

Analysis Of Thyroid Profile In Type-2 Diabetes Mellitus Patients

Abdur Rahim Abidi^a, Ravjit Kaur Sabharwal^b, Niamatullah Zaheer^c, Pranav Kumar Prabhakar^{d,*}

^a Department of Biochemistry, Faculty of Stomatology, Kunduz University, Afghanistan

^b Department of Biochemistry, Punjab Institute of Medical Sciences, Punjab India

^c Department of Internal Medicine, Faculty of Stomatology, Kunduz University, Afghanistan

^d Department of Medical Laboratory Sciences, Lovely Professional University, Panjab, India

*Corresponding Author: Dr. Pranav Kumar Prabhakar (Email: pranav.16113@lpu.co.in)

ABSTRACT: *Diabetes mellitus and thyroid gland abnormalities are interlinked and coexist with influencing each other. Current study was planned and conducted to evaluate thyroid status in patients with type-2 diabetics. The main aim of the study was to understand the relationship between diabetes mellitus and thyroid abnormalities. Total 100 known diabetic patients were studied, out of them 37 were males with the mean age 59.81 ± 12.8 years, and 63 females with average age of 55.31 ± 11.10 years. 50 non-diabetic healthy subjects included 13 males and 37 female of mean age 48.86 ± 12.9 and 48.86 ± 17.94 years respectively selected as a control. All the patients were evaluated for thyroid profile (TSH, FT3, and FT4) and diabetic profile (RBS and HbA1c) by using Cobas C-311 and Cobas E-411 fully automated immunoassay analyzer. The observations were recorded. The result showed that, out of 100 diabetic subjects 41.03% male and 58.97% female were faced with euthyroid and the remaining 22% had thyroid dysfunctions. Hypothyroidism was more common in females (78.97%) as compared to men (21.05%). The mean values for TSH, FT3 and FT4 at ($p > 0.05$) probability level shows statistically no significant difference. The relationship between diabetes and thyroid abnormalities was significantly difference, interdependency of these two conditions and evaluation of thyroid hormones status with the diabetic profile in the early days of diabetes is recommended. This will induce the management strategies of diabetes and can delay and avoid the progression of the secondary complications in diabetic patients with uncontrolled diabetes.*

Keywords: *Diabetics; thyroxine; secondary complications; thyroid disease*

INTRODUCTION

Diabetes mellitus and the thyroid abnormalities are the two most prevalent endocrine disease (Satyanarayana N., et al., 2014; Sharma et al., 2018). Diabetes is one the fastest growing noncommunicable metabolic syndrome which is characterised by the increased blood glucose level and mainly due to reduction of insulin secretion or suppression in insulin action (Nankar et al., 2017). Accordance with evaluation of International Diabetes Federation (IDF) in 2015 the diabetic population was 415 million across the world and will be 642 million by 2040, most of them (80%) live in developing countries with the highest number in China and on the Indian subcontinent (Prabhakar, 2016).

Thyroid, largest endocrine organ located in neck region, consist of two right and left lateral lobes associated with a narrow band of the thyroid tissue called Isthmus, it weighs about 25-30gr, usually larger in men than women (Neupane et al., 2017) and store a large amount of inactive hormones within extracellular follicles (Sharma et al., 2018)(Vyas, M. et al 2019).

These hormones play a vital role in the regulation of glucose metabolism, hepatic lipid cholesterol and mediate important physiological processes like growth and development (Singh. et al., 2011).

Pathological condition of the thyroid gland are hypothyroidism and hyperthyroidism, in hypothyroid condition the thyroid gland is unable to synthesize sufficient amount of T3 and T4 hormones and this is one of the most well-known thyroid disorders in the adult individuals (Vij., et al., 2012), on the other hand, in hyperthyroid condition the thyroid gland is more active and synthesizes an excessive amount of both T3 and T4 hormones and this is the less common type of thyroid disorder in this condition and it cause increases in rate of body metabolism which result in rapid heart-beats and sudden weight loss (Aneetha P., et al., 2015). Thyroid disorders increase with advancing age and its frequency is higher in women than men, which may be associated with estrogen and progesterone,(Usman, B. et al. 2019) there is a profound fundamental association between diabetes and thyroid dysfunction, both mutually effect each other (Bharat et al., 2013), the pathophysiological basis of this association is proved and a complex malfunction of chemical, genetic and secretory signaling pathways has been suggested.(Prabhakar, P. K. et al, 2014)

The pancreatic function is influenced by diabetes and thyroid hormones in various ways (Hage M. et al., 2011). The high amount of thyroid hormones decreases the insulin content of the pancreas and this might be due to a decreased level of proinsulin at mRNA stage (Chandel K. et al., 2016). Thyroid hormones and insulin are antagonists and both of them are involved in cellular metabolism, an increase or decrease in any one of them can cause a disturbance in the normal functions of the body (Aneetha P. et al., 2015). Diabetes mellitus affects thyroid functions at two sites; first, the release of thyroid stimulating hormone (TSH), controlled by the hypothalamus, poorly controlled diabetes results in an impaired response of TSH to thyrotropin-releasing hormone (TRH) (Gurjeet Sing, et al., 2011), second T4 conversion to T3 which take place in the peripheral tissues. Diabetes is characterized by hyperglycemia which causes reversibly decrease in the hepatic concentration and activity of T4-5-deiodinase enzyme, decrease T3 serum concentration, increase the reverse T3 level and normal, low or high level of T4 (Neupane et al., 2017). Moreover, diabetic medication such as metformin has suppressing effect on TSH. Thyroid disorder causes poor glycemic control and adversely affects diabetes.(Singh, A. P., et al. 2019) In hypothyroidism the synthesis and secretion of insulin are suppressed, while in hyperthyroid condition to compensate the increased degradation of insulin there would be an increase in insulin secretion (Nagaraju K, et al., 2013) (Kaur, P. et al, 2018). Elevated concentration of free thyroid hormones in the blood circulation cause hyperglycemia by upgrading the gastrointestinal assimilation of glucose, increased insulin resistance more insulin degradation and stimulation of glycogenolysis (Sing P., et al., 2014), this result in worsening glycemic control in diabetic patients,(Bashary, R. et al. 2020) while decreased levels of thyroid hormones cause susceptibility to hypoglycemia resulting in complicating the management of diabetes (Aneetha P., et al., 2015; Sing P., et al., 2014). Evaluation of thyroid status in diabetic patients not only help in early recognition and treatment of thyroid diseases but also play a vital role in the better control of diabetes and complications (Sathish R and Mohan V., 2003; Duntas LH., et al., 2011; Shah., et al. 2017).

MATERIALS AND METHODS

The focus of the present study were all Type II diabetes mellitus (DM) patients, who attended the outpatient department (OPD) or admitted to wards of PIMS Punjab, India. All Type II DM patients categorized in to two part based on their gender male and female. Total, 100

known diabetic patients, 37 males with the average age of 59.81 ± 12.8 years, and 63 females with average age of 55.31 ± 11.10 years and 50 non-diabetic healthy subjects, 13 males with mean age of 48.86 ± 12.9 years and 37 females with mean age 48.86 ± 17.94 years were selected as a control.

“Known Type II diabetic patients of both sexes, irrespective of treatment with the age group of 30-85 years were included, patients below 30 years and elderly adults beyond 85 years, anemic patients, patients from ICU were not taken into consideration for the study. Subsequently collected blood samples of all patients were scrutinized for HbA1c, RBS, thyroid profile TSH, FT3, and FT4 level and diagnosis of diabetes mellitus, according to American Diabetes Association (ADA) criteria, using Cobas e 411 fully automated immunoassay analyzer on the bases of electrochemiluminescent technology, using ruthenium complex and the measuring cell for thyroid profile HbA1c was estimated by Turbidimetric Inhibition Immunoassay (TINIA) methods and Random blood sugar (RBS) by enzymatic method with hexokinase using Cobas C 311 fully automated analyzer. All evaluations were done in the laboratory of (PIMS). Any kind of elevation in the TSH associated with the decrease in the serum thyroid hormone is considered as Subclinical hypothyroidism.”

RESULTS

The frequency and percentage of thyroid disorder in diabetic subjects were evaluated, out of 100 diabetic subjects studied (78%) were euthyroid and the remaining (22%) had thyroid dysfunction. Among them, 19% was found to be having hypothyroidism and the rest 3% were having hyperthyroidism. Hypothyroidism was more common (19%) as compared to hyperthyroidism 3% in diabetic subjects (Table 1. figure 1).

Table1: Frequency and percentage of Thyroid disorders in diabetic patients

Thyroid Status	Frequency	Percentage	Male	Female	Male %	Female %
Euthyroid	78	78%	32	46	41.03	58.97
Hypothyroid	19	19%	4	15	21.05	78.95
Hyperthyroid	3	3%	1	2	33.33	66.67
All Sample	100	100 %	12.333	21	31.803	68.196

The types and sex wise percentage of thyroid disorders in diabetic patients are shown in Table 1. figure 2. out of 100 diabetic subjects studied 78 individuals were euthyroid and the rest 22 had thyroid dysfunction and out of 78 individuals 32 (41.03%) were male with euthyroid and 46 (58.97%) were female. Among 22 thyroids patients, 19 persons were found to be having hypothyroidism and remaining 3 individuals were having hyperthyroidism. Hypothyroidism was more common in female 15(78.97%) as compared to men 4 (21.05%). Similarly, hyperthyroidism was also more common in women 2 (66.67%) compare to men 1(33.33%).

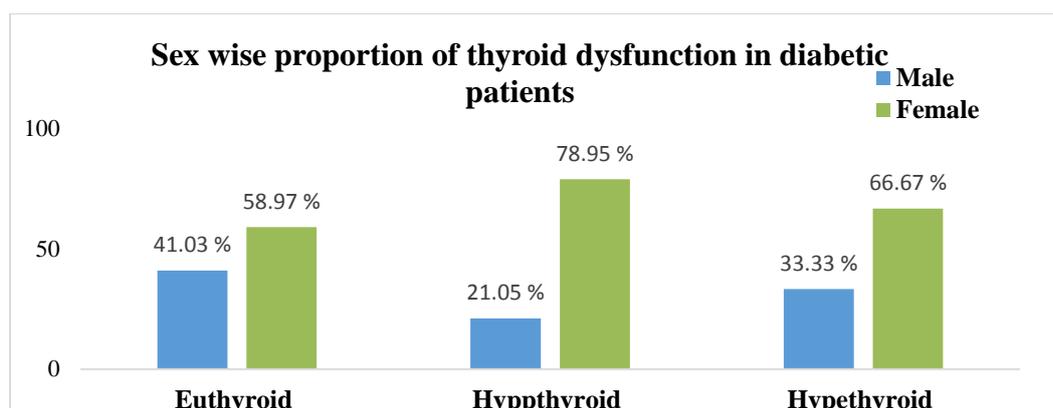


Figure 2: Sex wise distribution of thyroid dysfunction in diabetic subjects

The comparison of diabetic and thyroid profiles parameters in diabetic and non-diabetic control subjects were done by using Independent sample t-test. The mean value of TSH in diabetic patients were 2.87 ± 2.92 (uIU/ml), more as compared to non-diabetic healthy subjects 2.08 ± 1.19 (uIU/ml) and this difference was not statistically significant at ($p > 0.05\%$) probability level. The mean value of FT3 in diabetic patients were less 3.87 ± 3.81 (pmol/l) as compared to non-diabetic healthy subjects 4.25 ± 0.90 (pmol/l) and this difference were not statistically significant at ($p > 0.05\%$). The FT4 mean value in diabetic patients were 17.15 ± 8.98 (pmol/l), more than non-diabetic healthy individuals 16.35 ± 2.09 (pmol/l) and this difference was not statistically significant at ($p > 0.05\%$) (Table 2. figure 3). The mean values of RBS in diabetic subjects (N=100) were found to be 218.95 ± 80.37 mg/dl, which is higher as compared to non-diabetic healthy subjects (N =50), 103.14 ± 12.95 mg/dl and this difference was statistically highly significant ($p < 0.05\%$), Similarly, the mean value of HbA1c in diabetic subjects were $9.13\% \pm 2.60$, while in non-diabetic healthy subjects the mean value of HbA1C were $5.26\% \pm 0.44$ and this difference was statistically significant ($p < 0.05\%$).

Table 2: Comparison of mean values \pm SD of biochemical parameters in diabetic and Non diabetic control subjects

Parameter	Control Group		DM Group		Total	Std. Deviation		Std. Error		p-values
	Male	Female	Male	Female		DM	Control	DM	Control	
TSH (uIU/ml)	37	13	37	63	150	± 2.92	0.169	0.292	0.169	0.066 NS
FT3 (pmol/l)	37	13	37	63	150	± 3.81	0.127	0.380	0.127	0.488 NS
FT4 (pmol/l)	37	13	37	63	150	± 8.98	0.296	0.898	0.296	0.535 NS
RBS (mg/dl)	37	13	37	63	150	± 80.37	1.831	8.037	1.831	.000 SN
HBA1c (%)	37	13	37	63	150	± 2.60	0.062	0.260	0.062	.000 SN

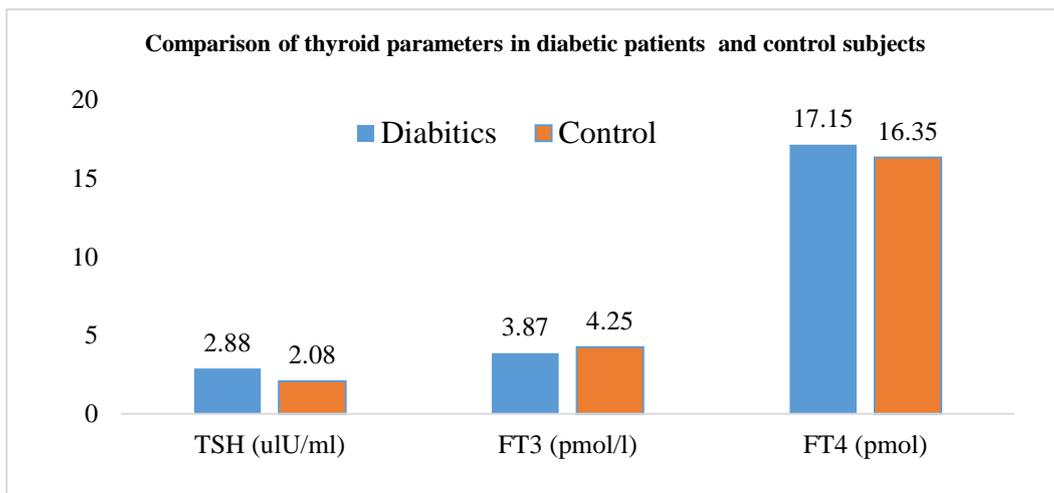


Figure 3: Comparison of Thyroid Parameters in Diabetics and Control Subjects

Karl Pearson’s correlation between HbA1c and thyroid profile

The correlation between HbA1c and thyroid profile was found by Pearson’s correlation. The HbA1c in diabetic patients were negatively correlated with TSH, the r-value was found to be (-0.055) and the p-value was (0.585) which is greater than 0.05%. It shows a negative correlation which is not significant. The HbA1c in diabetic patients were positively correlated with FT3, the r-value was found to be (0.165) and the p-value was (0.101) which is greater than 0.05, and the correlation was not significant.

The HbA1c in diabetic patients were negatively correlated with FT4, the r value was found to be (-0.005) and the p value was (0.976) which is greater than 0.05% and the correlation was not significant (Table 3: figure 4).

Karl Pearson’s correlation between RBS and thyroid profile

The RBS in diabetic patient was negatively correlated with TSH, the r value was found to be (-0.017) and the p value was (0.868), which is greater than 0.05% and the correlation was not significant. The RBS in diabetic patient was negatively correlated with FT3, the r value was found to be (-0.132) and the p value was (0.0.361) it shows the correlation was not significant (p>0.05%). The RBS in diabetic patient was positively correlated with TSH, the r value was found to be (0.083) and the p value was (0.409) which is greater than 0.05% and the correlation was non-significant at (p > 0.05%), (Table 3. figure 4).

Table 3: Pearson’s correlation between HbA1c and RBS with thyroid profile

Relationship	R-values	p-values	Relationship	R-values	p-values
HbA1c vs TSH	-0.055	0.585NS	RBS vs TSH	-0.017	0.868NS
HbA1c vs FT3	0.165	0.101NS	RBS vs FT3	-0.132	0.361NS
HbA1c vs FT4	-0.005	0.976NS	RBS vs FT4	0.083	0.409NS

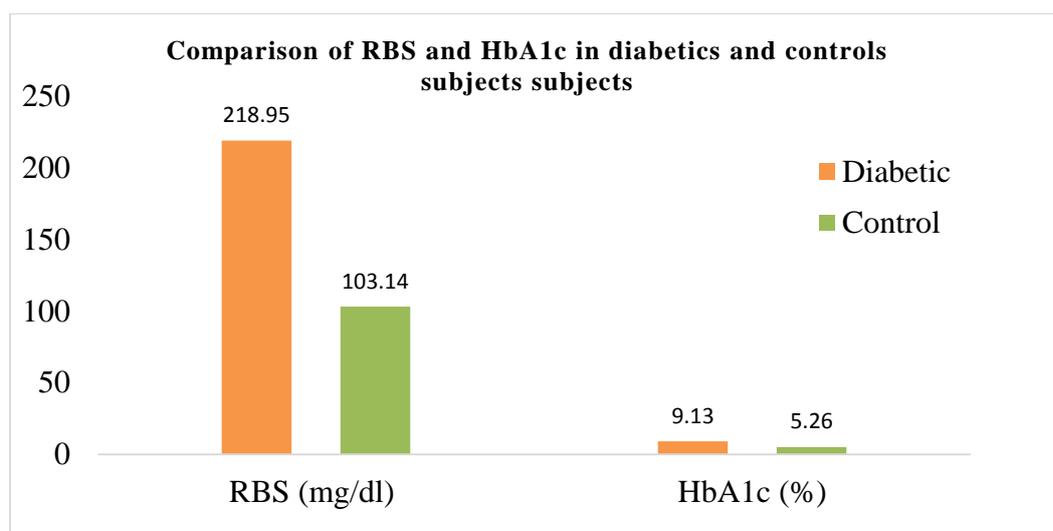


Figure 4: Comparison of RBS and HbA1c values in diabetic and control subjects.

DISCUSSION

Diabetic mellitus is an important health problem affecting major population worldwide (Sharma A and Shavgotra VK., 2017). It is a global health anxiety and its incidences are increasing (Deokar PG., et al., 2016). This study was conducted to evaluate the thyroid status and to understand the association between thyroid disorders and diabetes mellitus in Type 2 DM patients that have been recruited at outpatient department of biochemistry, Punjab Institute of Medical Sciences (PIMS), Jalandhar Punjab, India. The result showed an increased level of serum TSH in diabetic patients as compared to nondiabetic control subjects. Serum FT3 level was lower in diabetic patients than nondiabetic subjects but FT4 was comparatively high in diabetic patients than nondiabetic control. Similarly, in diabetic subjects significantly increased level of RBS and HbA1c were observed as compared to non-diabetic control subjects. These observations were correlated with other study conducted by (Islam S., et al., 2008).

Thyroid hormones levels may be altered by various medications that diabetic subjects used to take. Insulin significantly induces the production of FT4 and suppresses the generation of FT3 by halting the conversion of T4 to T3 in the liver and reduced TRH production in the diabetics. Insulin influenced glycemic status, which modulates TRH and TSH level.

In our study, the overall prevalence of thyroid dysfunction among the diabetic patient was 22%, out of them, 19% was found to be having hypothyroid and 3% hyperthyroid the rest 78% of diabetic patients were found euthyroid. Hypothyroidism was more common in women (15%) than men (4%), Similarly, hyperthyroidism was also common in women compare to men. These results are agreed to the findings of (Uppal V., et al., 2013). The occurrence of thyroid abnormality was found to be higher in female when compared to males; 78.95% vs 21.05% hypothyroidism and hyperthyroidism 66.67% vs 33.33%. Female diabetics are more susceptible to thyroid disorder and they are at higher risk as compare to male. These observations agree with the reports of (Khurana A., et al., 2016, Papazafiropoulou, et al., 2010), their result has shown high prevalence of thyroid disorder in females' diabetics as compare to male diabetics.

Conclusion

One of the important reason for the abnormal glycaemic control in diabetics are the thyroid dysfunction. There is a critical need to reduce thyroid disorders in both diabetic and non-diabetic patients for their current and future diabetic risks by increasing their thyroid glance health and making them more resilient to ill impact of thyroid disorder. The prevalence of thyroid disease is more common in diabetics when compared to nondiabetics. In diabetic patients, the thyroid function level changes and abnormal thyroid hormone level in the diabetic patient causes poor management of diabetes, which is evidenced in some treated diabetics. The association between diabetes and thyroid disorder was found to be significant. By considering this association and interdependence of these two conditions, evaluation of thyroid hormone level along with the diabetic profile in the early stage of diabetes and avoiding consumption of fermentable carbohydrates, sedentary habits, obesity and high blood pressure will not only help in the management of diabetes but it will delay and avoid the progression of the secondary complications in diabetic patients, particularly those with uncontrolled diabetes in addition, it will improve the quality of life and decrease morbidity and mortality rate in diabetic patients. Therefore, the diabetic patient should be screened for thyroid dysfunction as frequent as possible, preferably every year for T1DM and every five years for T2DM.

Conflict of Interest

The authors proclaim no conflict of interests related to this manuscript.

References

- Anveetha, P., Rao, K. P., & Chittimoju, V. K. (2015). Study of thyroid profile in patients with type 2 diabetes mellitus. *Int J Pharm Biol Sci*, 5, 24-30.
- Bharat, H. D., Gangte, D., Lalnunpui, P., Devi, I., & Singh, G. W. (2013). Thyroid status in diabetes mellitus. *J Glycomics Lipidomics*, 3(1), 1-4.
- Chandel, K., Singh, R. B., Kumar, S., Gupta, A., & Nath, K. (2016). Evaluation of thyroid hormone dysfunction in patients of type 2 diabetes mellitus. *Indian Journal of Clinical Anatomy and Physiology*, 3(1), 21-23.
- Deokar, P. G., Nagdeote, A. N., Lanje, M. J., & Basutkar, D. G. (2016). Prevalence of thyroid disorders in a tertiary care center. *International Journal of Current Research and Review*, 8(9), 26.
- Duntas, L. H., Orgiazzi, J., & Brabant, G. (2011). The interface between thyroid and diabetes mellitus. *Clinical endocrinology*, 75(1), 1-9.
- Hage, M., Zantout, M. S., & Azar, S. T. (2011). Thyroid disorders and diabetes mellitus. *Journal of thyroid research*, 2011.
- Islam, S., Yesmine, S., Khan, S. A., Alam, N. H., & Islam, S. (2008). A comparative study of thyroid hormone levels in diabetic and non-diabetic patients. *Southeast Asian J Trop Med Public Health*, 39(5), 913-916.
- Khurana, A., Dhoat, P., & Jain, G. (2016). Prevalence of thyroid disorders in patients of type 2 diabetes mellitus. *J Indian Acad Clin Med*, 17(1), 12-15.
- Nagaraju, K., Pirouz, A., Sadeghi, T., & Esmaeili, P. (2013). Prevalence of thyroid dysfunction and its management in diabetic patients attending outpatient clinic of KIMS hospital. *International research journal of pharmacy*, 4(9), 132-35.
- Nankar, R., Prabhakar, P. K., & Doble, M. (2017). Hybrid drug combination: Combination of ferulic acid and metformin as anti-diabetic therapy. *Phytomedicine*, 37, 10-13.
- Neupane, N., Kaur, M., Prabhakar, P.K. (2017). Treatment of Hashimoto's thyroiditis with herbal medication. *International Journal of Green Pharmacy*. 11(3), S343-S347.

- Papazafiropoulou, A., Sotiropoulos, A., Kokolaki, A., Kardara, M., Stamataki, P., & Pappas, S. (2010). Prevalence of thyroid dysfunction among greek type 2 diabetic patients attending an outpatient clinic. *Journal of clinical medicine research*, 2(2), 75.
- Prabhakar. P.K., (2016). Pathophysiology of secondary complications of diabetes mellitus. *Asian Journal of Pharmaceutical and Clinical Research*, 9 (1), 32-36.
- Sathish, R., & Mohan, V. (2003). Diabetes and thyroid diseases-A Review. *Int J Diab Dev Ctries*, 23(4), 120-3.
- Satyanarayana, N., Ashoka, M. A., & Seetaram, K. J. (2014). Prevalence of thyroid dysfunction in patients with type 2 diabetes mellitus in tertiary care centre. *J Evol Med Dent Sci*, 3, 4160-6.
- Shah, A., Yadav, P. P., Chaudhari, M., Vataliya, A., Kantharia, N. D., & Mehta, R. (2017). A prospective study of adverse drug reactions in patients with bipolar disorder in psychiatry outpatient department of a tertiary care hospital. *Journal of clinical and diagnostic research: JCDR*, 11(5), FC24.
- Sharma, A., & Shivgotra, V. K. (2015). Prevalence of thyroid disease among the diabetic patients: a meta analysis. *Journal of Medical science and Clinical Research*, 5(6), 1-5.
- Sharma, A., Devi, S., Singh, K., & Prabhakar, P. K. (2018). Correlation of body mass index with thyroid-stimulating hormones in thyroid patient. *Asian J. Pharm. Clin. Res*, 11, 65-68.
- Singh, G., Gupta, V., Sharma, A. K., & Gupta, N. (2011). Evaluation of thyroid dysfunction among type 2 diabetic Punjabi population. *Adv biores*, 2(2), 3-9.
- Singh, P., Khan, S., & Mittal, R. K. (2014). Evaluation of thyroid dysfunction among type-2 diabetic mid and far western Nepalese population. *J Coast Life Med*, 2(11), 903-6.
- Singh, R., J Hamada, A., & Agarwal, A. (2011). Thyroid hormones in male reproduction and fertility. *The open reproductive science journal*, 3(1).
- Uppal, V., Vij, C., Bedi, G. K., Vij, A., & Banerjee, B. D. (2013). Thyroid disorders in patients of type 2 diabetes mellitus. *Indian Journal of Clinical Biochemistry*, 28(4), 336-341.
- Vij, V., Chitnis, P., & Gupta, V. K. (2012). Evaluation of thyroid dysfunction among type II diabetic patients. *Ijpbs*, 2(4), 150-155.
- Prabhakar, P. K., Kumar, A., & Doble, M. (2014). Combination therapy: a new strategy to manage diabetes and its complications. *Phytomedicine*, 21(2), 123-130.
- Kaur, P., Mittal, A., Nayak, S. K., Vyas, M., Mishra, V., & Khatik, G. L. (2018). Current strategies and drug targets in the management of type 2 diabetes mellitus. *Current Drug Targets*, 19(15), 1738-1766.
- Bashary, R., Vyas, M., Nayak, S. K., Suttee, A., Verma, S., Narang, R., & Khatik, G. L. (2020). An Insight of Alpha-amylase Inhibitors as a Valuable Tool in the Management of Type 2 Diabetes Mellitus. *Current Diabetes Reviews*, 16(2), 117-136.
- Vyas, M. (2019). Physicochemical analysis of leaves of *Eriobotrya japonica* and antioxidant and antidiabetic evaluation of its methanolic extract. *International Journal of Green Pharmacy (IJGP)*, 13(3).
- Usman, B., Sharma, N., Satija, S., Mehta, M., Vyas, M., Khatik, G. L., ... & Dua, K. (2019). Recent developments in alpha-glucosidase inhibitors for management of type-2 diabetes: An update. *Current pharmaceutical design*, 25(23), 2510-2525.
- Singh, A. P., Khatik, G. L., Mishra, V., Khurana, N., Sharma, N., & Vyas, M. (2019). Formulation development and in vitro antioxidant and antidiabetic evaluation of *eriobotrya japonica* based self nano emulsifying drug delivery system. *International Journal of Applied Pharmaceutics*, 11(4), 313-319.