et al.* 2003, Henrichs *et al.* 2010).

In the present study 2% mothers had neurological deficit in neonate which was not statistically differing from control group.(Table 19).

One study has also shown increase in fetal death rates among mothers with severe hypothyroidism (Allan *et al*. 2000), but no association has been seen in other studies concerning subclinical hypothyroidism and fetal deaths (Casey *et al.* 2005, Cleary-Goldman *et al.* 2008). Our results had 4.44% neonatal death in hypothyroxinemic mothers which was not significant. (Table 21).

Some investigators have evaluated pregnancy loss, i.e. miscarriages and fetal death together (Ashoor *et al.* 2010a, Negro *et al*. 2010a), although early pregnancy miscarriage and late fetal death are of totally different aetiology (Fretts 2005).

In the present study, 2% hypothyroxinemic mothers had congenital anomaly (VSD) in neonate (Table 18) and 6.67% had neonatal hypothyroidism (Table 17) which was statistically not significant.

Significant results have been found in hypothyroid mothers having low birth weight babies (31.11%) with p value of 0.02 in the present study(Table 16).

Overall fetal morbidity was significantly increased in hypothyroxinemic mothers in the present study (p=0.009).

Table 5 :History of Infertility Treatment vs. Group

H/O infertility treatment	Cases		Controls	
	No.	%	No.	%
Present	8	16	2	4
Absent	42	84	48	96
Total	50	100	50	100

χ^2 = 2.778; p = 0.092

Table 6 :History of Spontaneous Abortion vs. Group (n=68)

History of Spontaneous abortion	Cases(n=37)*		Controls(n=31)*	
	No.	%	No.	%
Present	15	40.54	2	6.45
Absent	22	59.45	29	93.54
Total	37	100	31	100

χ^2 = 8.71 ; p = 0.02

*Note=out of 100 subjects, 32 were primigravidae (13 cases+19 controls)

Table 7 :History of Gestational Diabetes Mellitus vs. Group

H/O GDM	Cases		Controls	
	No.	%	No.	%
Present	5	13.5	1	3.22
Absent	32	86.48	30	96.77
Total	37	100	31	100

χ^2 = 1.125 ; p = 0.209

Note: out of 100 subjects 32 were primigravidae (13 cases+ 19 controls)

Table 8 :History of Pregnancy Induced Hypertension vs. Group

H/O PIH	Cases		Controls	
	No.	%	No.	%
Present	7	18.91	2	6.45
Absent	30	81.08	29	93.54
Total	37	100	31	100

χ^2 = 1.326 ; p = 0.249

Note: out of 100 subjects 32 were primigravidae (13 in cases+ 19 controls)

Table 9 :Bad Obstetric History vs. Group

Bad obstetric history No.		Cases		Controls	
		%	No.	%	
Present	Spontaneous abortion	15	30	2	4
	Still birth	5	10	1	2
Absent		30	60	47	94
Total		50	100	50	100

χ^2 =11.814 ; p = 0.001

Table 10 :Hypertensive disorders in present pregnancy vs. Group

PIH in present pregnancy	Cases		Controls	
	No.	%	No.	%
Present	8	16	3	6
Absent	42	84	47	94
Total	50	100	50	100

χ^2 = 1.634; p = o.201

Table 11 : Gestational Diabetes Mellitus in present pregnancy vs. Group

Gestational Diabetes Mellitus	Cases		Controls	
	No.	%	No.	%
Present	6	13.3	1	2.04
Absent	39	86.67	48	97.95
Total	45	100	49	100

χ^2 =4.29 ; p =0.038

Note: In cases 5 and in controls 1 had spontaneous abortion

Table 12 :Spontaneous Abortion in present pregnancy vs. Group

Spontaneous Abortion	Cases		Controls	
	No.	%	No.	%
Present	5	10	1	2
Absent	45	90	49	98
Total	50	100	50	100

χ^2 = 1.596; p = 0.204

Table 13 :Mode of Delivery vs. Group (SVD vs. LSCS)

Mode of delivery	Case		Control	
	No.	%	No.	%
SVD	17	37.78	28	57.14
LSCS	28	62.22	21	42.85
Total	45	100	49	100

χ^2 = 2.403; p = 0.121

Note: 5 women in cases and 1 in controls had spontaneous

abortion

Table 15: Preterm Birth vs. Group

Preterm delivery (<37 wks)	Case		Control	
	No.	%	No.	%
Present	9	20	0	0
Absent	36	80	49	100
Total	45	100	49	100

χ^2 = 8.651 ; p = 0.003

Note: five in cases and one in controls had spontaneous abortion

Table 16: Birth Weight of babies vs. Group

Low birth weight	Cases		Controls	
	No.	%	No.	%
Present	14	31.11	4	8.16
Absent	31	68.89	45	91.83
Total	45	100	49	100

χ^2 =9.796 ; p =0.02

Note: five in cases and one in controls had spontaneous abortion

Table 17:Neonatal Hypothyroidism vs. Group

Neonatal hypothyroidism	Cases		Controls	
	No.	%	No.	%
Present	3	6.67	0	0
Absent	42	93.33	49	100
Total	45	100	49	100

χ^2 = 2.971; p = 0.243

Table 18 :congenital anomaly vs. Group

Congenital anomaly	Cases		Controls	
	No.	%	No.	%
Present*	1	2	0	0
Absent	49	98	50	100
Total	50	100	50	100

χ^2 = 1.010; p = 1.000

*Ventricular Septal Defect

Table 19 :Neurological deficit in the Neonate vs. Group

Neurological deficit in the neonate	Cases		Controls	
	No.	%	No.	%
Present	1	2.22	0	0
Absent	44	97.78	49	100
Total	45	100	49	100

χ^2 = 0.970; p = 1.000

Table 21: Neonatal mortality vs. Group

Neonatal mortality	Cases		Controls	
	No.	%	No.	%
Expired	2	4.44	0	0
Survived	43	95.56	49	100
Total	45	100	49	100

χ^2 =0.603; p=0.226

Note: five in cases and one in controls, had spontaneous abortion

Table 22 :Subsequent Thyroid Disease in mother vs. Group

Subsequent thyroid disorders *	Cases		Controls	
	No.	%	No.	%
Present	3	6	0	0
Absent	47	94	50	100
Total	50	100	50	100

χ^2 = 2.971; p = 0.243

*mothers were followed upto 3 months post partum