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HYPOTHYROID PREVALENCE DURING PREGNANCY IN LAST ONE DECADE IN INDIA

Biotechnology

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ABSTRACT

Hypothyroidism during pregnancy is the most commonly found endocrine disorder. Its effect during pregnancy has widely been studied among women to understand the pathophysiology, outcomes, and prevalence. We collected data from several studies of last One Decade from separately studied population among all across the country regarding hypothyroid abundance. We compared more than 61 online available studies for the validation of data prevalence and to understand the status of associated risks to the mother and child in current scenario. Various risks like preeclampsia, preterm labor, anemia, IUGR, spontaneous birth, still birth, low birth weight infants, have been claimed associated in more than thirty five studies from the nation, few of them also lighted shed on developmental disorders in neonates born under such conditions. This study conserves biggest data of 43,282 women studied for such condition. Here we found 6,952 women effected by hypothyroid, which makes an average prevalence of 14.2% and it ranges from 2.5% (lowest) - 33.82% (highest) in different places in pregnant women. This figure is higher than the reported global prevalence. These studies also found increased number of bad obstetric outcome for antenatal and postnatal risks in mothers. To prevent consequences universal screening should be acquired.

KEYWORDS

Hypothyroid. Pregnancy, Adverse outcome, Prevalence, Preeclampsia, low birth weight

secreted into the bloodstream and then carried to every cell of the human body. Thyroid hormone helps the body use energy by regulating metabolism and keep the brain, heart, muscles, and other organs working normal. Fetal functional thyroid does not mature until 10-12 gestational weeks, so the fetus is dependent on the maternal thyroid hormone. This makes the mother overburdened and might led to hypothyroidism during pregnancy and results in later complications like abortion, anemia, pre term delivery (PTL), low birth weight (LBW) babies and many more if requirement remains unfulfilled.

Pregnancy is a general phenomenon. In normal pregnancy a number of important physiological and hormonal changes occur that alter metabolism. Mother wears extra load for nutritional supply to the fetus. In the initial phase, several endocrine glands are absent or underdeveloped in the developing fetus. One of them is thyroid, which is essential for metabolism and normal growth and development of the fetal organs mainly it functions in fetal brain development (Landers and Richard 2017). The mother nurtures the entire fetus development and tries to fulfill nutritional, metabolic, hormonal and genetic supply. Prior to the development of the fetal thyroid gland, mother is the only source of thyroid hormone for the fetus.

Over thirty years, hypothyroidism is emerged one of the most common endocrine disorders during pregnancy. That is why; many studies have taken place to examine the developmental effects of thyroid hormone (TH) deficiency on various systems in the mother, fetus and child. Their results have provided better understanding of disease pathogenesis and also helped in the treatment of TH insufficiency during prenatal or antenatal period.

1.1 Thyroid Pathophysiology and subtypes:

Thyroid is easily detectable in the serum by an inexpensive biochemical lab testing of Thyroid Stimulating Hormone (TSH), Free Thyroxins (FT4, FT3) level. Its functional test changes during pregnancy due to the imbalance of the two main hormones: human chorionic gonadotropin (hCG), a hormone that is measured as a biomarker of pregnancy and estrogen, the main female hormone. hCG can weakly stimulate the thyroid and the high circulating hCG levels in the first trimester may result in a slightly low TSH (called subclinical hyperthyroidism). This may show little decrease in TSH during early pregnancy but it comes back under range after a while in later pregnancy and remains normal throughout. Estrogen increases the amount of thyroid hormone binding proteins in the serum which increases the total thyroid hormone levels in the blood because more than 99% of the thyroidhormones are bound to these proteins. The low levels of thyroid hormone production is termed as hypothyroid converts in to secondary level of Overt Hypothyroidism (OH) in 2-5% of cases. TSH level goes high TSH > 10mIU/L [Begum *et al.* 2016].

However, measurement of hormone level, which is not intact to the protein ("Free Hormone": represents its active form) usually remain normal. The thyroid functions normally if the TSH, Free T4 andFree T3 are all normal throughout the pregnancy. Calcitonin stimulates the thyroid nodule growth which increases the size of thyroid gland for over production of the hormone during pregnancy.

Embryonic neurodevelopmental process is crucial for the brain development until onset of fetal thyroid function. Maternal hypothyroidism has been reported to impair the astrocyte maturation by epigenetic silencing of G*fap* which is a marker of mature astrocyte. Overt maternal hypothyroidism study reported from Kashmir over 82 early neonates of 3-4 weeks of age found related with abnormal neurobehavioral development of the affected child [Ganaie *et al.* 2015]. This is in particular visible while the maternal hypothyroidism is due to iodine deficiency, which also impacts the baby. However, recent research have cautioned that certain brain developmental abnormalities can be present in children born to the untreated hypothyroid mothers in antenatal period. At this time there may be no popular consensus of opinion regarding screening all pregnant females with hypothyroidism.

However, some physician groups and several studies recommend examination of a woman's TSH value either before conceiving (pre-pregnancy counseling) or as soon as pregnancy is confirmed and provide a trimester specific dose [Dhanwal *et al.* 2016]. Screening becomes more important for the women having increased risk of thyroid disorders or on prior medication of hyperthyroidism or contains a family history of thyroid disease of goiter.

1.2 Disease management:

Woman with established hypothyroidism/ with earlier history of hypothyroidism must have TSH test done once pregnancy is confirmed. Antenatal checkups for Thyroid function tests (TFT) may be more frequent as in every 6-8 weeks approximately throughout pregnancy.

This is to ensure that the woman has normal thyroid function throughout pregnancy, as thyroid hormone requirements increase during pregnancy. This issue should be discussed further with the health care provider, particularly if patient is contemplating pregnancy. Once hypothyroidism has been detected, the woman can be treated with hormone replacement usually levothyroxine to normalize her TSH and Free T4 values.

The treatment of hypothyroidism in pregnancy also gets change due to increment in requirement by the trimester unlike the non-pregnant woman [Murthy *et al.* 2015], occasionally, the levothyroxine dose may double, and it might continue even after delivery with more than half of regular dose [Begum *et al.* 2016]. If a change in levothyroxine dose is required, thyroid levels should be measured 4 weeks later. As soon as the child is delivered, the hypothyroid woman may go back to her usual pre-pregnancy dose of levothyroxine. Prenatal iron and calcium level examination is equally important because vitamins may play a role in thyroid hormone absorption in gastrointestinal (GI) tract.

Consequently, levothyroxine and prenatal vitamins should not be taken at the same time and should be separated by at least 2-3 hrs of duration for proper absorption of the hormone and supplements.

2. MATERIAL AND METHOD:

We searched on Google Scholar, Pub Med, Scopus, Medline, Research gate, using a combination of text words to generate two subsets of quotes combined with "AND", one indexing thyroid disorders and the other indexing adverse maternal and fetal outcomes. Studies from 2008 to 2019 were scrutinized and primary focus was on to collect prevalence data for hypothyroid women during pregnancy. Other information on their maternal age (Avg ±SD), gestation age (Avg ±SD), classification in groups for study and conclusion of study were noted for our reference. Zonal division was made to understand the scatteredness of disorder.

Language restrictions were applied and authors only have considered English language full articles. All other incomplete articles having main focus on other disorders were excluded. Online search results were sorted and scrutinized for obtaining full material and were considered relevant to our study. Few have been cited from the journal itself. References have been framed by the ENDNOTE X9.

RESULTS:

Result of our study consolidates data of 43,282 Women from 61 different studies of past 10 years which were executed in more than 61 centers from 16 states/union territories of country.

We noticed a great variability between cities, the prevalence of hypothyroidism, as assessed by individualized investigations, ranges from 33.82% [Goel *et al*. 2015] in Uttar Pradesh to 2.5% in Hyderabad [Rao *et al.*2008], this provides a combined mean of 14.2 % in total thyroid dysfunction during pregnancy. Total numbers of subjects 43,282 pregnant women were studied by research groups where 6,952 were diagnosed Hypothyroid.

This indicates an average prevalence of 14.2% (overlying values were excluded from 5 studies consisting case control patients data to not affect prevalence calculation) spread among.

Most of the studies were focused on analysis of prevalence and relation of hypothyroidism with adverse outcomes. Table 1 contains the gathered data from those studies.

Table 1: Hypothyroid prevalence studies in last one decade from various centers of India

SR NO	YEAR	GROUP	NO OF SUBJECTS n= (hypothyroid/total)	PLACE-(State/ Union territory of INDIA)	TYPE OF STUDY	Gestational age (wks)	Mean age of women (yrs)	Total hypothyroidism present count (%)	Sub Group Division-count (%)	Main Finding (significant association with "&")
1	2008	R. K. Marwaha *et al.*	86/541	New delhi, INDIA	Cross sectional study	I, II, III trimesters all	-	86 (15.9) %	SCH 78(14.2%) & OH 7 (1.3%)	Trimester specific range of FT3, FT4, TSH(I, II, III)
2	2008	V.R. Rao *et al.*.	8/337	Hyderabad, Telangana, INDIA	Case control study		25.19 ± 4.01 yrs	8 (2.5%)	RPL (163) & Control (170)	RPL & Hypothyroid(significant relation)
3	2009	R. Gayathri *et al.*.	14/495	Chennai, Tamil Nadu, INDIA	Cross sectional single center study	I, II, III trimesters all	23.8±3.7 yrs	14 (2.8%)	SCH 14 (2.8%) TPO 42(8.5%)	SCH doesn't depend on TPO –universal screening recommend
4	2009	Abraham *et al.*.	58/505	Pondicherry, INDIA	Population based survey (Random Selection)			58 (11.5%)	SCH 58 (9.5%), OH 9 (1.8%)	
5	2010	M.T. Sahu & V. Das *et al.*.	70/633	New Delhi, Lucknow, U.P. INDIA	Prospective evaluation bi-centric study	13-26 wks	28.4±4.6 yrs	81 (12.8%)	SCH 41(6.47%) & OH 29(4.58%)	PIH, IUGR, IUD, LSCS & OH (sig relation)
6	2011	V. Nambiar *et al.*.	24/483	Mumbai, Maharastra, INDIA	Prospective Cohort study	10.03± 1.87 wks	25.19 ± 4.17 yrs	24 (4.8%)	TSH Range 6 groups	Hypothyroid & miscarriage
7	2012	P. Goel *et al.*.	63/ 1005	Chandigarh, India	Prospective Study	-	27.6±2.9 yrs	63 (6.3%)	SCH 34 (3.4%) & OH 29 (2.9%)	34 new case due to lower cutoff
8	2012	M. Pradhan et al.	196/ 2479	Lucknow, Uttar Pradesh, INDIA	Prospective Study	Ist, IIn & IIIrd trimester	-	196 (7.91%)	167 (6.7%) SCH & 29 (1.17%) OH (2 Groups-TPO+/TPO	High Risk was present more in TPO+ Vs TPO-group
9	2013	Dhanwal *et al.*.	143/ 1000	Pant Hospital, New Delhi, India	Prospective Observational uni-centric study	9.2±3.4wks	25.6±11.1 yrs	143 (14.3%)	SCH (13.5%) & OH (0.7%)	SCH is higher in North INDIA
10	2013	Jayaraman *et al.*	109	Hyderabad, Telangana, INDIA	Prospective Cohort Study	17.6 wks	24.8 yrs	98	SCH - 98	No sig diff in APO b/w groups with medication
11	2013	K.Lata *et al.*.	51/200	Chandigarh, INDIA	Prospective Study	38 wks	27.0±3.1	51 (25.5%)	Groups with Miscarriage history	TPO+ was higher in recurrent abortions

12	2013	Bandela *et al.*	18/139	Nandyal, Andhra Pradesh, INDIA	Random selection Prospective study	Mean- 8.5 wks	17-35 yrs	18 (12.87 %)	14(10.0%) SCH, 4(2.87%) OH	
13	2014	S.N. Ajmani *et al.*	48/400	New Delhi India	Prospective study	13-26 wks	25.84±4.97 yrs	48 (12%)	SCH 36 (9%) & OH 12 (3%)	Adverse pregnancy and fetal outcome reported
14	2014	A Dave *et al.*	30/305	Indore, Madhya Pradesh, INDIA	Prospective Cohort Observational Study	9.09 ± 4.09 wks	24.46±2.0 yrs	(9.8%)	Eu thyroid (89.83%)& hypo thyroid (9.8%)	TSH & adverse peri natal outcome (sig relation p<.001)
15	2014	Tej Ram Jat	-	Madhya Pradesh, INDIA	Epidemiology and global Health	Pregnant women	±		SCH (%) & OH (%)	
16	2014	V R Murty *et al.*.	89/322	Ranga Reddy, Telengana, INDIA	Prospective uni-centric study	IInd trimester	<20, 20-25, 25-30, >30 yrs groups	89 (26%)	SCH (22%) & OH (4.02%)	Universal screening recommended
17	2014	M.Rupali et al.	35/800	Burdwan, Kolkata, West Bengal, INDIA	prospective analytical study	36-38 wks	25.2 ± 3.22 yrs	35 (4.8%) Hypothyroid (HOTH)	SCH 35 (4.8%) & 765 cases Euthyroid (ETH)	SCH is associated with bad obstetric outcome in comparison to Euthyroid
18	2015	M. Goel *et al.*	208/ 615	Ghaziabad, Uttar Pradesh, India	Prospective Observational uni-centric study	9.81±.66 wks	25.4 (± 3.61) years	208 (33.82%)	SCH 200 (32.5%) & OH 8 (1.3%)	Local population based reference range required
19	2015	R. Rajput *et al.*	105/ 461	Haryana, INDIA	Prospective cross sectional uni-centric study	8±5 wks	23.79 ± 3.47 yrs	105 (22.7%)	SCH 99(21.5%) & OH 6 (1.3%)	High Anti TPO-universal screening required
20	2015	K. Velayutham *et al.*.	161/ 1292	Madurai District, Tamil Nadu. INDIA	Prospective Cross sectional study	-	18-25 years	161 (12.5%)	125 (77.6%) SCH & 17 (10.6%) OH	More aggressive screening is required
21	2015	N.V.R. Murty *et al.*.	260/ 1340	Hyderabad, Telengana, INDIA	Prospective Uni-centric Observational study	All Diff Ist& IInd trimesters	<20 to >30 all age groups	260 (19.41 %)	216 (%) SCH & 44 (%) OH	Higher prevalence found Universal screening desired
22	2015	S Sogani	35/70	Indore, M.P. INDIA	Case Control Uni-centric study	35.85 ± 2.65 wks	22.94 ± 3.25 yrs	35 (50%)	35 (50%) Hypothyroi 35 (50%) control group	Preeclampsia & Elevated level of TSH
23	2015	D. Joshi *et al.*.	66/132	Indore, M.P. INDIA	Prospective Cross sectional study	<20 wks	23.9±3.1 yrs	66 (50%)	Higher TSH &Control	TSH range for Isttrimester
24	2015	M.A. Ganaie*et al.*	82/133	Kasmir, J&K, INDIA	Prospective Cohort study	36 ±1.75wks	29.4 ± 3.5 yrs	82 (61.65%)	Hypothyroid & Euthyroid	NBD & OH
25	2015	K.P. Singh *et al.*	92/400	Imphal, Manipur	Prospective study	Ist & IInd trimester	26.8 ±8.2 yrs	72(18%) SCH, 18(4%) OH	Hypothyroid (SCH & OH)& Euthyroid	Higher prevalence of SCH
26	2015	A. Bose *et al.*	151/ 1152	Indore, Madhya Pradesh, INDIA	Prospective study	Ist trimester	26.25 ± 4.39	151(13.1%) = 125 (10.85% SCH & 26(2.25%) OH	Clinical & subclinical hypothyroid	Routine thyroid screening recommended
27	2015	A Pavangang a *et el.*	168/ 1663	Bangalore, Karnataka, INDIA	Observational study	14-20 wks	20-30yrs	10.1% 156 (9.3% SCH) & 12 (0.72%) OH	Autoimmunity in SCH & OH (Hypothyroid groups)	PE, GDM, PTL, IUGR cases were increased in study group
28	2015	Umadevi N.	116/ 400	Chennai, Tamil Nadu, INDIA	Cross sectional study for Master's Thesis	34.7 ± 2.9 wks	24.36 ± 4.25 yrs	116 (29%) =110 (27.5%) SCH & 6 (1.5%) OH	Normotensive and Preeclampsia group	Strong correlation between PE & Hypothy
29	2016	P Bhatia *et al.*	32/249	Bhopal, M.P. INDIA	Cross Sectional Study	-	17-25 yrs	32 (12.85%)	Hypothyroid & Euthyroid	7.63% in collage girls
30	2016	D K Dhanwal *et al.*	404/ 2599	11 Cities in 9 States of INDIA	Cross Sectional Multi-centric Study	19.3 ± 15.9 wks.	25.5 ± 5.6 yrs	388 (13.13%)	Trimester specific TSH cutoff	hypothyroi 44.3%, 32.0%, and 34% in I II,III trimest

31	2016	F Begum	1671/ 9117	Kolkatta, W.B. INDIA	Prospective Observational study	IInd trimester	20-30 yrs majorly	1671 (18.33%)	Euthyroi, Hypothy & Hyper thyroids	PE, PTL, LBW vs Hypothyroidism
32	2016	A.P. Kaundinya *et al.*.	54/500	Goa, INDIA	Prospective observational study	±	27.35 yrs	54 (10.8%)	SCH 35 (%) & OH19 (%) & Hyper O&C	Universal screening is required for saving APO
33	2016	U. Agrawal *et al.*.	35/110	Bhopal, M.P. INDIA	Retrospective observational study	8.3 wks	26.34 yrs	35 (31.81%)	Hypothyroid & Control	Anemia & hypothyroidism
34	2016	R.C. Mandal *et al.*.	168/ 510	West Bengal, INDIA	Prospective observational study	7.6 ± 1.12 wks	18.7 ± 3.52 yrs	168 (32.94%)	SCH & diff TSH Levels	SCH is higher in WB
35	2016	D. Tiwari *et al.*.	102/ 1000	New Delhi. INDIA	Prospective cross sectional	20-35yrs	26.06 ± 3.85 yrs	102 (10.2%)	SCH 48(6.4%), &OH 21 (3.8%)	PE, GDM, PTL, FD,
36	2016	S. Chittamuri *et al.*	50/100	Visakhapatnam, Andhra Pradesh, INDIA	Observational, prospective, Cohort Study	Ist& IInd trimester	≥18 years	50 (50%)	SCH 50 (50%) & 50 (50%) Euthyroid	PTL, PIH, LSCS were higher but non significant
37	2016	A. Khatri *et al.*.	473/ 2492	Safdarjang, New Delhi, INDIA	Cross sectional study	-	Mean age 26.5 yrs (18-45 yrs)	473 (18.98%)	SCH 388 (15.56%), & OH 85 (3.41%)	Timely management of HT is required
38	2016	R. Saraladevi et al	92/ 1000	Warangal, Telangana, INDIA	Prospective Study	<12 wks	-	92 (9.2%)	64 (6.4%) SCH & 28 (2.8%) OH	Universal screening required to reduce APOs
39	2016	S. Rao *et al.*.	215/ 1062	Sanathnagar, Hydrabad, Telangana, INDIA	Retrospective Study	Ist& IInd trimester	Mean age 22.1 yrs	215 (20.1%)	SCH 149 (14.9%) & OH 66 (6.6%)	Very high prevalence of hypothyroi
40	2016	M. Shivanagappa *et al.*	170/ 1000	Mysore, Karnataka, INDIA	Observational Study	Irrespective of gestational age	Irrespective of maternal age	170 (17%)	126(12.6%) SCH & 44(4.4%) Hypothyroi	Hypothyroid has relation with adverse fetomaternal effect
41	2017	P.U.Kadushkar *et al.*	452	Bangalore Karnataka, INDIA	Prospective Study	13.81 ± 9.12	25.74 ± 4.29	256 (9.04%)	New cases 256 (56.64%), & in 196 (43.36%) Pre pregnancy Hypothyroid present	LSCS was higher in cases but not significant
42	2017	J. Mulik *et al.*.	102/864	Nagpur, Maharashtra, INDIA	Observational Study	Ist, IInd& IIIrd trimester	18-40 years	102 (11.8%)	88 (83.8%) SCH & 14 (13.3%) OH	Anemia, PIH & Abortions are linked to hypothyroi
43	2017	J.K. Gedam *et al.*	41/ 350	Parel, Mumbai, Maharastra, INDIA	Prospective study	7.96 ± 2.01 weeks	18-40 years	41 (11.7%)	SCH 27 (7.7%) & 14 (4%) OH	Universal screening recommended due to high prevalence of SCH found
44	2017	Dr.S Suganthi & Dr. R Monika	30/500	Royapuram, Chennai, TN INDIA	Prospective study	Ist, IInd& IIIrd trimester	20-35yrs	30 (6%)	30 (6%) SCH & Euthyroid group	Early detection may reduce APOs
45	2017	M. Beenish et al.	114/ 902	Srinagar, Kashmir, INDIA	Prospective Study	Pregnant women	28.3 ± 4.2 yrs	114 (12.6%)	Control group & Study group	High prevalence of SCH & universal screening advocated
46	2018	B. Kalra *et al.*.	70/569	Karnal, Haryana, INDIA	Retrospective review	At Term	27.33 ± 3.78 yrs	70 (12.3%)	Full term delivered pts with TSH profile	Level observed in term pregnancy
47	2018	V.R. Korde *et al.*.	98/705	Pune, Maharashtra, INDIA	Prospective Study	Term delivered reports	Mean age 23.45 yrs	98 (13.9%)	90 (12.76%) Hypothyroidism and 8 (1.13%) hyperthyroidism	Universal screening required due to higher prevalence
48	2018	Pillai et al	92/ 1000	Kerala, INDIA	Prospective Study	6-10 wks	Mean age 26.66 yrs	(9.2%)	92 (9.2%) = SCH 85 (8.5%) & OH 7 (0.7%)	Recommendation of universal screening need

49	2019	D. Goyal *et al.*	18/140	New Delhi, INDIA	Case Control Study		26.76 ± 6.66 yrs	18 (12.85%)		
50	2019	P. Agrawal et al.	15/250	New Delhi, INDIA	Prospective Study	<12 wks Ist trimester	20-45 yrs	15 (6%)	13 (5.8%) SCH & 2 OH (0.2%)	Prevelence pregnancy duration, gravid,& socioeconomic status
51	2019	Aishwarya R.	50/ 400	Theni, Tamil Nadu, INDIA	Single centre prospective study for Master Thesis	36-40 wks	25.33 years	50 (12.5%)	34 (8.5%) SCH & 16 (4%) OH	Universal Screening is Important to avoid missing 1/3 affected patients

Table1: table summarizes the studies conducted in last ten years from 2008 to 2019 all across the country which includes 48 super specialty centers from 14 different state and union territories. Values are given in mean ± SD, Abbreviations: PTL, pre term labor; LBW, low birth weight; SCH, subclinical hypothyroidism; OH, overt hypothyroidism; PE, preeclampsia; PIH, pregnancy induced hypertension; LSCS, longitudinal caesarian section; TSH, thyroid stimulating hormone; NBD, neonatal birth defects; FD, fetal distress; GDM, gestational diabetes mellitus ;TPO, thyroid peroxide antibody.

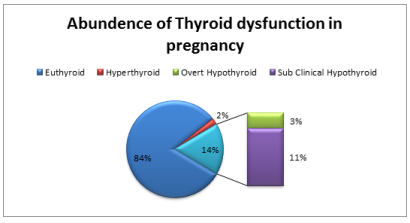

Figure 1: Distribution of hypothyroidism in women (%) with subtype of disease from the studies in last one decade has been observed in INDIA

Pie chart in Figure 1. shows percentage distribution of hypothyroid during pregnancy in Indian women which was found higher as per global data. 84% women ware euthyroid whereas 14% found hypothyroidism and 2% reported with hyperthyroidism. Subclinical hypothyroidism was more with 11% prevalence and 2% cases was diagnosed as overt hypothyroid.

All the studies further categorized in countries zonal boundaries to understand overall scenario in country, Data revealed many places missing from the various parts to still provide the clear view. We found 16 states and Union Territories were probing in the right direction to find out necessary cause and working towards to draw a wide picture over it from all the six zones.

Table 2 includes 61 studies from 6 zones and 16 states performed 61 studies. Most of the studies were available from north zone and south zone 21-21 respectively and 7-7 studies were reported from central and west zone, whereas east and north east has conducted 4 and one study at different centers on different time during the last 10 years.

Table 2:Summariesed Zonal classification of studies from different parts of INDIA in last one decade from 2008-2019.

Zone	Region	Study no.	Name of state / Union Territory	No of centers (where Study was conducted)	Total No of Studies	Prevalence (AVG %)
1	NORTH ZONE	1	Jammu & Kashmir	3	21 Studies	39.75%
		2	Haryana	3		18.13%
		3	Uttar Pradesh	4		17.55%
		4	Chandigarh	2		28.65%
		5	New Delhi	9		11.45%
2	NORTH EAST ZONE	6	Manipur	1	1 study	18%
3	EAST ZONE	7	West Bengal	4	4 study	13.51%
4	SOUTH ZONE	8	Karnataka	3	21 studies	12.05%
		9	Tamil Naidu	6		11.25%
		10	Puducherry	1		11.5%
		11	Andhra Pradesh	3		23.94%
		12	Telangana	7		14.3%
		13	Kerala	1		9.2%
5	CENTRAL ZONE	14	Madhya Pradesh	7	7 studies	11.16%, 20.67%
6	WEST ZONE	15	Goa	1	7 studies	10.8%
		16	Maharashtra	6		12.34%
INDIA		TOTAL	16 states/UTs	61 centers	61 Studies	14.2%

3. DISCUSSION:

Thyroid hormone is secreted by the thyroid gland present in the neck. It's an extremely important hormone for the conventional development and metabolic regulation of virtually every organ of the physical body and specifically for neonate brain. It's required for maturation of the many target tissues. The under and over-production of this hormone has significant effects on the human body.

Similarly, inadequate treatment of expectant mother already known to possess hypothyroidism from a range of causes, or over-treatment of a hyperthyroid woman with anti-thyroid medications and former abortions should be addressed with utmost care [Joshi *et al.* 2015]. Untreated, or inadequately treated hypothyroidism has been related to maternal anemia (low red blood corpuscle count) [Ganaie *et al.* 2015], myopathy (muscle pain, weakness), congestive coronary failure , pre-eclampsia, low birth weight infants, postpartum hemorrhage (bleeding), spontaneous abortions, still birth or perinatal death , placental abruption and pre term labor. Women with sever hypothyroidism history witnesses complications more likely. Mostly females with mild hypothyroidism may not have any symptoms or attribute unnoticed symptoms during the pregnancy.

Thyroid hormone is critical for fetus brain development. The children who have congenital hypothyroidism (CH: no thyroid function at birth) may face severe cognitive, neurological and developmental abnormalities [Bhatia *et al.*2016] if the condition isn't recognized and treated promptly. Immediately after birth recognition of abnormalities may prevent developmental malfunctioning in neonates.

The fetus remains hooked in to the mother for ingestion of adequate amounts of iodine, which is important for the assembly of thyroid hormones. Any irreversible brain damage like cretinism is often avoided in cases of TH insufficiency. The planet Health Organization recommends iodine intake of 200 micrograms/day during pregnancy to take care of adequate hormone production. That's why; many studies have suggested that accurate thyroid screening with trimester specific reference ranges should be warranted, particularly in areas with reported mild to moderate iodine deficiency [Kadushkar *et al.* 2017]. Variable prevalence of hypothyroidism in pregnancy has been reported from various parts of the country. Table 1 lists recently published data on this aspect of thyroidology [1-51]. A good heterogeneity was witnessed in results, it may be due to differing TSH cut offs for diagnosis they opted during screening. One epidemiological study data has not been included within the calculations due to having varied

objectives [Tej Ram Jat, 2014].

This review consolidates data of 43282 Women from 61 studies of last 10 years and over 61 centers 16 states of country. There's great variability between cities. The prevalence of hypothyroidism, as assessed by centralized investigations, ranges from 32.94% in West Bengal [Mandal *et al.*2016] to 2.5% in Hyderabad [Rao *et al.*2008]. We couldn't report city-specific adverse outcome for all, though this might have provided meaningful insight into the epidemiological features. Nonrandomized design and lack of clinical data were also important limitation during this study.

We addressed an epidemiological study from 11 different cities of India trying to find prevalence of hypothyroidism reported a significantly higher ($P < 0.05$) proportion of females vs. males (15.86% vs. 5.02%) [Dhanwal *et al.*2016]. Another study from Pondicherry, a complete 505 women were examined where 15.8% found thyroid dysfunction and 84.2% were euthyroid among them 11.5% had hypothyroidism where as 9.5% sub-clinical and a couple of ha overt hypothyroidism [Abraham *et al.* 2009]

A study from Karnal Haryana records the prevalence of hypothyroidism 12.3%, of which 15.5% were diagnosed during pregnancy of all women who had delivered there in April 2016 to March 2017. Hypothyroidism is common in term with pregnancies. If treated adequately, healthy feto-maternal outcomes will be achieved (Kalra*et al.* 2018).

A big study from south India has given prevalence of 1 in every eight women shows thyroid dysfunction and concluded for raising the importance of universal screening (Velayutham*et al*. 2015). The incidence of congenital hypothyroidism (CH) during a study conducted by Abraham & group screened nearly 40,000 newborns and located 1 in 2,640 affected with CH which may be a preventable explanation for retardation found in neonates, where as in another regional study from Mumbai area Desai *et al.* found CH incidence 1:2804 from the study of n=25244 samples (Desai*et al.* 1994), these findings indicates a way higher prevalence than the worldwide average of 1 in 3,800 (Rose *et al*. 2006). The common reason found was delay in diagnosis because of lack of awareness in primary health care practitioners and family physicians (Kalra*et al.* 2018).

Many previous studies suggests that accurate thyroid screening with trimester specific reference ranges should be warranted, particularly in areas with mild to moderate iodine deficiencies (Altomare, *et al.* 2013). Kalra *et al.* 2018 has also mentioned in his study from Delhi that hypothyroidism is common in term pregnancies. If treated adequately, healthy feto-maternal outcomes are often achieved (Kalra,*et al.* 2018). Aishwarya R. 2019 in her recent study from south India over 400 subjects observed the importance of Universal screening to avoid undiagnosed one third part of affected populations. (Aishwarya R.2019)

CONCLUSION:

Universal screening of the patients as per the trimester wise requirement should be done to scale back the infant mortality rate (IMR), perinatal mortality rate (PMR) and congenital hypothyroidism. More studies are required from missing regions across the country to decode the prevalence of related adverse pregnancy outcomes. We've gathered most number of studies as biggest collection during this particular criteria from last 10 years in best my knowledge nobody from India has published data with this huge collection. Screening for antenatal hypothyroidism should be made universal to manage the cases affected by irreversible brain damage as its consequence. Proper treatment of maternal hypothyroidism will increase the survival rates of premature fetuses and early postnatal treatment are often initiated for neonates with congenital hypothyroidism to cut back the severity of neurological damage and developmental delays.

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Abbreviations:

Preterm Labor (PTL), Low Birth Weight (LBW), Subclinical Hypothyroidism (SCH), Overt Hypothyroidism (OH), Thyroid Stimulating Hormone (TSH), Intra Uterine Growth Retardation (IUGR), Intra Uterine Death (IUD), Neonate Development (NBD), Pregnancy Induced Hypertension (PIH), Longitudinal cross section (LSCS), Thyroid (TPO), Rupture Placental (RPL), Gestational Diabetes Mellitus (GDM), Fetal Distress (FD), Preeclampsia (PE), Adverse Pregnancy Outcome (APO), Hypo Thyroid (HT)

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