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EDITORIAL OPEN ACCESS

Challenges of being a diabetic in Nepal

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Diabetes mellitus burden has been escalating throughout the globe. By end of 2018 approximately 425 million adults (20-79 years) are living with diabetes and the most troublesome statistics is that 79% of adults with diabetes are living in low and middle income countries.[1] The global prevalence of diabetes is 8.8% and is expected to increase every decades especially contributed by increasing prevalence from low and middle income countries.[2] Nepal reports prevalence of diabetes above 8% from studies done at communities' level by different medical schools.[3-5] The true burden is likely to be beyond the published data. Comprehensive quality care at low cost to patient seems to be one of the challenges in developing nation like Nepal. The point of care facilities for diabetic patients in Nepal are either less or inaccessible compared to the burden of disease. This is likely to increase the indirect cost of illness of a diabetic patient in terms of travel and accommodation which is again not easier as compared to high income country. The major gaps at current situation are first inadequate manpower in terms of primary physicians trained on diabetes at primary health care and districts hospitals, and diabetic team (diabetic physician, dietician, counselor and nurses) at zonal and tertiary hospitals. Second laboratories facilities that can monitor beyond plasma sugar level in primary care are a few in Nepal. Some of the endocrinology faculties in Nepal has taken initiative to train primary physician regarding comprehensive diabetes care however these is need of incorporation of such training in national policy level. Diabetes is not a priority disease in terms of expense of budget by health ministry in Nepal though it is public health problem that runs parallel with infectious disease. This is so because infectious disease are still priority public health issue at ministry and ministry is fighting against elimination or eradication of the infectious diseases. Private health care facilities are bridging these gaps in diabetes but still they are focused at urban areas making a rural diabetic Nepalese inaccessible. These all gaps is going to bring a diabetic patients to care point at either acute or chronic complicated status. This could be the reason for high burden of coronary artery disease, strokes and renal failure in young adults in developing nations. Diabetes with complication is going to exacerbate the cost of illness with compromised quality of life. Nepal GDP per capita income is around $1003.64 and Nepal spends around 6% of its GDP in health.[6] Literature on direct cost of illness of outpatient door (OPD) diabetes in developing countries is more than $150 per annum.[4],[7-9] If we consider global prevalence as national the direct cost of illness of an OPD based diabetic patient will account for 1.3% of Nepal GDP that is 21.6% of current health budget.2,6 Thus diabetes is high economic burden disease in Nepal.

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Correlation between Body Mass Index, Thyroid Function Test and Neck Ultrasound in Euthyroid and Thyroid Disorder patients: a Centre Based Retrospective Study

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Abstract

Background: Thyroid dysfunction is a major health issue among the Nepalese population. It is the prone region for iodine deficiency disease. Altered living status, sub-urbanization and behavioral factors among the people are believed to be thyroid sufferers. The effects of hypothyroidism and hyperthyroidism on body weight have been clinically clearly demonstrated however there are only few literatures published showing the relationship between BMI and thyroid function among the two groups of population (euthyroid and thyroid dysfunction).
Objective: This study aims to study the relationship of TSH (thyroid stimulating hormone) and thyroid hormones with BMI and neck ultrasound findings in euthyroid and thyroid dysfunction subjects.
Methods: This is a centre based retrospective study carried out in Diabetes, Thyroid and Endocrinology Care Centre (DTECC), Pokhara Nepal. The study used the archives of the laboratory and patient clinical information on the Centre during the years 2016 March to 2017 March. Detailed information regarding patientís age, medical history and previous history of smoking and alcohol consumption data, patients BMI (Body Mass Index) and neck ultrasound findings were obtained.
Results: Of the total five hundred and six cases, four hundred and forty cases were females and sixty six cases were male. 59.4 percentages of the cases had increased body mass index and about 48 percentages of the total cases had abnormal thyroid function tests. Of the total, neck ultrasound revealed findings suggestive of Hashimoto Thyroiditis in two hundred and forty four cases.
Conclusion: Thyroid dysfunction is associated with some components of metabolic syndrome. The thyroid function disorders in conjunction with the strong influence of various environmental factors can increase body weight and lead to obesity. Increased in BMI has strong influence on thyroid hormone level.

Key Words: Body Mass Index, Euthyroid, Thyroid dysfunction,

Introduction:

Thyroid dysfunctions are the second most common endocrine disease, being next only to diabetes mellitus. Depending upon the level of thyroid hormones in blood it manifests ranging from hyperthyroidism to hypothyroidism.[1] Abnormal Thyroid functions can be induced either by excessive or deficient of iodine intake. Study shows that almost one-third of the world's population lives in areas of iodine deficiency.[2] Dietary Iodine deficiency is an important underlying cause of thyroid dysfunction, especially among the people who resides in hilly region.[3]

Thyroid dysfunction is a major health issue among the Nepalese population as it is the country of

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Himalaya, landlocked and surrounded by two giant countries China and India; is the prone region for iodine deficiency disease. Altered living status, sub-urbanization and behavioral factors among the people are believed to be thyroid sufferers. Lack of country's census in regarding the prevalence of thyroid suffers and government policy for prevention and disease control, lots of information and the proper data to compare the study is beyond our dream. However, few research data has been published in different parts of the Nepal regarding the prevalence rate and status.[1,4,5]

This study aims to correlate the relationship of TSH (thyroid stimulating hormone) and thyroid hormones with BMI and at the same time its correlation with the neck ultrasound findings.

Methods:

This is a centre based retrospective study carried out in Diabetes, Thyroid and Endocrinology Care Centre (DTECC), Pokhara Nepal. Patients who visited the centre during the period, 2016 March to 2017 March, either for thyroid screening purpose or for medication purpose was randomly included. Irrespective of patientís age, cast and ethnicity patients were recruited. Data were collected from the archives of the laboratory and patient clinical informationís file. Detailed information regarding patientís age, medical history and previous history of smoking and alcohol consumption data, patients BMI (Body Mass Index), fasting serum thyroid function test report and neck ultrasound findings were obtained. Sonographic findings of the neck ultrasound were further compared with the clinical diagnosis and serum thyroid report. Ethical permission for the study was obtained from the board of DTECC. Descriptive analysis was done for statistical interpretations. All the data were first input in Microsoft Excel software (version 2003) which was further analyzed by SPSS, Version 23 (Chicago, USA).

Results

There were in total, five hundred and six patients who fulfilled the criteria for the study were enrolled. The patient mean age was 42.43 years, ranging from 8 to 88 years. There were four hundred and forty female cases (87%) and only sixty-six male cases (13%). Female predominance was common (Figure 1). Thyroid dysfunction was more common in women above forty years of age.

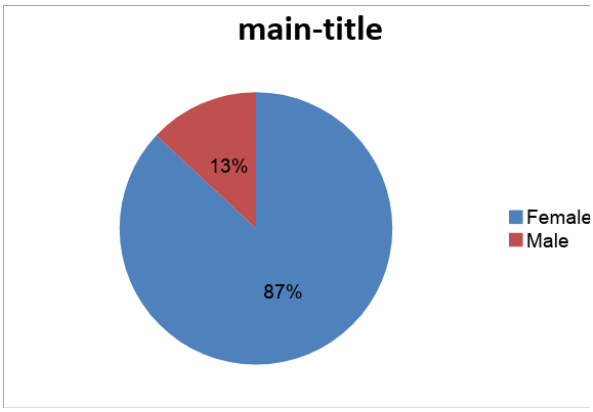

Figure 1 Male and female participant for the study

Most of the patients who visited the centre for thyroid dysfunction examination or for screening purposes revealed obese status. Of the five hundred and six cases, forty percentage of cases had normal Body Mass Index (<25), thirty six percentage of the total cases were overweight (25-30). Similarly 19% of the cases were categorized as obese (30-35). Only 5% of the total cases (24/506) were categorized under morbidity (Figure 2).

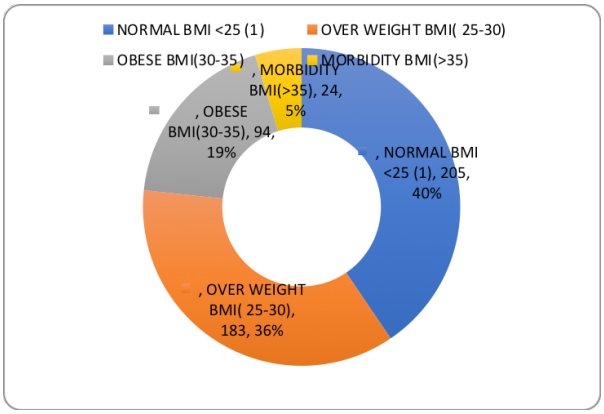

Figure 2 Levels of BMI

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Our study revealed that of the total 506 cases that had serum thyroid function test in our centre using CLIA(Chemiluminescence Immunoassay) methods in fasting status had high TSH in one hundred and ninety-seven cases (38.93%), low in 57 cases (11.26%) and normal in 252 cases (49.80%) (Figure 3).

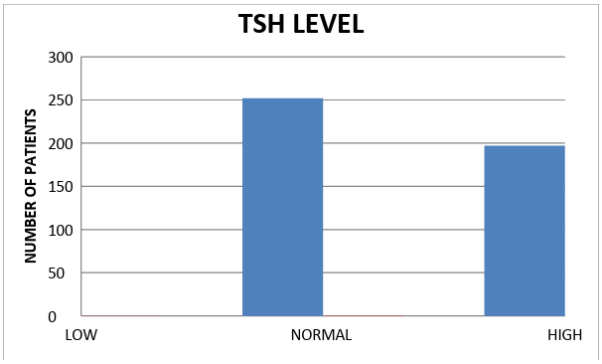

Figure 3 . TSH levels distribution in the population

Male and female distribution of serum thyroid hormone level as per the biochemistry report were further categorized as low, normal and high as shown in table 1.

Table 1. Distribution of Thyroid serum TSH levels in male and female population

	SERUM TSH VALUES			
	Low	Normal	High	Total (n=506)
Male (n=66)	6 (9.0%)	28 (42.42%)	32 (48.48%)	66
Female (n=440)	51 (11.59%)	224 (50.90%)	165 (37.5%)	440

All of the enrolled cases underwent neck ultrasound. Neck ultrasound was performed in the transverse and longitudinal planes using an Esaote Mylab 90 US scanner equipped with 7.5-13.0MHz liner-array transducer. Sonographic features of thyroid parenchyma, vascularity, presence or absence of lesion, features of lesions (size, shape, margin, calcification etc), presence/ absence of lymph node enlargement, presence/absence of intra-tumoral blood flow etcetra were recorded according to the guidelines provided by American College of Radiology (ACR) TIRADS (Thyroid Image Reporting and Data System) 2017.[6] Ultrasound findings for all the cases were shown in below diagram (Figure 4). The most common finding on ultrasound was Hashimoto Thyroidtis. 48.22 percentages of the cases had features of Hashimoto Thyroidtis (HT) (Figure 5). Sonographic features of HT typically showed diffusely altered parenchyma, with heterogeneously hypoechoic and echogenic septations with oftenly mild enlargement of thyroid gland with increased in parenchmyal vascularity.[7-10]

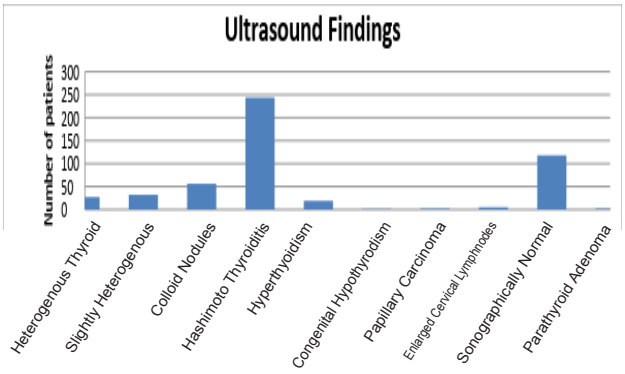

Figure 4. Illustrating the ultrasound findings

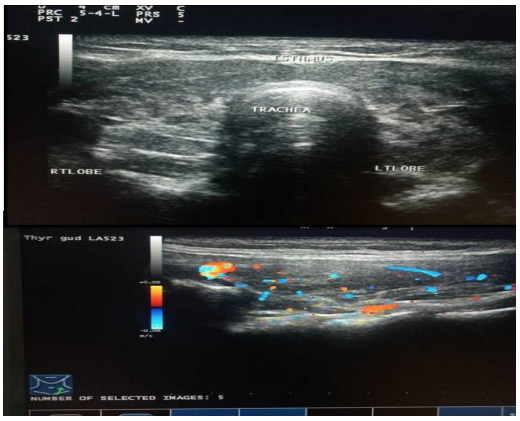

Figure 5. Neck ultrasound showing the typical appearance of Hashimoto Thyroiditis on ultrasound.

Transverse scan image A revealed diffusely altered parenchyma with heterogeneously hypoechoic and echogenic septations. Image B showing increased in parenchymal vascularity on Color Doppler imaging.

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Similarly, below figure showed the relation of BMI with thyroid function test. TSH increases as BMI increases. Most of the disorder or increased in TSH was noticed in obese group, however no normal thyroid function was noticed in morbidity group (BMI>35)

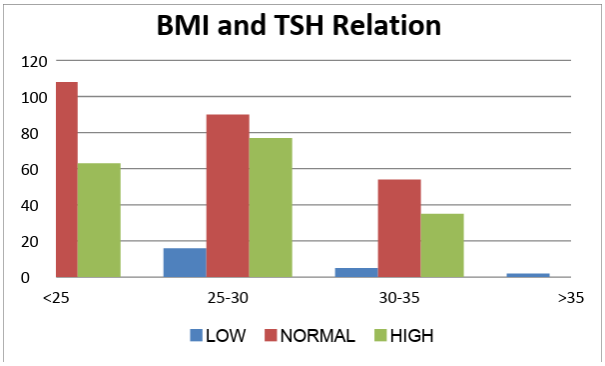

Figure 6. Relation of BMI and TSH

Discussion

Obesity and Overweight are defined as an excessive or abnormal fat accumulation in body that presents a risk to health. Generally, obesity of the body is measured by the body mass index (BMI), a person ís weight (in kilograms) divided by the square of his or her height (in meters). A person with a BMI of 30 or more is generally considered obese. A person with a BMI equal to or more than 25 is considered overweight.[11] A BMI of <18.5 is considered underweight while BMI>=30 is considered obese. Obesity leads to the risk for different diseases, study revealed that etiology of obesity is an imbalance between the energy ingested in food and the energy expanded.[12]

Drastic changes in life style, living style, socio-economic status and adopting western culture might be one of the cause for obesity Thyroid hormones regulates metabolic processes essential for normal growth and development as well as regulating metabolism in the adult. It is well established that thyroid hormone status correlates with body weight and energy expenditure.[13] Our study revealed that there is a strong relationship between body mass index and TSH as given in figure 6. As BMI increases, the level in TSH hormone increases leading to hypothyroidism as similar to study conducted by Fathima et al in 2016.[14] In our study as BMI is over 35, no cases had normal TSH values. However, we have also found that normal thyroid function was found in 54 cases with obese which was quite similar to study by Strata et al,.[15] There he found that thyroid function was normal in obese. There was no normal TSH value in morbidity group , >35 BMI; Approximately 92% of the cases had increased TSH levels which was quite opposite to the Strata et al 15 and similar findings to other study.[16,17]

Recent advances in ultrasound technology have enhanced anatomical characterization of neck pathology offering higher diagnostic accuracy leading to an eminent role in lesion characterization and clinical decision making.[18] Ultrasound evaluation of thyroid gland is economically and technically a very convenient tool in assessing and evaluating the morphological features of thyroid nodules. Sometimes clinical and laboratory findings are not sufficient for identification of nature of lesions especially when they are non palpable.[19] Emerging techniques and recent advances of piezoelectric crystal with high definition of ultrasound probe has brought the revolution for even few millimeter of thyroid microcalcifcation.[20] As illustrated in figure 4 and figure 5, Hashimoto thyroiditis is the most common cause for thyroid dysfunction leading to hypothyroidism which is very similar to study conducted by Adhikari BR et al.[21] Female dominant with age more than 40 years old was seen in our population as well as in other study.[22,23]

Conclusions

Thyroid dysfunction is increasing throughout the world. Increased in BMI has strong influence on thyroid hormone level. Screening of thyroid function test is mandatory. Simple ultrasound tool can be very helpful diagnostically in determining the nature of lesion when clinically and laboratory findings creates dilemma.

Limitations

Our study was single institutional based centre.

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Sample size was good for this study; however more sample size would have been better to represent the entire western population to decrease the biasness. Other laboratory parameters like fT3, fT4, thyroglobulin, anti-thyroperoxidase, antithyroglobulin, TSH receptor antibodies would have been included to rule out thyroid disorders. As this is the preliminary study in western part of Nepal, we certainly will bring some good research paper regarding the thyroid dysfunction very soon.

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A Diabetic Foot Survey

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Abstract

Introduction: Diabetic foot has been defined by the International Working Group on the Diabetic foot and World Health Organisation as a Diabetic patient's foot, associated with neuropathy, ischaemia or both, which has lead to ulceration, infection and/or deep tissue destruction An association of diabetic retinopathy with risk factors of Diabetic foot ulcer has been seen. Hence it is important to assess diabetic patients for risk factors leading to diabetic foot and tally these risks with diabetic retinopathy to help early diagnosis and management of diabetic foot and diabetic retinopathy.
Methodology: This is a community based survey of a cohort of randomly presented patients examined on a first come first service basis limited to maximum of 100 patients to be reviewed in a day in a free health camp in Jaishi Dewal, Kathmandu, Nepal. The data of the patients were noted in a proforma documenting risks of diabetic foot and diabetic retinopathy. Results: Out of the 82 patients reviewed in the medical camp 38 were diabetic (type 2) with a mean age of 60.29 years being more common in females. Risk of Diabetic foot did have a definite association with level of education more common in the lesser educated and occupation (commonest in housewives). Awareness of risk of diabetic foot was only among 39.5% of the diabetic patients. Diabetic retinopathy was also seen only among 18.4% of the diabetic patients, being more common in the educated.
Conclusion: Education and awareness programmes towards diabetic foot protocol are important despite the level of education or occupation. In diabetic patients, it is important to screen for risks of diabetic foot especially if patient has a history of hypertension and also screen for diabetic retinopathy.

Key Words: Diabetic Foot, Risk Factors, Diabetic Retinopathy

Introduction:

Diabetic foot has been defined by the International Working Group on the Diabetic foot and World Health Organisation as a Diabetic patient's foot, associated with neuropathy, ischaemia or both, which has lead to ulceration, infection and/or deep tissue destruction.[1] In developed countries foot ulcers have been seen to be prevalent in 4 to 10% of diabetic patients.[2] It has also been noted that approximately 15% of diabetic patients will develop ulcers in their lower extremity throughout their diabetic life history.[3, 4] Diabetes has been seen to be the commonest cause of non-traumatic lower limb amputation in US and Europe.[5,6] Diabetes and ethnicity has a significant contribution to the rate of lower limb amputation, being more common

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in Mexican, Native and African Americans than Caucasians.[5,7] The commonest cause of lower limb amputation in diabetic patients is foot ulcer.[8,9,10] The risk factors that could cause diabetic foot ulcerations are peripheral neuropathy, vascular disease, limited joint mobility, foot deformities, abnormal foot pressures, minor trauma, a history of ulceration or amputation, and impaired visual acuity.[11,12,13]

There is good evidence that Diabetic foot ulcer (DFU) is associated with Diabetic retinopathy especially if serum creatinine is elevated.[14] An association of diabetic retinopathy with risk factors of Diabetic foot ulcer (sensory neuropathy and neuropathy with vascular foot disease, foot deformity, prior history of ulcer and amputation) has also been seen.[15] Hence it is important to assess diabetic patients for risk factors leading to foot ulcers or diabetic foot and tally these risks with diabetic retinopathy to help early diagnosis and management of diabetic foot and diabetic retinopathy.

Methodology:

This is a community based survey of a cohort of randomly presented patients examined on a first come first service basis limited to maximum of 100 patients to be reviewed in a day. A medical camp was organised in Jaishi Dewal, a small locality in the heart of Kathmandu, Nepal on the ------. This free health camp, focussing on diabetic patients was advertised using banners and by word of mouth. It was managed and financially supported by a local social-service club. The patients were reviewed with the help of a team of Physicians, ophthalmologists, Orthopaedicians, a Dietician, para-medical and nursing staff and the club's members. The programme included an educational section to make the local community aware of Diabetes Mellitus and its management presented on power point by a consultant Physician and a Dietician. Awareness towards complications of Diabetes focussing on Diabetic retinopathy and Diabetic foot was also presented by an Ophthalmology and an Orthopaedic consultant.

The data of the patients was collected in a proforma after taking consent, which stored details like age, sex, height, weight, Body mass index (BMI), type of Diabetes (if previously known), years of Diabetes, random blood sugar, systolic and diastolic blood pressure (BP), level of education, occupation, use of tobacco products, whether under treatment for Diabetes, awareness of diabetic foot, history of foot problems and foot surgery in the past, foot examination clinical findings (looking for risks of diabetic foot and its presence) and findings for Diabetic retinopathy.

The criteria for diagnosing a patient newly with Diabetes Mellitus was if the random blood sugar (capillary blood using a glucometer) was 200mg/dl and above.[16] If random blood sugar was between 140mg/dl and 199mg/dl the patients were advised to confirm if they were diabetic using fasting and post-prandial blood sugar and HBA1C and following up with an endocrinologist in their respective hospital. Similar advice was also given to the newly diagnosed diabetic patients.[16]

Risk of Diabetic foot was analysed on the basis of neuropathy (loss of fine touch over the heel, big toe and little toe, loss of proprioception over first metatarsophalangeal joint), ischaemia (palpable arteria dorsalis pedis and posterior tibial artery), autonomic nervous system and microvascular circulation (skin texture and loss of hair on legs) and mechanical problem (foot deformity). [11,12, 13]

Diabetic retinopathy was diagnosed doing a fundoscopy and classified into mild, moderate, severe and proliferative diabetic macular retinopathy.

This data was transferred onto a SPSS21 data sheet for data analysis. For categorical variable, Chi Square test was used and for the violation of chi square assumption, Fisher Exact test was used.

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Results:

Among the patients who presented to the health camp we were able to collect data of 82 patients. Out of the total, 34 were previously diagnosed as diabetic patients and 4 were newly diagnosed in the health camp on the basis of the random blood sugar level.[16] Therefore, the data of 38 diabetic patients were analysed.

The mean age of the 38 diabetic patients was 60.29 years (95% CI: 55.90 to 64.67) with a male: female ratio of 1:1.38. The mean BMI was 27.25 (95% CI 25.64 to 28.86); mean random blood sugar 197.58 mg/dl (95% CI: 168.24 to 226.92), mean systolic and diastolic BP of 125 mm of Hg (95% CI: 117.92 to 132.08) and 77.11 mm of Hg (95% CI: 73.96 to 80.25) respectively. The level of education of these patients was variable ranging from illiterate to higher beyond bachelor level, highest frequency being illiterate (Table 1). The occupation of these patients was also variable highest being housewives (Table 1). Most of these patients were non-smokers (Table 2) and hypertension was the most common co-morbid condition although heart, lipid, kidney and thyroid pathologies were also present (Table 2)

Table 1: Demographic information of patients

Variables	Categories	Count	%
Sex of patient	Male	16	42.1%
	Female	22	57.9%
	Total	38	100.0%
Type of diabetes	Type 1	0	0.0%
	Type 2	34	89.5%
	Unknown (newly diagnosed DM)	4	10.5%
	Total	38	100.0%
Education level of patient	Illiterate	7	20.0%
	Literate	4	11.4%
	Primary level	1	2.9%
	Secondary level	5	14.3%
	Intermediate	6	17.1%
	Bachelor	6	17.1%
	Higher	6	17.1%
	Total	35	100.0%
Occupation of patient	Farmer	0	0.0%
	Government officer	1	2.8%
	Businessman	7	19.4%
	Labourer	1	2.8%
	Housewife	14	38.9%
	Self-employed	5	13.9%
	Unemployed	3	8.3%
	Others	4	11.1%
	Teacher	1	2.8%
	Total	36	100.0%

Note: 3 people (7.9%) of Education and 2 people (5.3%) of Occupation were unspecified.

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Table 2: Smoking and Comorbidities of patients

Variables	Categories	Count	%
Smokes or takes betel	Yes	10	27.8%
	No	26	72.2%
	Total	36	100.0%
Smokes and takes betel now	Yes	5	13.9%
	No	31	86.1%
	Total	36	100.0%
Co morbidities	Present	26	72.2%
	Absent	10	27.8%
	Total	36	100.0%
If present specify	HTN	15	57.7%
	Lipids	1	3.8%
	Peripheral neuropathy	1	3.8%
	HTN & peripheral neuropathy	2	7.7%
	HTN & lipids	1	3.8%
	Post nephrectomy donor	1	3.8%
	HTN & kidney	1	3.8%
	LIPIDS, heart & thyroid	1	3.8%
	HTN & heart	1	3.8%
	HTN, lipids, heart, anaemia & kidney	1	3.8%
	HTN, kidney & stroke	1	3.8%
	Total	26	100.0%

Note: There were 2 (5.3%) people were unspecified.

Considering the patients who were previously diagnosed with diabetes (no: 34), the mean years since being diagnosed with the disease was 99 months (95% CI: 59.34 to 138.88), all of them being non-insulin dependent. The remaining four newly diagnosed diabetic patients were non-insulin dependent too. Most of the patients (82.1%) were managed using tablets and 17.9% used insulin and tablets (Table 3).

Table 3: Treatment of Diabetes Mellitus patients

Variables	Categories	Count	%
Under treatment for diabetes	Yes	28	75.7%
	No	9	24.3%
	Total	37	100.0%
If having treatment of DM, specify	Tablets	23	82.1%
	Tablet & insulin	5	17.9%
	Diet control	0	0.0%
	Total	28	100.0%
If not having treatment of DM, specify	Nothing	3	33.3%
	Diet Control	6	66.7%
	Total	9	100.0%

Note: One patient (2.6%) was unspecified.

Considering Diabetic foot, 15 (39.5%) were aware of the condition, 4 (10.5%) had foot problem in the past and 2 (5.3%) had had foot surgery. With relation to the skin condition, hair loss on leg, loss of palpable pedal pulse, loss of fine touch and proprioception in foot and foot deformity; risk to develop diabetic foot was seen in 17 (56.7%) patients (Table 4) with a male: female ratio of 1:2.4. ANS and microcirculation pathology (26.3%) was the commonest risk to develop Diabetic foot (Table 5).

Table 4: Cross tabulation of risks for Diabetic foot with Gender

Gender	Yes Count	%	No Count	%	Total Count	%	p value
Male	5	29.4%	7	53.8%	12	40.0%	
Female	12	70.6%	6	46.2%	18	60.0%	0.176
Total	17	100.0%	13	100.0%	30	100.0%	

Table 5: Types of risks for Diabetic foot

Risks for diabetic foot	Frequency	Percent
Vascular pathology	1	5.9%
ANS & microcirculation pathology	10	58.8%
Mechanical	1	5.9%
ANS, microcirculation and mechanical pathology	2	11.8%
ANS, microcirculation & neuropathy	2	11.8%
ANS, microcirculation, vascular & mechanical	1	5.9%
Total	17	100.0%

Risk of Diabetic foot did have a definite association with level of education (more common in the lesser educated) (Table 6) and occupation (commonest in housewives followed by businessman) (Table 6). Awareness of risk of Diabetic foot was only among 5 of the 17 patients who had the risk of Diabetic foot. None of the patients had Diabetic foot.

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Table 6: Diabetic foot with relation to education and occupation of patient

		Does patient have risk of diabetic foot					
		Yes Count	%	No Count	%	Total Count	%
Level of Education	Illiterate	3	17.6	2	15.4	7	20
	Literate	4	23.5	0	0	4	11.4
	Primary level	1	5.9	0	0	1	2.9
	Secondary level	2	11.8	2	15.4	5	14.3
	Intermediate	3	17.6	2	15.4	6	17.1
	Bachelor	2	11.8	4	30.8	6	17.1
	Higher	2	11.8	3	23.1	6	17.1
	Total	17	100	13	100	35	100
Occupation	Government	1	5.9	0	0	1	2.8
	Businessman	4	23.5	3	23.1	7	19.4
	Labourer	1	5.9	0	0	1	2.8
	Housewife	6	35.3	5	38.5	14	38.9
	Self-employed	1	5.9	3	23.1	5	13.9
	Unemployed	2	11.8	1	7.7	3	8.3
	Others	2	11.8	1	7.7	4	11.1
	Teacher	0	0	0	0	1	2.8
	Total	17	100	13	100	36	100

Diabetic retinopathy in either of the eyes was seen in 7 patients (18.4%) with a male: female ratio of 1.33:1 (Table 7). Retinopathy was seen more in the educated though not significant. (Table: 8). Out of the 17 patients who had risk of diabetic foot, 2 had an association with ANS and microcirculation as a risk of diabetic foot as well as diabetic retinopathy.

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Table 7: Diabetic Retinopathy

Variables	Categories	Count	%
Does patient have right diabetic retinopathy	No	32	84.2%
	Yes	6	15.8%
	Total	38	100.0%
If yes, specify	Mild	3	50.0%
	Moderate	2	33.3%
	Proliferative diabetic macular retinopathy with macular oedema	1	16.7%
	Total	6	100.0%
Does patient have left diabetic retinopathy	No	31	81.6%
	Yes	7	18.4%
	Total	38	100.0%
If yes, specify	Mild	1	14.3%
	Moderate	5	71.4%
	Proliferative diabetic macular retinopathy	1	14.3%
	Total	7	100.0%
Retinopathy either eye	Yes	7	18.4%
	No	31	81.6%
	Total	38	100.0%

Table 8: Diabetic retinopathy with relation to education and occupation of patient

		Retinopathy either eye					
		Yes Count	%	No Count	%	Total Count	%
Education level of patient	Illiterate	1	20.0%	6	20.0%	7	20.0%
	Literate	0	0.0%	4	13.3%	4	11.4%
	Primary level	0	0.0%	1	3.3%	1	2.9%
	Secondary level	1	20.0%	4	13.3%	5	14.3%
	Intermediate	1	20.0%	5	16.7%	6	17.1%
	Bachelor	0	0.0%	6	20.0%	6	17.1%
	Higher	2	40.0%	4	13.3%	6	17.1%
	Total	5	100.0%	30	100.0%	35	100.0%
Occupation of patient	Farmer	0	0.0%	0	0.0%	0	0.0%
	Government	0	0.0%	1	3.3%	1	2.8%
	Businessman	1	16.7%	6	20.0%	7	19.4%
	Labourer	0	0.0%	1	3.3%	1	2.8%
	Housewife	1	16.7%	13	43.3%	14	38.9%
	Self-employed	1	16.7%	4	13.3%	5	13.9%
	Unemployed	1	16.7%	2	6.7%	3	8.3%
	Others	2	33.3%	2	6.7%	4	11.1%
	Teacher	0	0.0%	1	3.3%	1	2.8%
	Total	6	100.0%	30	100.0%	36	100.0%

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There was no association seen between risk of diabetic foot and diabetic retinopathy considering no statistical significance (Table 9). Similarly, no association was also seen in patients with 10 years or more of diabetes with risk of diabetic foot (Table 10) and Diabetic retinopathy (Table 11) but diabetic patients who had history of hypertension showed risk of developing Diabetic foot (Table 12). Hypertension in Diabetic patents however did not have association with Diabetic retinopathy (Table 13).

Table 9: ASSOCIATION OF DIABETIC RETINOPATHY WITH RISK OF DIABETIC FOOT

Cross tabulation

DOES PATIENT HAVE RISK OF DIABETIC FOOT	RETINOPATHY EITHER EYE				p value
	Yes		No		
	n	%	n	%	
Yes	2	50.0%	15	57.7%	1.00
No	2	50.0%	11	42.3%	
Total	4	100.0%	26	100.0%	

Table 10: ASSOCIATION OF 10 YEARS AND MORE OF DIABETES WITH RISK OF DIABETIC FOOT

Cross tabulation

10 YEARS AND MORE THAN 10 YEARS OF DIABETES	DOES PATIENT HAVE RISK OF DIABETIC FOOT				p value
	Yes		No		
	n	%	n	%	
Yes	4	28.6%	2	16.7%	0.652
No	10	71.4%	10	83.3%	
Total	14	100.0%	12	100.0%	

Table 11: ASSOCIATION OF 10 YEARS AND MORE OF DIABETES WITH DIABETIC RETINOPATHY

Cross tabulation

10 YEARS AND MORE THAN 10 YEARS OF DIABETES	RETINOPATHY EITHER EYE				p value
	Yes		No		
	n	%	n	%	
Yes	3	42.9%	6	23.1%	0.358
No	4	57.1%	20	76.9%	
Total	7	100.0%	26	100.0%	

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Table 12: ASSOCIATION OF HYPERTENSION WITH RISK OF DIABETIC FOOT
Cross tabulation

HYPERTENSION OF PATIENTS	DOES PATIENT HAVE RISK OF DIABETIC FOOT				p value
	Yes		No		
	n	%	n	%	
Yes	14	82.4%	4	30.8%	0.004
No	3	17.6%	9	69.2%	
Total	17	100.0%	13	100.0%	

Table 13: ASSOCIATION OF HYPERTENSION WITH DIABETIC RETINOPATHY
Cross tabulation

HYPERTENSION OF PATIENTS	RETINOPATHY EITHER EYE				p value
	Yes		No		
	n	%	n	%	
Yes	5	83.3%	17	56.7%	0.370
No	1	16.7%	13	43.3%	
Total	6	100.0%	30	100.0%	

DISCUSSION:

The prevalence of type 2 Diabetes Mellitus in Nepal is 8.4% [17] with higher prevalence in the urban population.[18] The prevalence of Diabetic retinopathy in Nepal has been seen to range from 19.3 to 78% [19,20] and the prevalence of Diabetic foot in Nepal was noted to be 21.4% .[21] Compared to these studies [17,18,19,20,21], this is a small pilot study in a small population. This can however be considered acceptable and representing a larger population considering patients were reviewed randomly from a population on a first come first service basis. Advertisement for the medical camp targeted to diabetic patients can be considered selection bias.

In this study, only type 2 diabetic patients have been reviewed, which however is the common type.[21,22] Diabetes Mellitus was seen to be more common in the female sex, the finding being comparable to other larger studies [15,21, 22] although diabetic foot was observed to be commoner in males.[23] In our study, risk of diabetic foot was seen to be more common in females, which does not match other larger studies.[23,24] The possible difference could be owing to the small sample studied. It is therefore a worthwhile question, why diabetic foot is more common in males[24] even though diabetes mellitus is more common in females. It may be due to gender inequality at work as only 26% of the paid employees are females and 8.3%of females fall in the paid labour category in Nepal.[25] In addition males are exposed to more trauma and may be wearing inappropriate footwear.[26] Thus, it may be important to consider protective gears[27,28] if the work place is influencing this male predominance of diabetic foot.

Awareness programmes[28] and education towards Diabetic foot care protocols[29] are vital too as only a small proportion of patients were aware of risks of diabetic foot in our study also considering that the commonest risk of diabetic foot noted was ANS and microcirculation pathology which is an important commonly influencing risk factor.[11,12,13]

Considering that Diabetic patients and patients with

risk of diabetic foot were mainly from the lesser-educated cohort and frequently more common among housewives, it becomes more compelling for us to approach these patients at the community level not only with local clinics but also with education programmes.[29]

Surprisingly, as diabetic retinopathy was more inclined towards the educated it can be suggested that awareness programmes are necessary even if people are educated. Diabetic retinopathy being more common among housewives also suggests the importance of education programmes at the community level.

As the number of smokers among the diabetic patients was small no positive findings was considered.

With relation to comorbidities, chance of risks of diabetic foot was seen to be significant if there was a history of hypertension. This finding has been supported by a previous study; which has also suggested hypertension as a risk factor to develop foot ulcers, gangrene and amputation in diabetic patients.[30]

Although our study has not shown significant association of hypertension with diabetic retinopathy there is evidence to prove the same.[31] Similarly, though no association was seen between patients who had 10 years or more of diabetes and risk of diabetic foot and diabetic retinopathy previous studies have shown good association between them.[32,33] This study has also not confirmed the association of Diabetic retinopathy and risk factors of Diabetic foot, though there is good evidence for the same.[15] These differences between available literature and our study are probably owing to the small sample size.

It does however show the importance to check all diabetic patients for risks of diabetic foot, and diabetic retinopathy and the importance of thinking of either, if one is present especially if accompanied with risk factors. This may help to diagnose either of the conditions early for earlier management.

CONCLUSION:

Education and awareness programmes towards diabetic foot protocol are important despite the level of education or occupation. In diabetic patients, it is important to screen for risks of diabetic foot especially if patient has a history of hypertension and also screen for diabetic retinopathy.

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Clinical Profile of Thyroid Disorders – A retrospective study at BPKIHS

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Abstract

Background: The thyroid gland produces two key metabolic hormones which regulate metabolic rate, growth and development. They play vital roles in digestion, heart and muscle function, brain development and maintenance of bones. People suffering from thyroid disorders may have autoimmune disease, ranging from primary hypothyroidism, Hashimoto's thyroiditis, to hyperthyroidism caused by Graves' disease.

Objectives: To study clinical profile of thyroid disorders in endocrinology clinic of BPKIHS, Nepal.

Methods: This is a hospital based retrospective study of past five years (2012 – 2017) done in department of internal medicine at B.P. Koirala Institute of Health Sciences, in which thyroid disorder patient records from the endocrinology clinic will be compiled together will be analyzed after classifying them according to the guidelines of the American Thyroid Association (ATA). **Results:** Among 584 thyroid disorder cases that were sampled, higher prevalence of thyroid disorders was seen in females, and the Male: Female ratio was 1:4.13. Most common type of thyroid disorder was Hypothyroidism (29.6%) followed by Subclinical hypothyroidism (28.3%).

Conclusions: Thyroid disorders are more common in females than males and hypothyroidism being commonest thyroid disorder in our setup. Subclinical hypothyroidism is second commonest followed by hyperthyroidism. In Subclinical hypothyroidism Anti TPO antibody is most commonly found to be positive.

Key Words: Hypothyroidism, Hyperthyroidism, Thyroid disorder

Introduction

The thyroid gland produces two key metabolic hormones viz. thyroxine (T4) and tri-iodothyronine (T3).[1] These hormones regulate metabolic rate, growth and development. The thyroid disorders include hypothyroidism, subclinical hypothyroidism, hyperthyroidism, subclinical hyperthyroidism and Secondary hypothyroidism.[2] Their clinical manifestations vary considerably from area to area and are determined principally by availability of iodine in the diet.[3]

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According to WHO, about 31% (1 900.9 million) of the world's population is estimated to have insufficient iodine intakes, with the most affected WHO regions being South-East Asia and Europe.[4,5] Within South-East Asia, Nepal is a mountainous landlocked country, which due to its geographical placement and high annual rainfall, has very low soil iodine content. This leads to an ever increasing number of iodine deficiency disorders and thyroid dysfunction in the general population.[6,7]

Though the clinical profile of thyroid dysfunction has previously been studied in other parts of Nepal, to the best of our knowledge, this is the first study to be reported from the eastern part of Nepal. The

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objective of this study is to assess the clinical profile of thyroid disorder in the eastern region of Nepal.

Methodology

This is a Hospital based retrospective cross sectional study done in Endocrinology clinic, Department of Internal Medicine, BPKIHS. Since this is a hospital based retrospective study of the medical records of thyroid disorders patients, presenting to the endocrinology clinic of BPKIHS in the past five years (2012-2017), so all the diagnosed cases of thyroid disorders of that duration will be taken as the sample size.

The Inclusion Criteria were all diagnosed case of thyroid disorders as per ATA guidelines visiting endocrinology clinic at BPKIHS were selected irrespective of age and sex.

The thyroid disorder patient records from the endocrinology clinic will be compiled together after permission from the institutional ethical committee. The records collected will be analyzed after classifying them according to the guidelines of the American Thyroid Association (ATA).

ATA/AACE guidelines 2011 (Bahn et al, 2011)

a. Primary Hyperthyroidism: There is constitutive activation of thyroid hormone synthesis & secretion leading to autonomous release of excess thyroid hormone. Raised FT3, FT4 and decreased TSH levels.
b. Secondary Hyperthyroidism: Occurs if thyroid is inappropriately stimulated by tropic factors. Decreased FT3, FT4 and raised TSH levels.
c. Subclinical Hyperthyroidism: Low or undetectable TSH with values within the normal reference range for both T3 and T4 estimates.
d. Graves' disease: Graves' disease is an autoimmune disorder. Thyrotropin receptor antibodies stimulate the TSH receptor, increasing thyroid hormone production.
e. Sub-acute Thyroiditis: Sub-acute thyroiditis is thought to be caused by viral infection and is characterized by fever and thyroid pain.
f. Euthyroid: Normal FT3, FT4 & TSH levels.
g. Hypothyroidism: Decreased FT3 and FT4 level and increased TSH level.
h. Had no change: FT3, FT4 and TSH value before and after the treatment has no significant change.
i. Graves Ophthalmopathy: Graves Ophthalmopathy is an inflammatory eye disease that develops in the orbit in association with autoimmune thyroid disorders.

TFT via immunofluorescence method (CLIA) was :
FT3: 1.21 to 4.18 picogm/ml
FT4: 8.9 to 17.2 picogm/ml
TSH: 0.3 to 4.5 micro IU/ml

Results

Table 1: Age distribution of the sampled thyroid patients (n=584)

Age Group (in years)	Frequency	Percentage
15-30	175	30.0
31-45	237	40.6
46-60	148	25.3
60-75	19	3.3
>75	5	0.9
Total	**584**	**100.0**

Table 1 above shows that out of the total 584 thyroid disorder cases that were sampled, higher prevalence of thyroid disorders was seen in the age group 31-45.

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Table 2: Sex distribution of the sampled thyroid patients (n=584)

Sex	Frequency	Percentage
Female	470	80.5
Male	114	19.5
Total	**584**	**100.0**

Table 2 above shows that out of the total 584 thyroid disorder cases that were sampled, higher prevalence of thyroid disorders was seen in females, and the Male: Female ratio was 1:4.13.

Table 3: Thyroid Disorder distribution of sampled thyroid patients (n=584)

Thyroid disorder	Frequency	Percentage
Hypothyroidism	173	29.6
Hypothyroidism Subclinical	165	28.3
Euthyroidism	28	4.8
Hyperthyroidism	80	13.7
Subclinical Hyperthyroidism	19	3.3
Secondary Hypothyroidism	53	9.1
Others (Thyroiditis, Goitre)	20	3.4
Sick Euthyroid Syndrome	46	7.9
Total	**584**	**100.0**

Table 3 above shows that out of the total 584 thyroid disorder cases that were sampled, most common type of thyroid disorder was Hypothyroidism (29.6%) followed by Subclinical hypothyroidism (28.3%).

Table 4: Distribution of Anti TPO Antibody test results of sampled thyroid patients (n=584)

Anti TPO Antibody	Frequency	Percentage
Not Tested	293	50.2
Negative (<30)	99	17.0
Positive (>30)	192	32.9
Total	**584**	**100.0**

Table 4 above shows that out of the total 584 thyroid disorder cases that were sampled, 293 patients were not tested for Anti TPO Antibody. Among the 291 tested patients, 99 tested negative, i.e. <30 and 192 tested positive, i.e. >30.

Table 5: Thyroid disorder distribution in Anti TPO Antibody positive patients (n = 192)

Thyroid disorder	Frequency	Percentage
Hypothyroidism	53	27.6
Subclinical Hypothyroidism	55	28.6
Euthyroidism	6	3.1
Hyperthyroidism	15	7.8
Subclinical Hyperthyroidism	3	1.6
Secondary Hypothyroidism	28	14.6
Others (Thyroiditis, Goitre)	7	3.6
Sick Euthyroid Syndrome	25	13.0
Total	**192**	**100.0**

Table 5 above shows that out of the total 192 thyroid disorder cases that tested positive for Anti TPO Antibody test, most common type of thyroid disorder was Subclinical Hypothyroidism (28.6%) followed by Hypothyroidism (27.6%).

Table 6: Differences in the characteristics of all thyroid disorder patients who underwent testing for Anti TPO Antibody (n = 291)

	Negative	Positive	Total	Value
Age				
15 – 30	35 (35.4%)	55 (28.6%)	90	
31 – 45	41 (41.4%)	79 (41.1%)	120	
46 – 60	20 (20.2%)	54 (28.1%)	74	0.250
60 – 75	2 (2.0%)	4 (2.1%)	6	
>75	1 (1.0%)	0 (0.0%)	1	
Sex				
Female	78 (78.8%)	155 (80.7%)	233	0.695
Male	21 (21.2%)	37 (19.3%)	58	
Type of Thyroid				
Hypothyroidism	24 (24.2%)	53 (27.6%)	77	
Subclinical Hypothyroidism	26 (26.3%)	55 (28.6%)	81	
Euthyroidism	12 (12.1%)	6 (3.1%)	18	
Hyperthyroidism	6 (6.1%)	15 (7.8%)	21	0.791
Subclinical Hyperthyroidism	6 (6.1%)	3 (1.6%)	9	
Secondary Hypothyroidism	12 (12.1%)	28 (14.6%)	40	
Others (Thyroiditis, Goitre)	3 (3.0%)	7 (3.6%)	10	
Sick Euthyroid Syndrome	10 (10.1%)	25 (13.0%)	35	
Total	**99**	**192**	**291**	

Table 6 above shows that out of 291 Thyroid disorder patients who were tested for Anti TPO Antibody, differences were seen in the characteristics for those who tested positive and negative. Among the most common age group, i.e. 31 – 45, almost equal distribution (41.4% for negative and 41.1% for positive) can be seen. Between sex distribution, the male: female ratio for negative and positive tested were approximately 3:11 and 4:17 respectively. For people tested for the antibody, the most common type of thyroid was Subclinical Hypothyroidism, whose distribution slightly varies with 26.3% for negative and 28.6% for positive tested.

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Table 7: Association between Type of Thyroid Disorders and Age group of sample size (n = 584)

Type of Thyroid	Age					Total	P value
	15–30	31–45	46–60	60–75	>75		
Hypothyroidism	51 (29.5%)	69 (39.9%)	46 (26.6%)	6 (3.5%)	1 (0.6%)	173	0.535
Subclinical Hypothyroidism	55 (33.3%)	61 (37.0%)	41 (24.8%)	6 (3.6%)	2 (1.2%)	165	
Euthyroidism	9 (32.1%)	10 (35.7%)	8 (28.6%)	0 (0.0%)	1 (3.6%)	28	
Hyperthyroidism	24 (30.0%)	27 (33.8%)	25 (31.3%)	3 (3.8%)	1 (1.3%)	80	
Subclinical Hyperthyroidism	4 (21.1%)	8 (42.1%)	6 (31.6%)	1 (5.3%)	0 (0.0%)	19	
Secondary Hypothyroidism	11 (20.8%)	30 (56.6%)	12 (22.6%)	0 (0.0%)	0 (0.0%)	53	
Others (Thyroiditis, Goitre)	6 (30.0%)	11 (55.0%)	2 (10.0%)	1 (5.0%)	0 (0.0%)	20	
Sick Euthyroid Syndrome	15 (32.6%)	21 (45.7%)	8 (17.4%)	2 (4.3%)	0 (0.0%)	46	
Total	175 (30.0%)	237 (40.6%)	148 (25.3%)	19 (3.3%)	5 (0.9%)	584	

Table 7 above shows the association between type of thyroid disorders and age group, which has turned to be not significant (P > 0.05).

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Table 8: Association between Type of Thyroid Disorders and Sex of sample size (n = 584)

Type of Thyroid	Age		Total	P Value
	Male	Female		
Hypothyroidism	143 (82.7%)	30 (17.3%)	173	0.162
Subclinical Hypothyroidism	139 (84.2%)	26 (15.8%)	165	
Euthyroidism	22 (78.6%)	6 (21.4%)	28	
Hyperthyroidism	57 (71.3%)	23 (28.8%)	80	
Subclinical Hyperthyroidism	14 (73.7%)	5 (26.3%)	19	
Secondary Hypothyroidism	43 (81.1%)	10 (18.9%)	53	
Others (Thyroiditis, Goitre)	18 (90.0%)	2 (10.0%)	20	
Sick Euthyroid Syndrome	34 (73.9%)	12 (26.1%)	46	
Total	**470 (80.5%)**	**114 (19.5%)**	**584**	

Table 8 above shows the association between type of thyroid disorders and sex distribution, which has turned to be not significant (P > 0.05).

Discussion

The study was done in B. P. Koirala Institute of Health Sciences of Dharan in the Eastern region of Nepal. All diagnosed cases of thyroid disorders as per ATA guidelines visiting endocrinology clinic at BPKIHS were selected irrespective of age and sex. From our study, we found that maximum (80%) of the patients suffering from thyroid disorders are females. Our result was similar to all other surveys done in different parts of the country as well as outside the country.[8,9,10,11,12]

From our study, we found that the most common age group for thyroid disorders is 31 – 45 (40.6%), which was similar to the data obtained in Lumbini Medical College Teaching Hospital (LMCTH), where the mean age for males was 39.28 years (SD = 19.01) and that of female was 39.60 years (SD = 14.63).[11] The results from other studies varied slightly. In Charak Hospital, Pokhara higher prevalence was observed in the subjects whose ages were above 41-50 years.8 In Shree Puspanjali Hospital Pvt. Ltd, Bharatpur-10, mean age was 45.9±1.3 years.9 In Malankara Orthodox Syrian Church Medical College, in Kerala State, the highest proportion of cases was reported in 40-60 years.10 In Benazer Bhutto Hospital, Islamabad, the study showed that young adult in the range of 16-40 years are more likely to suffer from thyroid illness.[12]

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From our study, we found that the most common type of thyroid disorder is Hypothyroidism (29.6%) followed by Subclinical hypothyroidism (28.3%), which was similar but less than that found in Shree Puspanjali Hospital Pvt. Ltd, Bharatpur-10, which was 87%9 and in Benazer Bhutto Hospital, Islamabad, which was 63%.[12] Whereas in Charak Hospital, Pokhara, Subclinical hypothyroidism (10.50%) had higher prevalence,[8] in Lumbini Medical College Teaching Hospital (LMCTH), Euthyroid cases were 76.7%[11] and in Malankara Orthodox Syrian Church Medical College, in Kerala State, most commonly observed type of thyroid disorder was Non-toxic multinodular goiter (48.5%).[10]

Conclusion

Thyroid disorders are more common in females than males and hypothyroidism being commonest thyroid disorder in our setup. Subclinical hypothyroidism is second commonest followed by hyperthyroidism. In Subclinical hypothyroidism Anti TPO antibody is most commonly found to be positive.

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Diabetic Eye Disease Related Knowledge, Attitudes and Practices among Physicians in Nepal

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Abstract

Background:
Awareness of diabetic retinopathy amongst general physicians is a major factor for the prevention of diabetes-related ocular complications.They are most often the first line of contact of diabetic patients and their knowledge and attitude are the principal indicators of their level of awareness.
Methods:
This cross-sectional study was conducted in Kathmandu and is based on a structured questionnaire referring to Diabetic retinopathy formulated on Guideline for Conducting a Knowledge, Attitude and Practice Study by information, Education, and Communication expert.The questionnaire comprised of 18 questions and 45 physicians were enrolled. Significant differences and associations were determined by values of $P < 0.05$.
Results:
All of the physicians (100%) were aware that diabetes can damage the eye and can cause visual impairment. Most of them agreed that patients with diabetes should be sent for ophthalmic evaluations with majority mandating an immediate evaluation after the diagnosis. The majority (98%) of physicians disagreed that eye examination was required only once the vision was affected. Only 56% of the physicians agreed they routinely perform direct ophthalmoscopy to examine the retina (p 0.551). Among them, nearly half (44%) reported not knowing the importance of dilating the pupil .($p = 0.69$).
Conclusions:
The study shows a good level of diabetic retinopathy awareness and knowledge with positive attitudes toward the importance of diabetes care. At the same time, it has found that practice level despite good knowledge and attitude to be below average among the physicians who are managing diabetic patients.

Key Words: Knowledge, Attitude, Practice, Diabetes, Nepal, Diabetic Retinopathy

Introduction:
Diabetes mellitus has established itself as a fastest emerging epidemic globally.[1] It is a vicious pathology affecting the macro and the microvascular components of different target organs. As a result, it has climbed upthe ranking to also become one of the top causes of vision loss.[2]
In 2017, nearly half a billion people are estimated to be living with diabetes withlow and middle-income countries carry almost 80% of the diabetes burden.[3]this is almost quadruple the number within a period of around 35 years but reports suggest we are a long way from achieving a control. Large

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meta-analysis shows that roughly 50% of people with diabetes still remain undiagnosed.[4] Despite advancements in technology and investigative methods for early diagnosis and treatment, nearly 75% of them are living in less economically developed countries where the equipment and treatment facilities are limited. Indian subcontinent and China account for nearly 45% of the burden.[1]

Diabetic retinopathy (DR) should never be undermined. It is the most common complication of diabetes and can lead to irreversible blindness if not identified early [5] Depending upon the severity ,this can range screening intervals of 1 year to 6 months and have proven effective for early discovery and management.[3,4,6–9] Besides diabetic retinopathy, diabetic patients are also more prone to develop cataracts, glaucoma and fluctuating refractive errors.[10–12]

This success story is however different in developing countries.[13–17] The primary care physicians are often the first medical personnel for patients with diabetes. The knowledge of the attending physicians regarding diabetic retinopathy is crucial as they are the main source of referrals for these patients to ophthalmologists.Various studies around the world have been done to access the diabetic eye disease awareness among physicians.[18–23] Even in resource-richsettings, many of these studies have suggested that the knowledge and awareness of physicians about diabetic retinopathy is inadequate and have recommended more robust training.[20,24]

Most of diabetes-relatedKAP studies in Nepal have focused on patientswith DM. One of the studies from Western Nepal showed KAP scores of the diabetic patients to be low.[25] Another KAP study from Kathmandu showed 33% had satisfactory knowledge about diabetes and 17.6 % reported low.[26] Another study done in Nepal regarding knowledge of diabetic retinopathy among patients by Thapa R et al [27]concluded that nearly two-fifths of the patients had no awareness that diabetes could affect the eye which could result in blindness and only50% of who were aware of DR claimed to have received information from physicians.

We do not have any data on the current status of this matter in amongst physician Nepal.The gravity of this problem is yet to be determined.This study aims aim to evaluate the current knowledge, awareness, and practices about DR among physicians in Nepal treating patients with diabetes. We expect the results will help us address "loopholes" and to construct efficient strategies to strengthen eye care of diabetic patients.

Methodology:

We conducted this cross-sectional study in Kathmandu on the 2nd day of "SAARC Diabetes 2016", on 10th September, in Kathmandu and included 45 physicians. The study is based on a structured questionnaire referring to Diabetic retinopathy.This study was performed with consent from participating physicians in compliance with the Declaration of Helsinki and maintains the confidentiality of the participants. A set of questionnaire formulated based on Guideline for Conducting a Knowledge, Attitude and Practice (KAP) Study by Kaliyaperumal K (I.E.C. Expert)[28] the questionnaire comprised of 18questions in 3 sections on knowledge, attitude,and practices.

Physicians involved in the care of patients with diabetes (registered hospital physicians, general practitioners) working at different tertiary health centers in Nepal were asked to fill the questionnaire. Data were coded and entered into "Statistical Analysis" by Statistical Program for Social Sciences (SPSS) version 20 (IBM SPSS Inc.) and were analyzed using frequencies and percentage. Continuous variables were summarized using mean, percentile, range, and standard deviation. Significant differences and associations were determined by values of $P < 0.05$.Chi-square / Fisher exact test was used wherever applicable.

The written and informed consent from all the participants was taken and the confidentiality of the participants maintained.

Results:

We evaluated a total of 45 physicians who were involved in the care of patients with diabetes (registered hospital physicians general practitioners

and endocrinologists) working at different tertiary health centers in Nepal. Twenty(22.4%) of the physicians worked in government hospitals, twenty one (46%) at a private hospital, three (7%) at NGO run hospitals and one (2%) at the community-basedhospital.(Figure 1) The mean number of patients evaluated by each physician was 16.3(SD 4.7) daily.

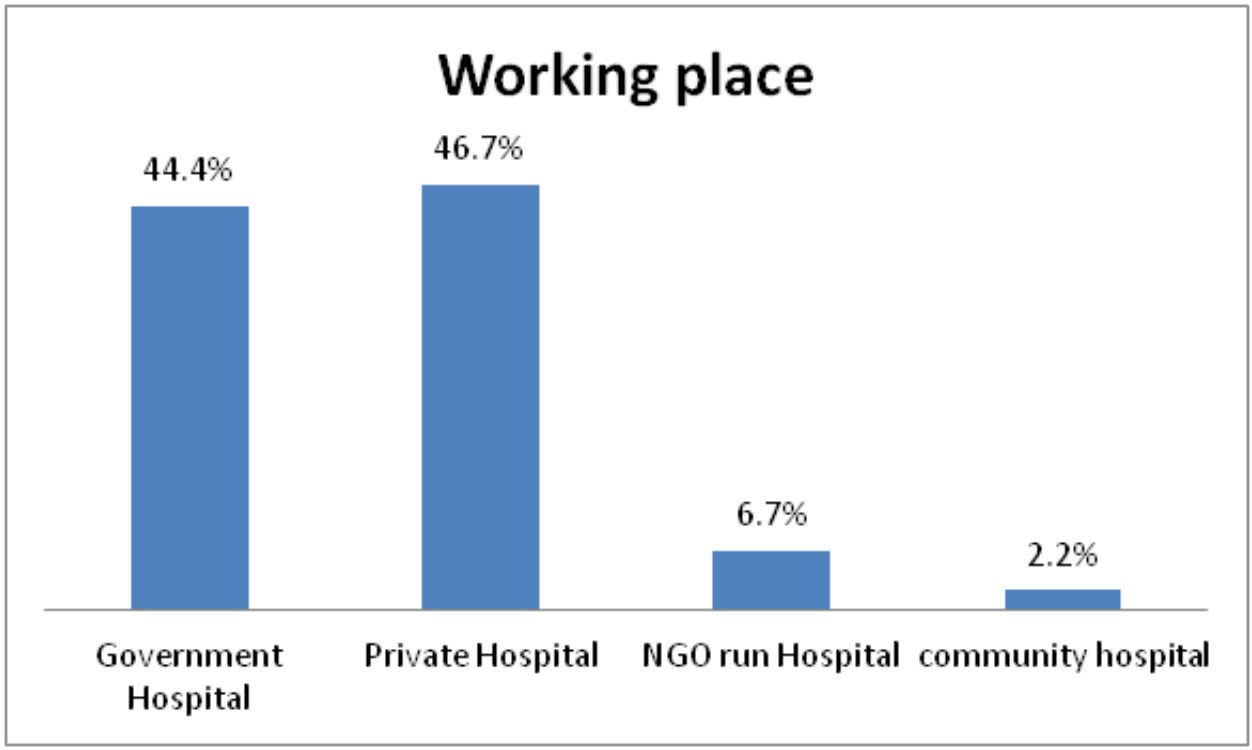

Figure 1. Graph illustration the place of practice of the physicians.

Knowledge about eye examination for diabetes

All of the physicians(100%) agreed that patients with type II diabetes should be sent for ophthalmic evaluations with 87% of them mandating an immediate evaluation after the diagnosis. In contrast, in type, I diabetes,Forty-one (91%)of the physicians thought ophthalmic evaluation to be important with 58% of the physicians agreeing that the first evaluations should be done immediately after the diagnosis. Thirty-nine out of 45 (87%) physicians answered that they would refer their pregnant patients with diabetes to an ophthalmologist for evaluation (Table1)

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Table 1. Physicians Knowledge on Diabetes and screening for Diabetic retinopathy

Type of Diabetes	Type I Diabetes	Type II Diabetes	Gestational	All Patients of Diabetes
Should be referred to an Ophthalmologist (Agreement)				
Yes	41(91%)	45 (100%)	39(87 %)	41(91%)
No	4(9%)		5(11%)	3(7%)
Don't Know			1(2%)	1(2%)
When to Refer				
Immediately after diagnosis	26(58%)	39(87%)	NA	NA
After 6months	8(18%)	4(9%)	NA	NA
After 1 year	7(15%)	2(4%)	NA	NA

All of the physicians(100%) were aware of the fact that diabetes can damage the eye and can cause impairment in vision. Eleven(24.4%) of them identified retinopathy alone as a complication of diabetes while thirty-four (85.6%) identified that diabetes could cause a refractive error, cataract, glaucoma and diabetic retinopathy. When queried about the treatment options for diabetic retinopathy, majority 25(55%) pointed laser therapy as the only possible treatment followed by intravitreal agents 10(22%). (Table 2)

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Table 2 Physicians knowledge on Diabetic retinopathy, its potential ocular manifestations, and

Is there any effect of diabetes mellitus to eyes?	
Yes	45 (100%)
No	
Does diabetes mellitus damageeyesight ?	
Yes	45 (100%)
No	
The eye conditions that a diabetic patient can have	
Diabetic Retinopathy	11(25%)
Refractive Error	-
Cataract	-
All of the above	34(75%)
Are you aware of the treatment options available for the management of Diabetic Retinopathy?	
Intravitreal Injection	10(22%)
Photocoagulation	25(55%)
Surgery	1(2%)
All	8(19%)
Don't know	1(2%)

Table 3. Physicians' attitude regarding diabetic retinopathy

Attitude	Disagree	Neutral	Agree	p-value
An eye examination is needed only when vision is affected	44(98%)	-	1(2%)	P<0.001
When diabetes is well controlled, there is no need to be concerned about diabetic retinopathy	37(82%)	3(7%)	5(11%)	P<0.001
If the disease is treated early on, diabetic retinopathy can be prevented/ delayed	1(2%)	2(4%)	42(94%)	P<0.001

Attitudes

98% of physicians disagreed that eye examination was required only once the vision was affected. 82% agreed that despite a good glycemic control, screening for diabetic retinopathy should still be performed and 94% of them agreed that if diabetes was treated early, diabetic retinopathy and its complications could be prevented or delayed (p<0.001) (Table 3)

Practices of retinal examination of diabetics

56% of the physicians said they routinely perform direct ophthalmoscopy to examine the retina (p 0.551). However, among them, nearlyhalf (44%) didn't know the importance of dilating the pupil for (p= 0.69). Only 49% of participants said they refer six monthly for an eye examination.(Figure 2) 64% of the participant said that they refer pregnant diabetic patients for eye examination (p =0.072). 11% of the participants said that they did not need to worry about ocular complications when blood sugar is well controlled. In regards to the barrier for screening, the factors were lack of exposure (53%), lack of adequate time (42%), both (5%) (P<0.001). (Table 4)

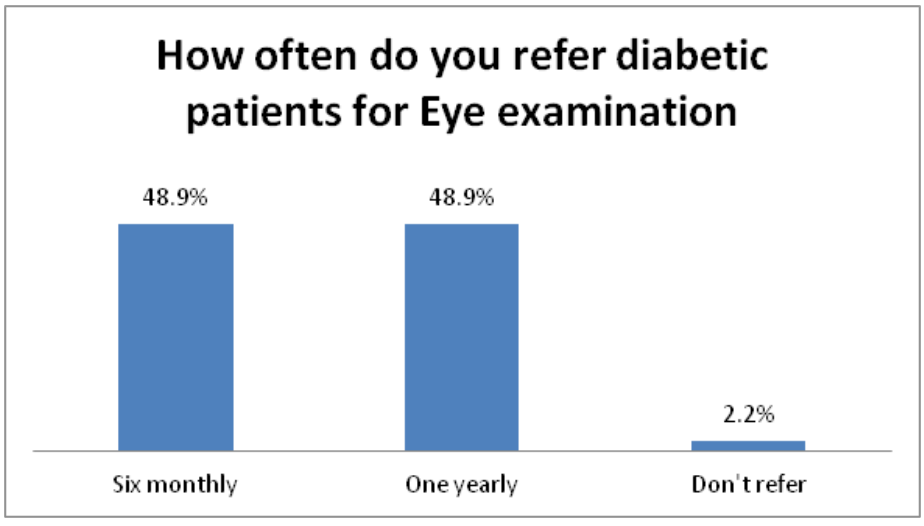

Figure 2. Graph eliciting the frequency of follow-ups that the physicians recommend to their diabetic patients.

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Table 4. Physicians practice for screening and ocular examination for diabetic eye changes in their patients

Do you perform Ophthalmoscopy to examine fundus?		
Yes	25(56%)	
No	20(44%)	p = 0.551
If You answered yes, do you dilate the pupil		
Yes	14(56%)	-
No	11(44%)	p = 0.69
Do you refer a pregnant diabetic patient for an eye check up		
Yes	29(64%)	
No	16(36%)	P=0.072
Frequency of referring		
First Trimester	7(15%)	
Second Trimester	7(15%)	
Third Trimester	3(8%)	p=0.017
All	14(31%)	
Do not refer	14(31%)	
The reason for not having Retinopathy screening at your practice		
Lack of time	19(42%)	
Lack of training	24(53%)	
all the above	2(5%)	P< 0.001

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Discussion:

Diabetic retinopathy often damages the retina and can trigger a series of cascading effects, which can result in full vision loss. Screening can catch this disease before irreparable damage is done. DR is a specific microvascular complication of DM and affects 1 in 3 persons with DM.[29] Most protocols agree that the patients with type 2 diabetes mellitusshould receive screening first eye examination at the time of diagnosis and must undergo a dilated fundus examination to rule out evidence of diabetic retinopathy by an ophthalmologist.[30] DR develops with time and is associated with poor control of blood sugar, blood pressure, and blood lipids.

The longer someone has had DM, and the poorer their control, the higher their risk of developing DR.[31] Our study found that all of the physicians agreed that patients with type II diabetes should be sent for ophthalmic evaluations with 87% agreeing on an immediate evaluation after the diagnosis. In contrast, in type, I diabetes, 91% of the physicians thought ophthalmic evaluation to be important with 58% of the physicians agreeing that the first evaluations should be done immediately after the diagnosis. Vision-threatening retinopathy is rare in type 1 diabetic patients in the first 3–5 years of diabetes or before puberty. During the next two decades, nearly all type 1 diabetic patients develop retinopathy. Up to 21% of patients with type 2 diabetes have retinopathy at the time of the first diagnosis of diabetes, and most develop some degree of retinopathy over time.[31]

In this study, majority of the physicians answered that they would refer their pregnant patients with diabetes to an ophthalmologist for evaluation. Approximately 12% of women with no retinopathy at the start of pregnancy will develop mild retinopathy consisting of a microaneurysm but regression after delivery is usually the rule.[32, 33]

However, there is a certain group which can have a very aggressive variant mandating urgent pan-retinal photocoagulation (PRP) to slow down the progression.[34]

All of the physicians were found to have awareness that diabetes can damage the eye and can cause impairment in vision. Majority of the physicians were found to have knowledge of the effect of DM that there are other structures besides retina that can be affected but it was worrying that nearly quarter of the physicians identified DR as the only possible ocular complication of DM. Physicians were also found to have inadequate knowledge regarding management of diabetic. More than half answered laser as the only modality. In today's anti-VEGF era, only around a quarter were able to identify it as one of the major treatment options. This could possibly due to lack of update of GP's on the management of DR.

The general rule now for screening for DR is that even if there is little or no evidence of DR, with normal or near-normal visual acuity and with good glycemic control at the initial time of evaluation. Persons with diabetes should have an annual eye examination.[31] The U.K. Prospective Diabetes Study (UKPDS) demonstrated that for every percentage point decrease in HbA1c, there was nearly 35% reduction in the risk of microvascular complications. Almost all of the physicians in our study agreed that glycemic control could slow down the progression but the patients should still be screened for DR at least on a yearly basis. They also acknowledged that vision impairment could be slowed or prevented if the patients with diabetic retinopathy are treated early.

This study also shows the need for training of physicians, general practitioners (GPs) and endocrinologists about diabetic retinopathy and its detection with a direct ophthalmoscope. Our study found that nearly half of them do not perform ophthalmic examinations and from those who do perform it, again, nearly half of them do not perform fundus examination under dilatations. Our study points that there needs urgent addressing regarding the importance of fundus examination

and the need for a dilated eye examination. One of the factors could be due to lack of mydriatic agents and lack of confidence in detecting changes even when examining dilated eyes. Knowledge of the guidelines of screening and management of diabetic retinopathy is another important factor to be considered. Bachelor and Residency programs should focus on providing the importance of ophthalmic examinations for detection of DR and also exposure to ophthalmoscopy.

The response from the doctors on screening for DR during pregnancy received a mixed practice pattern. Nearly 1/3rd of the doctors never sent their patient for DR screening or think it is necessary to be done irrespective of the gestation period. The knowledge that "Diabetic patient with pregnancy and gestational diabetes" has a different pathology, disease course and outcomes seems to require more robust dissemination. Most of the physicians also agreed on this regard as more than 50 percent of them agreed that their current trend in practicing diabetic eye care is mostly due to lack of training in performing eye screening for diabetic retinopathy.

Conclusion

The study shows a good level of diabetic retinopathy awareness and knowledge with relatively positive attitudes toward the importance of diabetes care. At the same time, it has found that practice level despite good knowledge and attitude to be below average among the physicians who are managing diabetic patients.

There is a need to carry out large-scale awareness programs, after identifying the appropriate means to spread the message mainly focusing on the protocols, examination techniques and updates regarding various approaches of managing a potential case of diabetic retinopathy. There is also a requirement for practice to be improved by the supplementing adequate information, increasing the availability of educational materials, proper guidance, and training among physicians who are managing diabetic patients.

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Burden of Thyroid and Lipid disorders among Elderly Depressed Patient: A cross sectional study in Nepal

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Abstract

Background and Objectives: Depression is common psychiatric illness among geriatric population however it remains underdiagnosed and undertreated. Majority of thyroid and lipid disorders are asymptomatic or have vague symptoms unless they land with emergency medical conditions. The burden of thyroid and lipid disorder are under reported in elderly population especially depressed one. The objective of the study was to measure the burden of thyroid and lipid disorders among Elderly Depressed Patient.

Materials and methods: A hospital based cross-sectional study was conducted at BP Koirala Institute of Health Sciences, Dharan. All written consent patients more than 60 years of age with diagnosed of depression using ICD 10 criteria were screened for thyroid and lipid disorders as per hospital protocol. Those cases found to have thyroid and lipid disorders were reevaluated by physician for possibilities to rule out the false positive causes.

Results: The prevalence of thyroid disorder and dyslipidemia was 29% and 62.7% respectively among 51 elderly depressed patient. Subclinical hypothyroidism was associated with 25% of the cohort. Hypertriglyceridemia (54.9%) was the most common form of lipid disorders followed by 47.1% increased total cholesterol level, 19.6% increased LDL level and 13.7% low HDL level. The presence of thyroid and lipid disorders were not significantly associated with types of depression (mild, moderate, severe and recurrent).

Conclusion: Low threshold should be kept to screen subclinical hypothyroidism and dyslipidemia among geriatric depressed population due to alarming burden and adverse impact on quality of life and longevity.

Key Words: Dyslipidemia, Depression, Elderly, Thyroid Disorder.

Introduction

The average life expectancy of mankind is increasing mainly due to better nutrition, safe drinking water, improved sanitation, effective preventive public health interventions and modern medicine however this has shifted the health burden on geriatric population, mental health, non- communicable diseases, malignancy and road traffic accidents.[1] The common chronic medical conditions associated with aging are heart disease, arthritis, cataract, stroke, cancer, diabetes and subclinical hypothyroidism.[2] In elderly, psychiatric illness like major depression is also common; 44% elderly in Canada and 17% elderly in Dutch have depression.[3,4] Depression is associated with increase morbidity and mortality of any other physical health problem.[5] Depression remains under-diagnosed and under-treated in elder as they

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have different presentations.[5]

The most common thyroid disorder is subclinical hypothyroidism (SCH). SCH is prevalent in the general population about 4-10%. It occurs about 15% in elderly women and 10% in elderly men.[6] SCH usually present with nonspecific vague symptoms and one of them could be depressive mood. Lipid disorder are usually asymptomatic unless they present with coronary artery disease, cardiovascular accidents and/or peripheral vascular disease. Hypothyroidism is one of the treatable cause for depression and/or dyslipidemia. There is an association between thyroid status and cognitive decline, depression and dementia in the elderly.[6]

Presence of depression in elderly increases the risk of coronary heart disease and total mortality; and also SCH.[7] On the other hand, prevalence of depression and SCH also increased with cardiovascular disease and other chronic physical diseases.[6] Depression is considered to be an independent risk factor for coronary artery disease, heart failure in older hypertensive patients and mortality.[7] The SCH is associated with cardiovascular risk factor and depression in the elderly.[8]

A large cross-sectional study in Colorado of 25,862 persons found that those with serum TSH concentrations of 5.1 to 10 mIU/L had higher serum cholesterol levels than those who were euthyroid.[9] The Nagasaki study found a 2-fold elevation in the risk of angina and MI in men but not in women with SCH.[10] A study of patients with SCH who were between the ages of 70 and 79 years showed 3-fold increased risk of congestive heart failure, but no increased risk of coronary or cerebrovascular disease or cardiovascular mortality.11 The Busselton Health Study in Australia revealed 3-fold increase in the risk of coronary artery disease and 2-fold increase in the risk of cardiovascular mortality in patients with SCH.[12] Women over 50 years of age with SCH with history of smoking have the highest risk for cardiovascular complications.[13] A 12-year study of 3, 233 aged 65 years and older found no significant difference in the risk of coronary heart disease, cerebrovascular disease, cardiovascular death, or all-cause death between euthyroid patients and those with subclinical.[14-18] Another studies suggest an increased risk of depression and panic disorder in SCH in elderly.[19,20] Both the conditions are bidirectional.[20]

The aim of our study is to measure the burden of thyroid and lipid disorders among elderly depressed patient and correlate the relationship among these entity with severity of depression in elderly.

Material and methods

The study was approved by the institutional review board of the hospital. This is a cross- sectional, hospital based study done at BP Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal for a period of one year. All consecutive depressed patients of age 60 years and above, diagnosed on the basis of ICD – 10 criteria coming in psychiatric services of BPKIHS were included. A written informed consent was taken before enrollment of the subject. Consent was received from care taker among those who were unable to provide written consent. Considering 10% prevalence of depression among elderly we calculated the sample size of 35 with 95% confidence interval and 90% power of the study. Adding 30% as biases the final sample size was 51. Epidemiological profiles (age, sex, ethnicity, occupation, education and geographical areas, etc) were noted using a semi-structured Performa developed for the study. Relevant investigations were done and interpreted as per hospital protocol. Patient under substance use or drugs that would altered thyroid functions (given for other than thyroid disease) and lipid profile (given for other than dyslipidemia) were excluded. Those patient with deranged thyroid and lipid profile were reevaluated by physician to rule out possible cause other than thyroid or lipid disorders. Data were collected and entered in Microsoft Excel Software. Analysis was done using SPSS Software.

Results

There were 51 patients enrolled. The mean age of the patients was 66.94 ±7.56. Two third of them

were female. Majority were illiterate, married, house maker and Hindu by religion. Family history of depression was associated with 15% of the cohort. (Table 1)

Among the types of depression, recurrent depression was noted in 39.2%, severe depression in 13.7%, moderate depression in 39.2% and mild depression in 7.8%. (Figure 1)

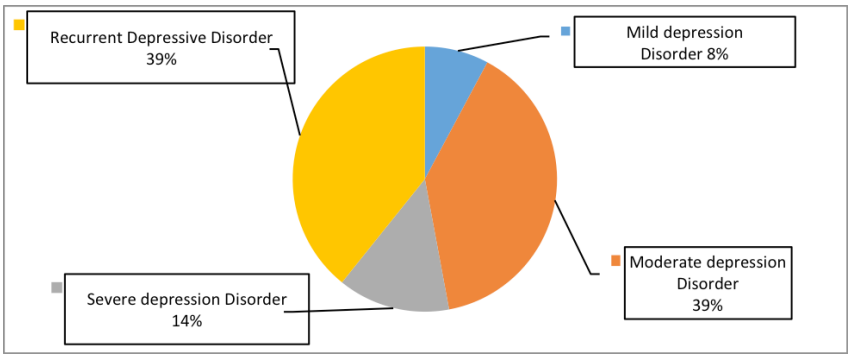

Figure 1: Types of depression

Table 1: Socio-demographic variables of the study group

Characteristics	Categories	Number	Percentage
Age group in years	60 – 69	35	68.6
	70 – 79	11	21.6
	≥80	5	9.8
Mean age of patient in years ± SD (Min – Max)		66.94 ±7.56 (60 – 89)	
Gender	Female	34	66.7
	Male	17	33.3
Educational level	Illiterate	26	51.0
	Can read and write	12	23.5
	Primary	6	11.8
	SLC and above	7	13.7
Occupation	Business	4	7.8
	Farmer	9	17.6
	House maker	25	49.0
	Service	7	13.7
	Unemployed	6	11.8
Religion	Bhuddhist	3	5.9
	Christian	3	5.9
	Hindu	43	84.3
	Kirat	2	3.9
Socio Economic Status	Low	19	37.3
	Middle	32	62.7
Marital Status	Married	42	82.4
	Widow	9	17.6
Family history	None	43	84.3
	Present	8	15.7
Total		51	100.0

Among 51 cases enrolled, thirty four cases (66.7%) had other comorbidities, most commonly systemic hypertension (35.3%), followed by type 2 Diabetes mellitus (15.7%). Ten cases (19.6%) had more than one multiple comorbidities. Among hypertensive cases two third were associated with isolated hypertension. Diabetes Mellitus (DM) was the second most common comorbidity accounting for 8 cases (23.53%). (Table 2) There was no statistical significance between types of depression and the above mentioned comorbidities. (Table 3)

Table 2: Burden of other comorbidities

Comorbidities	Frequency	Percentage
Overall comorbidities	34	66.6
Systemic Hypertension	18	35.29
Diabetes mellitus	8	15.68
Tuberculosis (treated cases)	4	7.84
Chronic obstructive pulmonary disease	3	5.88
Symptomatic gall stone disease	3	5.88
Heart disease	3	5.88
Parkinson's Disease	2	3.92
Hearing impairment 2	2	3.92

Table 3: Association between comorbidity and types of depression

Comorbidity	Type of depression				
	Mild	Moderate	Severe	Recurrent	Total
No	2	6	2	7	17
Yes	2	14	5	13	34
Total	4	20	7	20	51
χ^2 =0.69, p value = 0.87					

Seventy one percentage of the cohort were euthyroid followed by 25% subclinical hypothyroid (SCH) and 4% hyperthyroid. (Figure 2). SCH was more prevalent among females whereas hyperthyroidism were equally distributed with gender without statistical significance. (Table 4) The relation between thyroid status and types of depression was not statistically significant. (Table 5)

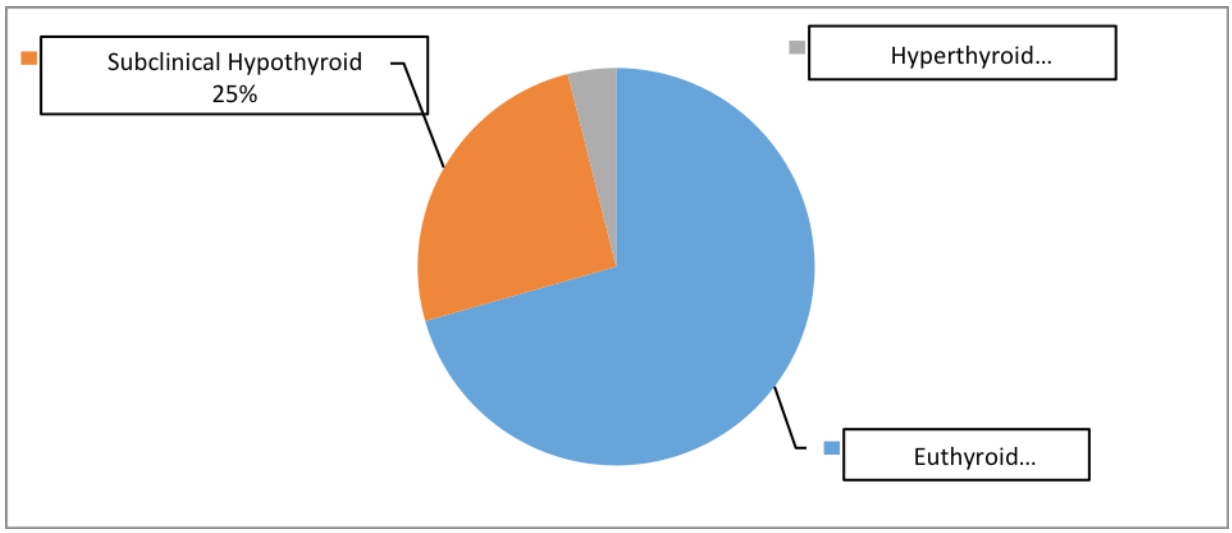

Figure 2: burden of thyroid disorder

Table 4: Thyroid profile and gender distribution

Gender	Thyroid Status			Total
	Euthyroid	SCH	Hyperthyroid	
Female	23 (67.64%)	10(29.41%)	1(2.94%)	34 (100%)
Male	13(76.47%)	3 (17.64%)	1(5.88%)	17 (100%)
	36(71%)	13(25%)	2(4%)	51 (100%)
χ^2 =0.99, p value = 0.69				

Table 5: Association between thyroid profiles and types of depression

Thyroid status	Type of depression				Total
	Mild	Moderate	Severe	Recurrent	
Euthyroid	2	17	6	11	36
Subclinical hypothyroid	1	3	1	8	13
Hyperthyroid	1	0	0	1	2
Total	4	20	7	20	51

The mean and median values of triglyceride and LDL was above normal limit. (Table 6) Hypertriglyceridemia (54.9%) was the most common lipid disorders followed by hyper cholesterolemia (47.1%), high LDL (19.6%) and low HDL (13.8%) levels. (Table 7)

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Table 6: Distribution of lipid profile

	Total cholesterol	Triglyceride	HDL	LDL
Mean±SD	198.26±53.02	197.09±149.05	49.24±14.44	124.96±44.19
Median	191	169	47	114
Mode	141	87	58	84
Range (min – max)	218 (95 -313)	795 (53 – 848)	66 (25 – 91)	162 (66 – 228)

There was no statistical significance between lipid disorders and types of depression. (Table 7)

Table 7: Association between lipid disorder and types of depression.

Lipid	Range	Type of depression				Total (%)
		Mild	Moderate	Severe	Recurrent	
Total Cholesterol	Normal	2	9	5	11	27 (52.9)
	Increased	2	11	2	9	24(47.1)
	Total	4	20	7	20	51
χ^2 =1.51, p value = 0.67						
Triglycerides TG	Normal	1	11	5	6	23(45.1)
	Increased	3	9	2	14	28(54.9)
	Total	4	20	7	20	51
χ^2 =5.24, p value = 0.15						
High density lipoproteins HDL	Normal	4	19	5	16	44(86.2)
	Decreased	0	1	2	4	7(13.8)
	Total	4	20	7	20	51
χ^2 =3.89, p value = 0.27						
Low density lipoprotein LDL	Normal	2	17	6	16	41(80.4)
	Increased	2	3	1	4	10(19.6)
	Total	4	20	7	20	51
χ^2 =2.74, p value = 0.43						

Discussion

According to the classification of the old age; [21] most of the cases were young old of 60 to 69 years age group comprising of 68.6%, followed by the middle old of 70 to 79 years comprising 21.6% and lastly the very old more than 80 years comprising 9.8%. This is similar to the age pyramid of Nepal.[22]

In our study, there was preponderance of female; the female to male ratio was 2:1. Female preponderance has been shown by other studies as well.[23-25]

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Forty nine percentage were literate which is comparable to Nepal's literacy rate of 57.4% where the female literacy rate is 46.7%.[26] As there was female preponderance most of the cases were housewife. Hindu (84.3%) was the commonest religion which is similar to the distribution of religion in the country.[27]

In the 51 cases of depression, 39.2% were recurrent. Severe, moderate and mild depression constituted 13.7%, 39.2% and 7.8% respectively. This is different from the study by Das BKL et al where the severe depression was the most common accounting for 36%.[26]

In our study, single comorbidity was present in 66.7% cases whereas 19.6% had multiple comorbidities. This is comparable to a population study where 24% aged 65 years or older; and 31.4% aged 85 years or older had multiple comorbidities.[28] The prevalence of comorbidities and number of comorbid conditions increase with age.[29] In this study, hypertension (35.2%) followed by Diabetes mellitus (15.3%) were the two most common comorbidities. This is similar to the study by Gerda G F et al where in a sample size of 4126 subjects, 57% reported hypertension, 20% diabetes, 15% coronary artery disease, 9% cancer, and 9% cerebrovascular diseases; 29% reported no disease conditions, whereas 29% multiple comorbidities.[30] Moreover, many older men and women experience a gradual decline in physical strength, gait speed, manual dexterity, memory, and cognitive skills, in the absence of a clinically manifest disease process. Coexistence of multiple such impairments complicates the diagnosis, treatment, and natural course of individual health conditions in older adults.[31] In our study, the presence of comorbidity was not related to the severity of depression which is similar to the findings of Polona Selic et al where the burden of somatic comorbidity was shown to be smaller than the impact of psychosocial determinants for depression and there was no significant difference in the comorbidity in depressed and non-depressed subjects.[32]

Most of the patients were euthyroid (71%) followed by subclinical hypothyroid (25%) and hyperthyroid (4%), but there were no cases of clinical hypothyroidism. This is similar to the study by Lokesh Jain et al where the prevalence of thyroid disorder in depression was 20% and subclinical hypothyroidism(13.3%) was more prevalent than clinical hypothyroidism (6.7%), but there were no cases of hyperthyroidism.23,24 A study by Vale´ria Bahdur Chueire et al showed that depression was observed in the subclinical hypothyroid patients (49%) and suggested that mood disturbances are frequent in the elderly with elevated serum TSH levels, but they do not differ in the primary hypothyroid and the nonthyroidal sick patients.33 Benedetta Demartini et al found that subclinical hypothyroidism is associated with the presence of depressive symptoms beyond the role of possible confounding factors.[34] In a study by Aeijaz Ul Noor et al, they found that major psychiatric disorders namely major depressive disorders had demonstrable changes in their thyroid functions and the prevalence of major depressive disorders was 30.77% in Sub-Clinical Hpothyroidism and 6 % in Clinical Hpothyroidism.[35]

In a prospective cohort study of 606 older adults, both baseline and persistent subclinical hypothyroidism were not associated with increased depressive symptoms; but results were consistent with a possible association between subclinical hyperthyroidism and increased depressive symptoms.[36] In our study also, the thyroid status was not associated with increased depressive symptoms. However, in a study of younger sample (15 to 60 years) by Das BKL et al, a multiple comparison testing between the groups of the patients of mild, moderate and severe depression showed significantly high TSH levels.[26]

Regarding dyslipidaemia a strong risk factor for cardio and cerebrovascular disease, more than half of the cases had increased level of triglyceride (54.9%) and similarly 52.9% had normal level of total cholesterol, but high density lipoprotein (86.2%) and low density lipoprotein (80.4%) were

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in most cases within the normal range. In our study, the relation between the lipid profile and types of depression was not statistically significant. This is similar to the study by Onuegbu A.J et al where there was significant increase in plasma triglyceride in depression, irrespective of the severity of disease, and showed that plasma lipid and lipoprotein levels did not demonstrate any definite pattern with increasing level of depression in patients.[37] This is in contrary to the study by Stefanos Tyrovolas et al where a considerable proportion of sample (53.2%) had hypercholesterolemia and hypercholesterolemia was correlated with depressive symptomatology.[38] Similarly, a study by Nikolaos Dimopoulos et al was done to examine the association of plasma lipid concentrations with changes in cognitive function and depressive states in elderly Greek individuals and it showed that an association existed between the plasma concentration of cholesterol and HDL and depression and/or cognitive impairment.[39] In a study on elderly Finnish men (n=470)by Sinikka Aijanseppa et al, it was also found that low total serum cholesterol was associated with a high amount of depressive symptoms independently of weight change or chronic disease.[40] In a study by Jae-Min Kim et al, it was shown that lower high-density lipoprotein level (but neither hypertension nor diabetes) were significantly associated with depression (independently of disability and cognitive function).[41]

Conclusion

Elderly depressed patient had high burden of thyroid and lipid disorder however these disorders were not associated with severity and recurrence of depressive disorders. Besides thyroid and lipid disorder these patient has higher burden of comorbidities like hypertension and diabetes. Nonspecific clinical signs and symptoms of thyroid and lipid disorder is likely to under screen these disorder at point of care. All the elderly depressed patients are recommended to be evaluated for thyroid and lipids biochemically. All the thyroid disorder in elderly patients are recommended to be evaluated for depression.

Limitations

This is a hospital based study. This is a cross sectional study among the depressed subjects. Further studies are recommended for causal and temporal associations.

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Knowledge Regrading Self-Administration of Insulin
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Lipid profile as a predictor of Neuropathy: The Sheffield Prospective Diabetes Study.

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Abstract

Background : Despite being a very common complication, the aetiology and potential risk factors of diabetic neuropathy (DN) have not been clearly determined in a prospective study. Aims: The aim of Sheffield Prospective Diabetes Study was to identify the abnormalities of physiological, biochemical, haemorrhelogical and cellular function for complications of diabetes in type 1 diabetes.
Materials and Methods: 66 newly diagnosed type 1 diabetic subjects (mean age 31± 9(SD) duration (3 years ± 2) were identified and followed for 9 years. They had detailed neurological assessment (symptoms and signs score, nerve conduction, vibration perception threshold, warm thermal discrimination threshold and autonomic function tests) and blood samples taken for detail biochemical and haemorrheological analysis at base line and at follow up.
Results: At the 9 years follow up, 51 subjects were studied of whom 18 were found to have DN using Dyck's criteria. As expected subjects with DN had significantly higher ($p < 0.01$) mean HbA1 over 9 years of follow up (11.8% vs 9.8%), but it was not significantly different at base line (10.2% vs 8.9%; $p = 0.37$). In addition, total cholesterol and LDL cholesterol at baseline were found to be risk factors for the development of neuropathy (5.9 vs 4.7 mmol; $p=0.01$ and 3.7 vs 2.8 mmol; $p=0.03$ respectively).
Conclusions: This prospective study confirms the findings of recent large epidemiological studies linking cardiovascular risk factors to the development of DN, and perhaps suggest a vascular aetiology for DN. Improvement of potentially modifiable risk factors for neuropathy may be useful for the development of risk reduction strategies.

Key Words: LDL - Low Density Lipoprotein, HDL - High density lipoprotein, DN - Diabetic Neuropathy, NN - Non- neuropath subjects, SD - Standard deviation

Introduction:

The pathogenic mechanism leading to Diabetic neuropathy (DN) in human is not fully understood. Animal studies have established the presence of a number of metabolic abnormalities such as oxidative stress, sorbitol accumulation, PKC activation, accumulation of advanced glycated products in DN.[4] Similarly vascular abnormalities such as endoneurial and epineurial vessels changes, nerve hypoxia etc have also been demonstrated. [8] Similar findings have also been demonstrated in human DN.[9]

Epidemiological and prospective studies have identified hypertension[6], increasing age, duration of diabetes and poor glycaemic control [1] as a significant risk factor for the development of DN. There has been association between lipids and DN but there is still a paucity of well-conducted prospective study in this field.

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Sheffield Prospective diabetes study was started with the aim of identifying risk factors associated with the development of diabetic complications in type 1 subjects. This study was approved and funded by Diabetes UK.

Methods:

In this prospective observational study, sixty-six (25 Females) newly diagnosed Type 1 diabetes subjects (mean age 31 - 9(SD) duration (3 years -2) were recruited from a busy diabetes clinic. All consecutive patients who were diagnosed with type 1 diabetes within the last 5 years were approached when they came to the diabetes clinic. Subjects were deemed to have type 1 diabetes if the age at diagnosis was less than 40 and needed insulin within six months of diagnosis. Only those subjects who agreed for detailed neurophysiological examination and long term follow up were included in the study. Subjects who were likely to leave the area, such as university students were excluded. They had clinical neurological assessment performed by neurological symptoms questionnaire and neurological examination. Nerve conduction velocity of median motor, median sensory, peroneal motor and sural sensory nerves was measured at 22 0C using Dantac 2000.[13] For qualitative sensory tests, vibration perception threshold over the great toe was measured using neurothesiometer and warm thermal detection threshold over the dorsum of right foot using thermo-aesthesiometer. Cardiac autonomic function tests were performed using O'Brien protocol. They also had fasting lipid profiles (serum cholesterol, fasting triglycerides, HDL cholesterol and LDL cholesterol) and HbA1c measured. The overall diabetes control (mean HbA1) was measured from the laboratory database by calculating the mean of all HbA1 performed over the study period.

They were treated in diabetes clinic as any other patients without any active intervention. At 9 years they were again invited for detailed follow up as above. Only 51 subjects (77%) attended for follow up as 15 patients had moved out of the area or refused to attend for detailed neurophysiologication (Figure 1). Diagnosis of diabetic neuropathy was made using Dyck's criteria (Dyck 1988).

Results:

At baseline visit 14 (21.2%) out of 66 subjects had evidence of neuropathy on detailed neurophysiological examination. Out of 52 subjects without neuropathy (NN) at baseline, 42 were followed up and 9 subjects (21.4%) developed new onset DN. At 9 years visit 33 subjects (64.7%) did not have neuropathy (NN) and 18 subjects (35.3%), 9 new and 9 established subjects, had DN.

When the lipid levels of 18 subjects with DN was compared with 33 subjects without neuropathy, the levels were raised in all visits (table 1). As expected the overall control over 9 years was poor in DN subjects (mean HbA1 11.8 +/- 2.1% vs 9.8 +/- 1.9%; $p < 0.01$) however this was not statistically significant on the first visit (10.2 +/- 3.2% vs 8.9 +/- 3.0%; $p= 0.37$).

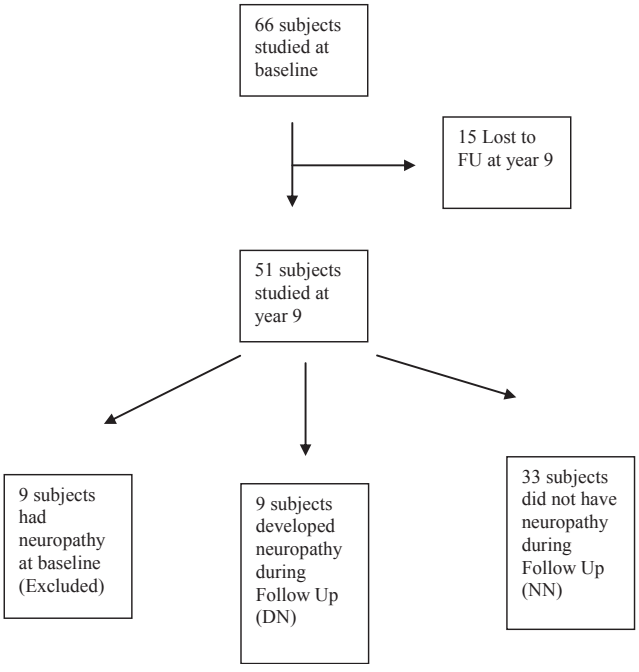

Figure 1: Flowchart of study

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Table 1: Lipid profile of subjects who have diabetic neuropathy at 9 years follow up in comparison to subjects who did not have neuropathy.

		Non-Neuropath		Diabetic Neuropathy		
		Mean	SD	Mean	SD	*p* Value
Triglyceride	Initial Visit	1.30	1.38	1.63	0.84	0.03
	Final Visit	1.06	0.45	1.89	1.44	0.05
Cholesterol	Initial Visit	4.73	1.12	5.57	1.18	0.02
	Final Visit	4.99	0.81	5.76	1.08	0.02
HDL Cholesterol	Initial Visit	1.36	0.34	1.29	0.47	0.34
	Final Visit	1.33	0.35	1.34	0.46	0.84
HDL / Total cholesterol Ratio	Initial Visit	3.67	1.40	4.71	1.53	0.01
	Final Visit	3.97	1.25	4.69	1.53	0.12
LDL Cholesterol	Initial Visit	2.83	1.08	3.55	1.06	0.02
	Final Visit	3.22	0.89	3.57	0.83	0.24

Nine subjects who were NN at first visit developed DN during follow up. In order to look into risk factors for the development of DN, the baseline lipid profiles of these subjects were compared with 33 NN subjects. We found that total cholesterol and LDL cholesterol was significantly raised in this group at baseline with a trend for elevated triglyceride and HDL / Total cholesterol ratio (table 2). There were no significant differences in the overall diabetes control at baseline between these groups (11.1 +/- 4.3% vs 8.9 +/- 3.0%; p= 0.15), however during follow up, the 9 year's mean HbA1, was raised (12.0 +/- 2.3% vs 9.8 +/- 1.9%; p=0.01). The baseline lipid profiles of subjects lost to follow up was statistically no different to those followed up for 9 years.

Table 2: Baseline lipid profiles of subjects who developed new onset diabetic neuropathy during follow up in comparison to those subjects without diabetic neuropathy

	Non - Neuropathy		New Diabetic neuropathy		
	Mean	SD	Mean	SD	*p* Value
Triglyceride	1.30	1.38	1.69	0.91	0.08
Cholesterol	4.73	1.12	5.88	1.06	0.01
HDL Cholesterol	1.36	0.34	1.42	0.55	0.78
HDL / Total Cholesterol Ratio	3.67	1.40	4.59	1.47	0.06
LDL Cholesterol	2.83	1.08	3.70	0.97	0.03

Discussion:

Previous studies have shown association of lipids to DN. In Eurodiab study Tesfaye et al[19] have shown baseline triglycerides to be associated with neuropathy and have shown both triglycerides and cholesterol to be a risk factor for the development of DN.[5] On the other hand Spallone et al [17] did not find any relation between autonomic neuropathy and lipids. Similarly Maser et al [14] did not find any relation between lipids and vibration threshold. In a recent epidemiological study in young people with diabetes, risk factors for neuropathy in Type 1 DM were older age, longer diabetes duration, smoking, increased diastolic blood pressure, obesity, increased LDL cholesterol and triglycerides, and lower HDL cholesterol. In youth with Type 2 DM, risk factors were older age, male sex, longer diabetes duration, smoking, and lower HDL-c.[11] Our study shows that at baseline both total cholesterol and LDL cholesterol is significantly elevated in subjects who later developed DN. Both total cholesterol and fasting triglycerides levels were significantly raised in subjects with Diabetic neuropathy. Microvascular abnormalities is thought to be the aetiology of neuronal damage.[18] It is possible that similar to hypertension, lipids also contribute to both macrovascular and microvascular complications. The elevated lipids may be in part responsible for reported raised mortality in diabetic neuropathy.[7]

The HbA1 was not statistically different between these two groups at base line, although the mean HbA1 was higher in subjects who later developed DN. The overall control of diabetes was poor in DN group during the 9 year follow up. We did not find any difference between the HDL levels in these two groups. This may be due to both male and female subjects being pooled together. HDL is higher in female subjects. We did not analyse the data separately as the numbers were smaller.

Elevated lipids have been associated with other microvascular complications of diabetes. Triglycerides has been shown to be a risk factor for the development of proliferative diabetic retinopathy.[2] In subjects with diabetic nephropathy, Zimmermann et al[20] demonstrated significantly higher concentrations of LDL-cholesterol, triglycerides and lower concentrations of HDL-cholesterol. In diabetic nephropathy deterioration of renal function has been retarded by LDL plasma apheresis.[16] Similarly HMG Co A reductase inhibitors have been shown to reduce the deterioration in renal function in experimental diabetic nephropathy[10,12], however, the mechanism is thought to be independent of its lipid lowering effect. Therapy with a statin or a fibrate was shown to have protective effect against the development of diabetic peripheral sensory neuropathy [3, 15]

Conclusion:

This prospective study confirms the findings of recent large epidemiological studies linking cardiovascular risk factors to the development of DN, and perhaps suggest a vascular aetiology for DN. Improvement of potentially modifiable risk factors for neuropathy may be useful for the development of risk reduction strategies.

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Chronic Calcific Pancreatitis Associated Diabetes.....
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CASE REPORT OPEN ACCESS

Chronic Calcific Pancreatitis Associated Diabetes Presenting as Involuntary Weight Loss and Multiple Soft Tissue Calcifications in a Young Male

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Abstract

Introduction: Chronic Calcific Pancreatitis, a rare form of secondary diabetes occurs due to recurrent alcohol induced acute pancreatitis.
Case Summary: A 28 year old male patient presented with significant involuntary weight loss associated with a history of passing clay colored sticky stools for the past 1 year. He was also detected to have deranged blood sugars on routine work up at a local hospital for increased thirst and increased urine output. There was a history of recurrent bouts of moderate to severe abdominal pain over the past 3 to 4 years. At the time of initial presentation his Random blood sugar values was 468 mg/dL. Other routine tests tests were within normal limits. His serum amylase levels were 185 U/L and serum Lipase levels were 467 U/L.
Conclusions: Chronic fibro calcific pancreatitis is a rare cause of diabetes in young patients but has a characteristic clinical picture with a young patient presenting with features of malabsorption and low BMI, low propensity for DKA , low beta cell reserve and sensitivity to Insulin .

Key Words: FPCD-chronic fibrocalcific pancreatic disease, TFCP-tropical fibrocalcific pancreatitis, TIGAR –o-toxic, idiopathic, genetic, autoimmune-obstructive

Introduction

Chronic calcific pancreatitis is a rare form of secondary diabetes.[1] Chronic calcific pan-creatitis most commonly occurs in adult patients due to recurrent alcohol induced acute pancreatitis. Tropical Fibro-calculus Pancreatitis is also an important cause in tropic coun-tries. In India the TFCP is most commonly seen in the south and east of the country, par-ticularly in Tamil Nadu and Kerala. Chronic pancreatitis and diabetes also occur in a rare form of Maturity Onset Diabetes of Young (MODY type 8) due to defect in the gene encoding cholesterol ester lipase.

Development of diabetes is a common complication of chronic pancreatitis and such pa-tients usually have significant weight loss due to the associated malabsorption.[2]

These patients show very low serum C-peptide levels due to decreased pancreatic beta cell reserve and have very high sensitivity to insulin, with glycemic control being achieved at very low doses of insulin therapy .

Case summary

A 28 year old male patient presented with significant involuntary weight loss associated with a history of passing clay colored sticky stools for the past 1 year. He was also detect-ed to have deranged blood sugars on routine work up at a local hospital for increased thirst and increased urine output. There was a history of recurrent bouts of moderate to

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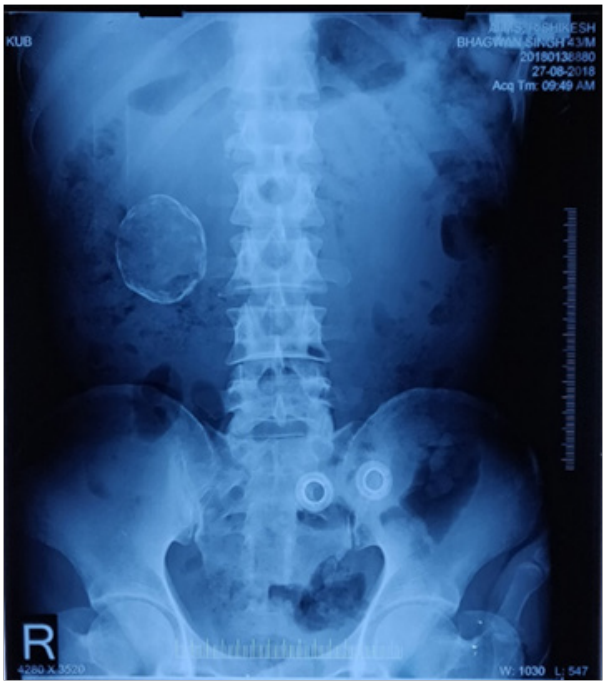
severe abdominal pain over the past 3 to 4 years.

There was no similar history in any first degree relatives. He had a history of only occa-sional alcohol intake and no history of binge drinking followed by onset of severe ab-dominal pain.

On examination he was conscious, oriented to time, place and person and was thinly built. His vital parameters were stable but his BMI was only 17.3. There was no pallor, icterus, cyanosis, clubbing or lymphadenopathy. Per abdomen was sound and there was a mass palpable just to the right of the midline in the epigastric and umbilical regions, which had a smooth surface, firm to hard consistency, did not move with respiration and became less prominent on contraction of the abdominal wall muscles. The respiratory, cardiovascular and neurological examination was within normal limits.



At the time of initial presentation his Random blood sugar values was 468 mg/dL.Other routine tests tests were within normal limits. His serum amylase levels were 185 U/L and serum Lipase levels were 467 U/L. Furthermore ,urinary ketone bodies were negative and Arterial blood gas analysis was not suggestive of any high anion gap metabolic acidosis. Stool examination revealed elevated fat content on examination . An AP X-ray radiogram of the abdomen showed a calcified cystic lesion to the right of the midline at the level of L2/3 vertebral bodies.

A CECT abdomen was done which showed extensive calcification and atrophy of the pan-creas with a 6.5*6.8*7.6 cm pseudo cyst involving the pancreatic head. There were similar but smaller pseudo cysts involving the body and tail of the pancreas.Multiple other calcific foci were also found in various soft tissue locations .His serum C-peptide levels were found to be 0.11ng/ml.

Based on the above presentation he was diagnosed to have chronic calcific pancreatitis related diabetes. He was started on Inj. Glargine 8 units HS and inj. human insulin regular 4units Thrice a day before each meal.

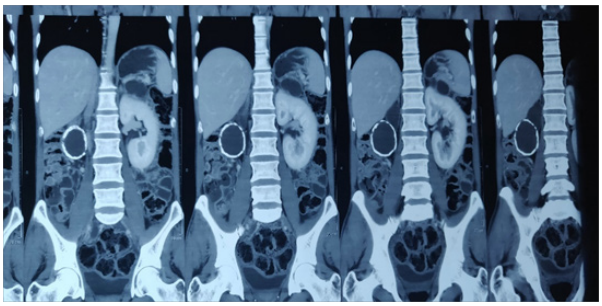


Figure 2: psuedocyst involving head and tail of pancreas

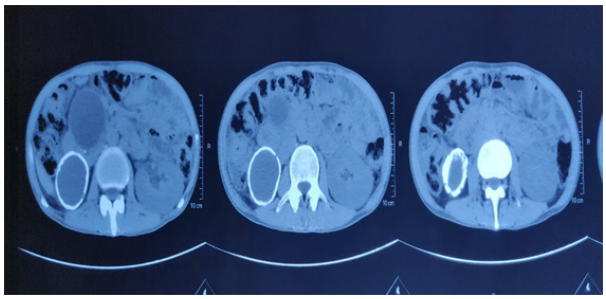


Figure 3: psuedocyst involving the head of pancreas showing calcification

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Discussion

Chronic pancreatitis is most commonly caused worldwide in adult patients by alcohol re-lated recurrent pancreatitis. In children the most common cause is cystic fibrosis . Presently the etiology of chronic pancreatitis is classified using the TIGAR-O classification (Toxic, Idiopathic, Genetic , Autoimmune, Recurrent and Obstructive) . In non-alcoholic young adults an important cause is tropical fibro-cacific pancreatitis which is relatively more common in the Indian states of kerala and Tamil Nadu . No cases have yet been documented from Uttarakhand. Autoimmune pancreatitis may occur with IgG4 related disease (type1)[3] and as [part of autoimmune polyglandular syndrome type 1 and 2. Rarer genetic causes of chronic pancreatitis include patients with mutations in the SPINK1 (encoding trypsinogen inhibitor) , CTRC(encoding chymotrypsin C) , PRSS1(cationic trypsinogen) and CaSR(calcium sensing receptor loss of function mutation).[4,5]

The etiology of tropical fibro-calcific pancreatitis is multifactorial and poorly understood with suspected causes being a genetic predisposition, selenium deficiency, cyanide toxicity secondary to chronic dietary ingestion. Criteria for diagnosis of tropical fibro calcific pan-creatitis are as follows
1)Occurring in a “tropical” country 2) established Diabetes mellitus based on ADA criteria 3) radiographic evidence of chronic pancreatitis and 4) absence of other causes of chronic pancreatitis.[6]

The diabetes associated with FCPD is associated with decreased serum C-peptide levels (as seen in this patient) and is usually severe in magnitude. However, the incidence of di-abetic ketoacidosis is very low which is largely a result of the low body fat content of the patients secondary to malabsorption. There is also a lower incidence of the macro vascular complications of diabetes. But the microvascular complications such as neuropathy, nephropathy and retinopathy are common and related to long term glycemic control.[7,8]
The mechanisms for development of diabetes in chronic pancreatitis are 2 fold -primary destruction of beta cells and decreased intestinal increasing secretion as a result of malabsorption.
Multiple soft tissue calcifications is a relatively uncommon radiological finding with many plausible causes which may be remembered using the pneumonic TIC MTV[9]
T- Tumor (Tumoral calcinosis , synovial osteochondromatosis , calcified lipoma/ hemangioma/sarcoma)
I- Inflammation (Systemic sclerosis, Dermatomyositis, pancreatitis with metastatic calcification , calcific myonecrosis , hydatid cysts)
C-congenital (Ehlers-Danlos syndrome, Myositis ossificans progressiva)
M-Metabolic (Hyperparathyroidism[primary/ secondary] ,calcium pyrophosphate deposition disease[CPPD], calcium hydroxyapatite deposition)
T-Trauma (Myositis ossificans, burns, hematoma)
V-Vascular (chronic venous insufficiency, arterial calcification)

Conclusion

Chronic fibro calcific pancreatitis is a rare cause of diabetes in young patients but has a characteristic clinical picture with a young patient presenting with features of malabsorption and low BMI , low propensity for DKA , low beta cell reserve and sensitivity to Insulin . The etiology of chronic pancreatitis can be varied and occasionally multifactorial and therefore requires a detailed structured work up . Timely diagnosis, insulin supple-mentation and tight glycemic control is required to prevent the development of microvascular complications of diabetes .

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National Consensus Statement for the Management of Hypothyroidism in Nepal

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Contents

From the President's Desk

"Gaining knowledge is the first step to wisdom and sharing it is the first step to humanity."

It is the need of the hour for us to unite to spread the knowledge we have gained in the past decades with our experiences so we can amalgamate it with the data and text from around the globe and use it to benefit our society which is unique in its ways from the rest of the world.

This is our first, albeit small, step in our academic journey. DEAN, with all its members, truly put in a great show of effort with this document, which only encourages the organization to take on more of such endeavors in the future. We hope this effort of ours travels far and wide to even the hard-to-reach corners of our healthcare system and helps the caregivers and health professionals to provide better care to the patients.

A heartfelt thanks to all DEAN members. A very special thanks to Dr Nitendra Sesodia and the team of Thieme Medical and Scientific Publishers for their relentless efforts in bringing this document to life, and to Dr Syed Abbas Raza (Endocrinologist, Lahore) for his significant contribution.

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Abstract

Hypothyroidism, most common of all the thyroid disorders, is estimated to have a worldwide prevalence of up to 4.6%. Although epidemiological data of hypothyroidism in Nepal is not available, several hospital-based studies have indicated a high prevalence ranging from 8 to 11.6%. Currently, there are no national guidelines in Nepal for the management of hypothyroidism. This document reviews the current international and regional guidelines and summarizes a consensus statement specifically for Nepal based on experts' opinion and evidence from literature.

Introduction

Thyroid is an important endocrine gland, which utilizes iodine from food and produces two hormones, thyroxine (T_4) and triiodothyronine (T_3). Thyroid gland also produces another hormone called calcitonin. While calcitonin regulates the level of calcium in the body, T_3 and T_4 play a major role in various metabolic functions. These metabolic processes get disrupted due to dysfunction of the thyroid gland. Common thyroid disorders include hypothyroidism, hyperthyroidism, goiter, thyroiditis, thyroid nodules, and thyroid cancer.[1]

Hypothyroidism is the most common of all the thyroid disorders with a worldwide prevalence ranging from 3.05 to 4.6%.[2–4] The global prevalence seems to be increasing over time, which could be due to several factors such as increase in iodine deficiency worldwide, better screening for the disease, and aging population.[3,5–7] This disorder of the thyroid gland is much more common in women than in men and is seen more frequently with increasing age.[2,8]

Although a large-scale study on general population to understand the epidemiology of hypothyroidism in Nepal is lacking, several hospital-based studies have indicated a high prevalence in this landlocked Himalayan country. The prevalence of hypothyroidism in various hospital-based studies from different parts of Nepal ranged from 8 to 11.6%.[9–12] Nepal lies in the iodine-deficient zone of the world and, therefore, several steps have been taken by the Government of Nepal to overcome the iodine deficiency issues.[13,14] Consequently, recent surveys have indicated an adequate intake of iodine in the general population of Nepal.[15] Although iodine deficiency was the main cause of hypothyroidism in Nepal until recently, with universal iodization of salt, autoimmune disease may now be an important cause. However, efforts to ensure adequate iodine intake should be continued.

There are several international/regional guidelines for the management of thyroid disorders including hypothyroidism.[16–18] However, there is no such guideline in Nepal. Thus, there is a need for development of guidelines specifically meant for management of hypothyroidism, which is the most common thyroid disorder in this region.

This consensus statement is an effort to bridge the existing gap and hopefully a guideline will be developed in the future.

Etiology of Hypothyroidism

The function of thyroid gland is controlled by the hypothalamic-pituitary-thyroid axis. Thyroid-stimulating hormone (TSH), released by the pituitary gland, controls the level of thyroid hormones. TSH, in turn, is controlled by the TSH-releasing hormone that is secreted by the hypothalamus. Hypothyroidism can occur as a result of primary failure of the thyroid gland or due to inadequate stimulation of the thyroid gland at the pituitary or hypothalamus level.

Primary causes of hypothyroidism include iodine deficiency; autoimmune diseases such as Hashimoto's thyroiditis and atrophic thyroiditis; congenital hypothyroidism; drugs such as lithium, amiodarone, interferon-α, antithyroid drugs; and iatrogenic factors such as radioactive iodine therapy, thyroidectomy, and external irradiation of neck for lymphoma or cancer. Secondary or central causes include hypothalamic and pituitary diseases such as tumors, trauma, or infiltrative disorders.

In Nepal, endocrine disruptors like insecticides and pesticides may have a role to play in the development of hypothyroidism; however, this area needs further study.

Signs and Symptoms of Hypothyroidism

Hypothyroidism can be asymptomatic in a large number of patients. In symptomatic patients, the most common presentation includes tiredness/weakness, dry coarse skin, cold sensitivity, menstrual irregularities, muscle cramps, hair thinning/hair loss, depression, hoarse voice, impaired concentration, memory impairment, weight gain, and constipation. With severe disease, additional findings such as delayed tendon reflex relaxation, carpal tunnel syndrome, edema, dyspnea, and even myxedema coma may be seen. Clinical presentation may vary depending on the age and sex of the patients. Thus, women may present more commonly with menstrual irregularities, children with lethargy and failure to thrive, and older patients with cognitive decline.[19] If left untreated, hypothyroidism can also lead to detrimental effects on the serum lipid profile and can cause cardiovascular problems. It can cause infertility/subfertility, cognitive impairment, and neuromuscular problems.[19]

Screening for Hypothyroidism

Measurement of serum TSH is the best screening test for hypothyroidism. Screening of general population for hypothyroidism has been a matter of debate. However, screening is recommended in following cases: type 1 diabetes, pernicious anemia, family history of autoimmune thyroid disorder, psychiatric disorders, and patients treated for hyperthyroidism.[16] For individuals with any autoimmune disorder (e.g., systemic lupus erythematosus) or any endocrine abnormality (e.g., premature ovarian failure), screening is recommended as they are at a higher risk. In addition, in Nepal, annual screening is recommended in population with no access to iodized salt and for those who are 50 years or older. Thyroid function test can be conducted at any time of the day without fasting.

Preconception

As per the most recent (2017) American Thyroid Association (ATA) guidelines for the diagnosis and management of thyroid disease during pregnancy and postpartum, "there is insufficient evidence to recommend for or against universal screening for abnormal TSH concentrations preconception, with the exception of women planning assisted reproduction or those known to have antithyroid peroxidase antibody (TPOAb) positivity."[20] However, the Indian Thyroid Society Guidelines support the view that screening should be carried out during prepregnancy evaluation.[21] Further, a study conducted in the United States found a high rate of subclinical hypothyroidism in women planning conception,[22] which implies that preconception screening could be an important step to identify and treat these women, and thus prevent adverse outcomes. Screening for TPOAb preconception has also been proposed (although supportive data are lacking), considering the high prevalence of TPOAb positivity in the women of reproductive age group. TPOAb test also helps in identifying women who are at risk of developing hypothyroidism during pregnancy.[20]

In Nepal, universal screening at preconception is strongly recommended specially in following high-risk cases: age greater than 30 years; body mass index (BMI) greater than or equal to 30 kg/m^2; presence of other autoimmune diseases; presence of symptoms of hypothyroidism; family history/past history of thyroid disease; previous head and neck irradiation; use of drugs such as amiodarone and lithium that interfere with thyroid function; presence of circulating TPOAb, history of previous miscarriage, preterm delivery, or infertility; women residing in an area of known moderate-to-severe iodine insufficiency; and a history of developmental delay in family.[23]

Diagnosis of Hypothyroidism

TSH, Free T_3, Free T_4, and Thyroid Antibodies

Diagnosis of hypothyroidism is made by measurement of blood levels of TSH and thyroid hormones. Most of the T_3 and T_4 is protein-bound and therefore, factors affecting the binding may affect the levels of total serum T_3 and T_4. Evaluation of free thyroid hormones instead of total hormones is, therefore, considered as a more accurate measure of thyroid function.[24] However, in certain cases, for example in pregnant women, measurement of total T_4 is recommended instead of free T_4 levels.[25] Thyroid antibodies may be a discerning factor in the differential diagnosis.

Reference Range for TSH

The reference range for TSH seems to vary with age, sex, race, ethnicity, and geographical area. In the ideal situation, upper limit of normal for a third-generation TSH assay must be determined by the reference range of a given laboratory. There are different methods of determination of TSH levels and each method has a slightly different reference range. Some methods along with the

reference values are listed in **Table 1**. In the absence of reference values, a range of 0.45 to 4.12 mIU/L should be used.[16] Recently, the National Indian Patient-Centered Thyroid Management group proposed patient-centered target TSH levels, that is, a low or a high target based on certain factors such as etiology, stage of life (e.g., lower TSH targets during preconception and pregnancy, and higher TSH targets for elderly), comorbid conditions, clinical course of the disease, patient's attitude toward therapy, and patient's ability to undergo frequent monitoring.[26]

Overt and Subclinical Hypothyroidism

Hypothyroidism can be overt or subclinical (**Table 2**). A high level of TSH, above the upper reference range, accompanied by a low T_4 level accounts to a diagnosis of overt hypothyroidism. In subclinical hypothyroidism, the serum TSH is elevated above the upper reference range with a normal fT_4 level. Subclinical hypothyroidism should be diagnosed only when thyroid function has been stable for at least 6 to 8 weeks. In patients with subclinical hypothyroidism TPOAb measurements should be considered.[16,18,32]

Table 1 Thyroid-stimulating hormone reference range by different methods[27–31]

Company/brand	Method[a]	TSH reference range in adults (mIU/L)
Roche Elecsys Cobas	Electrochemiluminescence immunoassay (ECLIA)	0.27–4.2
Siemens ADVIA Centaur TSH3-Ultra (TSH3-UL)	Chemiluminescent immunoassay (CLIA)[b]	0.55–4.78
Beckman Coulter Access	Chemiluminescent immunoassay (CLIA)[b]	0.45–5.33
Abbott Architect	Chemiluminescent microparticle immunoassay (CMIA)	0.45–4.12
DiaSorin TSH-CTK-3 IRMA	Immunoradiometric assay (IRMA)	0.25–3.51

[a] Other methods include radioimmunoassay (RIA), competitive protein-binding assay (CPBA), radioreceptor assay (RRA), enzyme-linked immunosorbent assay (ELISA), microparticle enzyme immunoassay (MEIA), fluoroimmunoassay (FIA).
[b] In Nepal, CLIA and ECLIA are preferred.

Table 2 Overt hypothyroidism and subclinical hypothyroidism

	Overt hypothyroidism	Subclinical hypothyroidism
Thyroid-stimulating hormone (TSH)[a]	High	High
Free thyroxine (fT_4)	Low	Normal

[a] Upper limit of normal for a third-generation TSH assay should be determined by the reference range of a given laboratory, in the absence of which an upper limit of 4.12 mIU/L should be used.

Primary and Central Hypothyroidism

When low fT_4 level is accompanied by a high level of TSH, the diagnosis is primary hypothyroidism, and if it is accompanied by normal or low TSH, the diagnosis is central hypothyroidism.

Iatrogenic Hypothyroidism

In patients who develop hypothyroidism as a result of treatment of hyperthyroidism, for example, in patients treated with antithyroid drugs, radioactive iodine, or surgery, TSH may remain elevated. Therefore, in these patients, low serum-free T_4 alone is diagnostic.[16]

Autoimmune Diseases

Autoimmune diseases can be diagnosed by detection of elevated antithyroid antibody titers, which include antithyroglobulin antibodies (TgAb), TPOAb, and TSH receptor antibodies (TSHRAb).[16] In Nepal, anti-TPO test may be relevant and it is recommended as it is more easily available and cost-effective.

Treatment of Hypothyroidism

Patients with hypothyroidism usually require treatment with lifelong thyroid hormone replacement. Although T_3 can also be used for treatment, it is generally not recommended and levothyroxine remains the treatment of choice.[16,17,33,34] Levothyroxine is recommended universally for its efficacy, favorable safety profile, ease of administration, and low cost.[17]

The initial daily dose of levothyroxine is determined based on the TSH level, age, sex, and weight of the patient.[17] Generally, an initial dose of 1.6 µg/kg/d is considered as a standard, which can be gradually titrated to achieve target TSH level.[35] In our population, a lower initial dose may be required. Dose adjustments may be required 4 to 8 weeks after starting levothyroxine based on the level of TSH. The usual starting dose of levothyroxine for an adult is 50 or 100 µg/d, which can be gradually increased to a maintenance dose of 100 to 200 µg/d[36] according to target TSH level.

It is well known that food may affect levothyroxine absorption. Therefore, levothyroxine must be taken either approximately an hour before a meal or at bedtime 3 to 4 hours after the last meal.[16,17] It is important to note that there are no food restrictions (such as for cabbage, cauliflower, soya, or broccoli). However, certain drugs that may affect the absorption of levothyroxine, such as proton pump inhibitors, calcium carbonate, and ferrous sulfate, should be taken with a gap of 4 hours, whenever possible.[17] If high levels of levothyroxine are required to maintain TSH within the reference range, after eliminating other causes that may interfere with levothyroxine absorption, patients must be evaluated for *Helicobacter pylori*, atrophic gastritis, coeliac disease.[17]

In addition, it has been found that noncompliance to treatment is fairly common. Therefore, if patients who are prescribed adequate doses of

levothyroxine have persistent high levels of TSH, patient noncompliance to treatment should be considered rather than malabsorption of the drug,[37] except in patients with severe hypothyroidism, cardiovascular disease, and the elderly. In patients with severe noncompliance issues, once-weekly dosing can be considered[38,39] followed by testing for free T_4 and TSH after treatment in the morning.

In order to get a consistent effect, it is recommended to use the same preparation of levothyroxine without switching between different brands as bioavailability differs with brands.[40,41] Switching between different preparations of levothyroxine may lead to variations in the dose, and therefore, should be avoided.[17]

Monitoring of Treatment and Follow-Up

Treatment adequacy should be evaluated based on the results of thyroid function tests.[17] Serum TSH level (TSH reference range 0.45–4.12 mIU/L) is the most reliable therapeutic end point for the treatment of primary hypothyroidism. Serum TSH measurements should be done 4 to 8 weeks after initiating treatment or after a change in dose. Once an adequate replacement dose has been determined, TSH measurements should be done 6 monthly. TSH measurements can be carried out more frequently, if required. It is recommended that dose adjustment is done if two consecutive abnormal values are obtained, except in pregnant women.

It must be ensured that optimum thyroid function is obtained following treatment. Care must be taken to prevent overtreatment of hypothyroidism, which may lead to cardiovascular effects (such as atrial fibrillation) and skeletal effects (such as osteoporosis). Therefore, proper precautions must be taken especially in older men and postmenopausal women. Likewise, it should also be remembered that undertreatment may also lead to untoward effects on the lipid profile and cardiovascular health.[42–44]

Referral

Although most cases of hypothyroidism can be managed by physicians, expert help by an endocrinologist must be sought for the following: pediatric patients, pregnant women or women planning conception, patients with cardiac disease, patients with goiter or thyroid nodule, patients with adrenal or pituitary disorders, patients with conditions that may affect the level of levothyroxine, unusual thyroid function test results, and patients in whom euthyroid state is difficult to achieve and maintain.[16]

Subclinical Hypothyroidism

As mentioned earlier, subclinical hypothyroidism is a condition when serum TSH is elevated with a fT_4 level within the normal reference range. Subclinical hypothyroidism is more common than overt hypothyroidism. Patients with

subclinical hypothyroidism may later develop overt hypothyroidism.[45] It has been found that subclinical hypothyroidism is associated with cardiovascular disorders including heart failure especially in the elderly and also with an increased risk of fatal and nonfatal coronary heart disease events. Moreover, it is also believed that treating subclinical hypothyroidism may be associated with cognitive benefits. It is well accepted that all patients with serum TSH levels more than 10 mIU/L must be treated.[16,46] However, whether all patients with TSH levels between 4.5 and 10 mIU/L will benefit from treatment has not been established. It is believed that certain patients, for example, those with associated cardiovascular risk factors may benefit from treatment.[47] In addition, treatment should also be considered for patients with symptoms suggestive of hypothyroidism and those with positive TPOAb.[2,16,17] If serum TSH levels are between 4.5 and 10 mIU/L on more than two consecutive times, treatment is considered.

While some experts advocate the treatment of subclinical hypothyroidism, others advise to be cautious and to weigh the risk–benefit ratio before initiating treatment.[16] In a recent multicenter randomized placebo-controlled trial in Europe (TRUST study; mean TSH level, 6.4 mIU/L), levothyroxine provided no apparent benefits in older persons with subclinical hypothyroidism.[48] It is advisable to decide whether to treat subclinical hypothyroidism depending on the risks and benefits involved in each case individually.

As per the Washington Manual of Medical Therapeutics (34th edition, 2014), subclinical hypothyroidism should be treated if any of the following is present: symptoms compatible with hypothyroidism, a goiter, hypercholesterolemia requiring treatment, or plasma TSH level of greater than 10 mIU/L. Untreated patients should be monitored annually, and treatment should be started if symptoms develop or serum TSH increases to greater than 10 mIU/L.[49]

Hypothyroidism in Pregnancy

Hypothyroidism during pregnancy is associated with serious risks to both the mother and the fetus. Maternal complications include spontaneous miscarriage, preterm delivery, preeclampsia, postpartum hemorrhage. Complications related to the fetus/infant include low birth weight, stillbirth, and impaired intellectual and psychomotor development. Subclinical hypothyroidism may also be associated with adverse pregnancy outcomes.[50–53]

The normal reference range for TSH during pregnancy is lower than the normal reference ranges for the general population. Ideally, trimester-specific reference range for TSH for the particular laboratory should be used. If this is unavailable, it is recommended to consider the upper reference range for TSH during the first trimester of pregnancy as 2.5 mIU/L and that during the second and the third trimester as 3.0 mIU/L and 3.5 mIU/L, respectively (2.5 mIU/L for first and 3.0 mIU/L for second and third trimesters as per the Indian guidelines).[16,17,23]

In pregnant women with TPOAb thyroid function testing is recommended. Levothyroxine should be prescribed if the level of TSH is more than the upper reference range. Further, TPOAb-positive pregnant women with history of miscarriage or past history of hypothyroidism, should be considered for treatment with levothyroxine even if the TSH level is normal.[16]

Indian guidelines recommend treatment with levothyroxine 25 µg/day for TSH between upper limit (for each trimester) and 10 mIU/L and 50 µg/d for TSH greater than 10 mIU/L.[23] It is recommended that the dose should be increased by about 30 to 50% (based on TSH level) as soon as a woman on thyroid replacement therapy is found to be pregnant.[54,55]

In pregnant women who are on thyroid replacement therapy, serum TSH and total T_4 should be checked every 4 weeks during the first half of pregnancy, and at least once between 26 and 32 weeks of gestation. Levothyroxine dose can be adjusted to ensure that the TSH levels remain within the trimester-specific reference range.[16] In the first trimester, dose of levothyroxine should not be adjusted based on low TSH alone as human chorionic gonadotropin (HCG) can lower the levels of TSH. Postpartum treatment and regular follow-up should be continued in women with TSH level greater than 10 mIU/L.[23]

Isolated hypothyroxinemia in pregnancy can occur without requiring treatment.

In pregnant women with previously undiagnosed/untreated hypothyroidism, counselling is strongly recommended with final decision being with the specialist.

Congenital Hypothyroidism

Congenital hypothyroidism is considered as the most common congenital endocrine disorder with an incidence of 1 in 4,000 live births.[56,57] It is also the leading cause of preventable intellectual disability.[57–59] Most common cause of congenital hypothyroidism is thyroid dysgenesis, which accounts for about 85% of the total cases.[57]

Every newborn should be screened for congenital hypothyroidism within 72 hours of birth (TSH reference range 1.3–19 mIU/L). Abnormal value at 72 hours should be reassessed after 1 week.

Once diagnosed, levothyroxine replacement should be started at a dose of 10 to 15 µg/kg/d.[17,57,60] Levothyroxine tablet should be crushed and given mixed with water or breast milk in the morning, and feeding should be withheld for 30 to 45 minutes after administering the medication.[60] The aim of the treatment should be to maintain level of fT_4 in the upper half of the age-specific reference range and that of TSH in the age-specific reference range.[17,60] After the target level of TSH is achieved, thyroid function test should be carried out every 6 weeks up to the age of 6 months, and every 8 weeks from 6 months to 1 year. From the age of 1 to 3 years, thyroid function should be checked every 3 months and thereafter every 6 to 12 months until growth is completed.[60] There is no evidence to suggest that children with normal tests at neonatal screening should be reassessed unless they are symptomatic.

Hypothyroidism in Pediatric Age Group

The management of hypothyroidism in children is mostly similar to that in adults. All children with overt hypothyroidism should be treated with levothyroxine. However, the weight-based dose of levothyroxine in children is higher as compared to adults and decreases gradually as the child grows. While newborns may need a dose as high as 10 µg/kg/d, children around the age of 1 year may require 4 to 6 µg/kg/d, and for adolescents a dose of 2 to 4 µg/kg/d may suffice.[17]

If subclinical hypothyroidism is diagnosed in the pediatric age group, it is considered safe to start therapy with levothyroxine to prevent detrimental effects on growth and development. Treatment is generally recommended when TSH level is greater than 10 mIU/L.[17]

Need to Develop National Hypothyroidism Guidelines for Nepal

Although a lot of literature and guidelines are available on hypothyroidism as described above, no standard protocol is currently being followed in Nepal. In addition, the ATA/American Association of Clinical Endocrinologists (AACE) or other international guidelines may not be completely applicable to Nepal. The types of resources available in Nepal are limited. Also, the disease scenario has been changing and so has medicine practice. Current medical practice needs evidence-based and easy-to-follow guidelines that will enable standardization of disease management. It is, therefore, important that all these factors are considered while developing country-specific guidelines, which will attempt to address the need for consensus-based management of thyroid disorders. It is important to note that due to lack of clinical data in Nepal, the hypothyroidism consensus statement summarized below are based on expert opinion and published evidence from other countries.

This consensus statement is but a step toward the guidelines which can hopefully be formulated in the near future.

Summary of Hypothyroidism Consensus Statement for Nepal

Based on the literature evidence and expert opinions, following are the recommendations for the management of hypothyroidism in Nepal.

Recommendations for screening

- In general population, annual screening for hypothyroidism by measurement of serum TSH level is recommended in following cases:
  - ◊ Individuals with no access to iodized salt.
  - ◊ Ageing population (more than 50 years of age).
  - ◊ Individuals with type 1 diabetes mellitus.

- ◊ Individuals with pernicious anemia.
- ◊ Individuals with a family history of autoimmune thyroid disorder.
- ◊ Individuals with psychiatric disorders.
- ◊ Individuals treated for hyperthyroidism.

- In preconception/pregnant women, universal screening is recommended specially in following high-risk cases:
  - ◊ Women older than 30 years.
  - ◊ BMI of greater than or equal to 30 kg/m^2.
  - ◊ Women who reside in areas of moderate-to-severe iodine insufficiency.
  - ◊ Presence of other autoimmune diseases.
  - ◊ Symptoms of hypothyroidism.
  - ◊ Family history/past history of thyroid disease.
  - ◊ Previous head and neck irradiation.
  - ◊ Use of drugs such as amiodarone and lithium that interfere with thyroid function.
  - ◊ Presence of circulating TPOAb.
  - ◊ History of previous miscarriage, preterm delivery, or subfertility.
  - ◊ History of developmental delay in the family.

Recommendation for diagnosis and treatment

- The diagnosis of hypothyroidism should be made by measurement of TSH level and free T_4 level (except in pregnancy when measurement of total T_4 instead of free T_4 is recommended).
  - ◊ Upper limit of normal for a third-generation TSH assay should be determined by the reference range of a given laboratory. In the absence of reference values, a range of 0.45 to 4.12 mIU/L should be used.
  - ◊ In pregnancy, trimester-specific reference range for the particular laboratory should be used, in the absence of which 2.5, 3.0, and 3.5 mIU/L should be considered as the upper reference range for TSH during the first, second, and third trimester, respectively.
  - ◊ For the diagnosis of autoimmune diseases, anti-TPO test is recommended.
- Patients should be treated with levothyroxine. Starting dose should be 50 to 100 µg/d. TSH level should be checked 4 to 8 weeks after starting treatment. The dose should be gradually titrated based on the level of TSH.
- Treatment for subclinical hypothyroidism should be carried out in following cases:
  - ◊ All patients with TSH level greater than or equal to 10 mIU/L.
  - ◊ Following cases, if TSH level is between 4.5 and 10 mIU/L:
    - ▪ Patients with cardiovascular risk factors.
    - ▪ Patients with symptoms of hypothyroidism.
    - ▪ Patients with positive TPOAb.

- Patients with psychiatric disorders.
- Patients with goiter.
- Patients with dyslipidemia.
- Preconception.
- Children with developmental delay.
- Preconception.
- Pregnant women.

◊ When TSH levels are between 4.5 and 10 mIU/L more than two consecutive times.

Recommendations for monitoring and follow-up

- Treatment should be monitored by TSH levels done at 4 to 8 weeks initially, and then 6 monthly once adequate dose of levothyroxine has been determined.
- In pregnant women, serum TSH and total T_4 should be checked every 4 weeks during the first half of pregnancy, and at least once between 26 and 32 weeks.
- Following hypothyroid patients should be referred to a specialist:
  - ◊ Pediatric patients.
  - ◊ Pregnant women or women planning conception.
  - ◊ Patients with cardiac disease.
  - ◊ Patients with goiter or thyroid nodule.
  - ◊ Patients with adrenal or pituitary disorders.
  - ◊ Patients with conditions that may affect the level of levothyroxine.
  - ◊ Patients with unusual thyroid function test results.
  - ◊ Patients in whom euthyroid state is difficult to achieve and maintain.

Recommendations for congenital hypothyroidism

- All newborn babies should have a heel prick (if available) or a venous blood screening test for TSH by 72 hours of birth.
- In babies diagnosed with congenital hypothyroidism, levothyroxine replacement must be started at a dose of 10 to 15 µg/kg/d.
- After the target level of TSH is achieved, thyroid function test should be carried out every 6 weeks up to the age of 6 months, and every 8 weeks from 6 months to 1 year. Between the age of 1 and 3 years, thyroid function should be checked every 3 months, and every 6 to 12 months thereafter.

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Notes

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