ORIGINAL ARTICLE

Clinico-demographic, Thyroid, and Lipid Biomarkers in Patients with and without Type 2 Diabetes Mellitus in a Paramilitary Hospital, Nepal

Mahendra Raj Shrestha[1], Apurba Shrestha[2], Dinesh Singh Bhat[1], Rajendra Maharjan[1]

[1] Department of Pathology, Nepal Armed Police Force Hospital, Balambu, Kathmandu, Nepal
[2] Department of Internal Medicine, Nepal Armed Police Force Hospital, Balambu, Kathmandu, Nepal

Corresponding Author:
Dr. Mahendra Raj Shrestha
Department of Pathology
Nepal Armed Police Force Hospital
Balambu, Kathmandu, Nepal.
Email: mahendrapath@gmail.com

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Abstract

Introduction: Diabetes disrupts the hypothalamic regulation of thyroid-releasing hormone and impacts the synthesis of triiodothyronine and thyroxine, leading to disrupted lipid biomarker levels. This study aimed how HbA1c correlates with body mass index, thyroid and lipid biomarkers in patients with and without type 2 diabetes mellitus.

Methods: This case-control study was conducted at the Paramilitary Hospital between July 2023 and June 2024, along with 202 type 2 diabetes mellitus patients (case) and 211 control. Ethical approval was taken from Ethical Review Board (Reference number: 3795). 202 Cases with Clinico-demographic and anthropometric variables were collected. Fasting venous blood samples were analyzed for HbA1c, thyroid, and lipid profiles. Data were analyzed using Statistical Package for the Social Sciences version 17.

Results: Among 2,488 hospital visitors, the prevalence of type 2 diabetes mellitus was 202 (8.12%) cases. The odds of having elevated HbA1c were significantly higher among patients with diabetes (OR = 64.7; 95% CI: 34.01–122.67). Additionally, increased body mass index showed (OR = 1.16; 95% CI: 0.78–1.72), while hypertriglyceridemia (OR = 6.4; 95% CI: 4.12–9.94) and elevated TSH levels (OR = 48.45; 95% CI: 11.64–200.25) were strongly associated with type 2 diabetes mellitus.

Conclusions: This study found that Type 2 Diabetes Mellitus prevalence was low in the paramilitary hospital. These patients had higher levels of HbA1c, body mass index, triglycerides, and thyroid stimulating hormone. Early identification and management of these parameters could improve clinical outcomes and reduce disease burden.

Keywords: *biomarkers; diabetes mellitus; dyslipidemia.*

Introduction

Diabetes mellitus is a chronic metabolic condition marked by elevated blood sugar levels, potentially leading to cardiovascular complications like coronary artery disease, atherogenic dyslipidemia, and stroke.[1,2] The global prevalence is rising, especially in Southeast Asian countries such as Nepal, India, and China.[3,4] Currently, about 537 million adults have diabetes, with projections reaching 783 million by 2045.[4] This increase impacts healthcare costs and morbidity, underscoring the need for effective management and prevention strategies.

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Type 2 diabetes mellitus (T2DM) develops due to insufficient insulin secretion or insulin resistance, where cells become less responsive to insulin.[1,4-7] Thyroid hormones play a crucial role in glucose metabolism and insulin sensitivity.[8,9] Excess thyroid hormones can increase glucose absorption and output, leading to reduced insulin efficiency and hyperthyroidism-related issues.[8] Conversely, hypothyroidism lowers blood glucose levels but increases insulin resistance.[8] Additionally, hypothyroidism reduces low-density lipoprotein (LDL) receptor activity in the liver, raising cholesterol and triglyceride levels and causing dyslipidemia.[10] Globally, about 50% of individuals with diabetes may be undiagnosed.[2] In 2012, 9.30% of the US population had diabetes, with around 28% undiagnosed.[2] The American Diabetes Association now recommends using glycated hemoglobin (HbA1c) to monitor and diagnose diabetes, as high HbA1c levels are linked to increased cardiovascular disease risk.[1]

Recent reports show a rapid rise in T2DM cases in Nepal, highlighting a research gap in the relationship between thyroid hormones and dyslipidemia in both T2DM and non-T2DM populations.[11] This study aimed to explore these complex interactions and stress the importance of early detection.

Methods

This hospital based retrospective case-control study was conducted between July 14th, 2023, and June 13th, 2024, at the Nepal Armed Police Force Hospital, Balambu, Kathmandu, Nepal, including 202 T2DM patients as cases and 211 controls, i.e., patients without T2DM. Ethical approval for the study was obtained by the Ethical Review Board (Reference number: 3795) of the Nepal Health Research Council, Kathmandu, Nepal. Written informed consent was obtained from study participants.

Patients with classic hyperglycemia symptoms like increased thirst, frequent urination, and fatigue along with HbA1c of ≥6.50%, who did not have known thyroid or lipid disorders and were not on thyroid-affecting medications, were included as cases. Those with an HbA1c of <6.50% were included as controls. Controls were matched with age, sex and demographics. This study excluded individuals with T1DM, pregnant women, and those who did not consent. Participants were recruited using simple random sampling.

A detailed history of participants regarding demographics (age and gender), anthropometrics [height, weight, and body mass index (BMI)], and laboratory findings [HbA1c, thyroid hormone levels {free triiodothyronine (T3), free thyroxine (T4), and thyroid-stimulating hormone (TSH)}, and lipid levels {total cholesterol, triglyceride, high-density lipoprotein (HDL), and low-density lipoprotein}] were collected following a comprehensive clinical examination using a pre-designed patient information.

Patients were classified based on their HbA1c values: those with HbA1c ≥6.50% had T2DM, while those with HbA1c <6.50% did not.[12] HbA1c levels were measured using the Finecare™ FIA Meter III Plus (Model: FS-205, Wondfo, Guangzhou, China), a semi-automatic fluorescence immunochromatographic system.

Anthropometric measurements

Participants' height (±1 cm) and weight (±100 g) were measured using a wall-mounted stadiometer and a calibrated electronic scale, respectively. BMI was calculated using the formula: mass (kg) / height² (m²). BMI classifications were made as: underweight (<18.50 kg/m²), normal weight (18.50–24.90 kg/m²), overweight (25–29.90 kg/m²), and obese (≥30 kg/m²).[13]

Serum collection and processing

Patients fasted overnight for at least 12 hours. Five milliliters of venous blood were collected in both EDTA tubes (for HbA1c) and plain tubes. Serum and plasma were separated by centrifugation at 3000 rpm for 10 minutes. Serum samples were tested for lipid markers and thyroid hormones, with control samples analyzed according to the manufacturer's instructions for each test run.

Thyroid assessment and diagnosis of thyroid dysfunction

Participants were examined for thyroid enlargement and underwent fundoscopy with an ophthalmologist. Peripheral neuropathy was assessed using a tuning fork (for vibration sense) and a tendon hammer (for deep tendon reflex). Primary hypothyroidism was indicated by elevated TSH and low free T3 and T4; primary hyperthyroidism was marked by low free TSH and high free T3 and T4; subclinical hypothyroidism and hyperthyroidism were characterized by elevated and lowered TSH, respectively, with normal free T3 and T4 levels.[14]

Thyroid hormones were measured using the Maglumi Fully-Auto Chemiluminescence Immunoassay Analyzer (Model: Maglumi X3, Sinbe, Shenzhen, China), with normal ranges for free T3 (2.0–4.2 pg/ml), free T4 (8.9–17.2 pg/ml), and TSH (0.3–4.5 μIU/ml).

Diagnosis of dyslipidemia

Lipid markers were measured using the Clinical Chemistry Analyzer (Model: Pictus 500, Diatron, Budapest, Hungary). LDL was calculated with Friedewald's equation: LDL = total cholesterol - (HDL

+ triglycerides / 5). The normal ranges were: total cholesterol <200 mg/dl, triglycerides <150 mg/dl, HDL >35 mg/dl, and LDL <100 mg/dl. Dyslipidemia was defined by elevated levels of cholesterol (typically LDL), triglycerides, or both.[15]

Statistical analysis

Data were analyzed with Statistical Package for the Social Sciences version 17. Continuous variables were summarized with mean and standard deviation (SD). Differences in quantitative variables between cases and controls were assessed using an independent t-test. Qualitative variables were tested with a chi-square test. A p-value of <0.05 was considered statistically significant.

Results

Prevalence and demographics of patients with T2DM

The study included 413 participants, including 202 patients with T2DM and 211 patients without T2DM. The prevalence of T2DM among visiting patients was 8.12% (95% confidence interval: 7.05-9.19%). The median age of T2DM patients was 51 years (interquartile range: 40–62.25). Most T2DM patients were male, 122 (60.40%) (p=0.800) and aged 50 to 59 were 53 (26.24%) (p=0.551). There were 83 (41.09%) (p=0.247) T2DM patients who were overweight (Table 1).

Table 1: Demographic and anthropometric details of the study population (n=413).

Demographics		T2DM			Dyslipidemia			Thyroid dysfunction		
		Yes (n=202)	No (n=211)	p-value	Yes (n=162)	No (n=211)	p-value	Yes (n=40)	No (n=373)	p-value
Age (years)	Median (IQR)	51 (40-62.25)	50 (45-66)	0.238	49.5 (41.75-63.25)	51 (42-64)	0.224	52.50 (42.25-63.75)	50 (42-64)	0.295
Age group (years)	20-29 (n=1)	1(0.50)	-	-	1(0.62)	0(0)	0.213	0(0)	1(0.27)	0.743
	30-39 (n=65)	44(21.80)	21(9.95)	01*	32(19.75)	33(13.15)	0.072	6(15)	59(15.82)	0.893
	40-49 (n=115)	45(22.28)	70(33.18)	0.014*	48(29.63)	67(26.69)	0.516	8(20)	107(28.69)	0.244
	50-59 (n=103)	53(26.24)	50(23.70)	0.551	35(21.60)	68(27.09)	0.208	12(30)	91(24.40)	0.436
	60-69 (n=88)	38(18.81)	50(23.70)	0.226	33(20.37)	55(21.91)	0.709	8(20)	80(21.45)	0.832
	70-79 (n=39)	19(9.41)	20(9.48)	0.980	12(7.41)	27(10.76)	0.256	5(12.50)	34(9.12)	0.487
	>79 (n=2)	2(0.99)	-	-	1(0.62)	1(0.40)	0.754	1(2.50)	1(0.27)	0.053
Gender	Female (n=161)	80(39.60)	81(38.39)	0.800	49(30.25)	112(44.62)	03*	11(27.50)	150(40.21)	0.117
	Male (n=252)	122(60.40)	130(61.61)		113(69.75)	139(55.38)		29(72.50)	223(59.79)	
BMI	Under weight (n=19)	4(1.98)	15(7.11)	0.013*	13(8.02)	6(2.39)	08*	1(2.50)	18(4.83)	0.505
	Healthy (n=171)	80(39.60)	91(43.13)	0.467	57(35.19)	114(45.42)	0.039*	17(42.50)	154(41.29)	0.882
	Over weight (n=158)	83(41.09)	75(35.55)	0.247	71(43.83)	87(34.66)	0.061	19(47.50)	139(37.27)	0.206
	Obesity (n=65)	35(17.33)	30(14.22)	0.386	21(12.96)	44(17.53)	0.213	3(7.50)	62(16.62)	0.132

T2DM=type 2 diabetes mellitus, BMI=body mass index, IQR=interquartile range, *statistically significant at 95% confidence interval

T2DM patients with dyslipidemia and thyroid dysfunction in patients with T2DM, dyslipidemia was present in 111 (54.95%) cases and thyroid dysfunction in 38 (18.81%). Males with T2DM had a higher risk of dyslipidemia 73(59.83%), and thyroid dysfunction 27 (22.13%). Dyslipidemia was most common in patients aged 30-39 which was 31 (70.45%), while thyroid dysfunction was more common in those aged 70-79 which was 11 (20.75%). Among T2DM patients with thyroid dysfunction, 30 (78.95%) had subclinical hypothyroidism, 6 (15.79%) had primary hypothyroidism, and 1 (2.63%) had subclinical or primary hyperthyroidism. All females with thyroid dysfunction had hypothyroidism. The median HbA1c levels were 7.50% in patients with dyslipidemia and 7.65% in those with thyroid dysfunction (Table 2).

Table 2: Dyslipidemia and thyroid dysfunction in patients with T2DM(n=413).

Metabolic disorders	Patients with T2DM (n=202)									
	Gender n(%)		Age group (years) n(%)							Median HbA1c
	Male (n=122)	Female (n=80)	20-29 (n=1)	30-39 (n=44)	40-49 (n=45)	50-59 (n=53)	60-69 (n=38)	70-79 (n=19)	>79 (n=2)	
Dyslipidemia (n=111) ^	73 (59.83)	38 (47.50)	1 (100)	31 (70.45)	23 (51.11)	30 (56.60)	18 (47.37)	7 (36.84)	1 (50)	7.50
▪ ↑ Total cholesterol (n=11)*	10 (13.70)	1 (2.63)	-	2 (6.45)	3 (13.04)	4 (13.33)	1 (55.56)	1 (14.29)	-	9
▪ ↑ Triglyceride (n=103)*	69 (94.52)	34 (89.47)	-	29 (93.55)	23 (100)	28 (93.33)	16 (88.89)	6 (85.71)	1 (100)	7.60
▪ ↓ High density lipid (n=17)*	12 (16.43)	5 (13.16)	1 (100)	4 (12.90)	2 (8.70)	4 (13.33)	3 (16.67)	3 (42.86)	-	7.90
Thyroid dysfunction (n=38)^	27 (22.13)	11 (13.75)	-	6 (13.64)	8 (17.78)	11 (20.75)	8 (21.05)	4 (21.05)	1 (50)	7.65
▪ Primary hypothyroidism (n=6)*	6 (22.23)	-	-	1 (16.67)	-	2 (18.18)	2 (25)	1 (25)	-	7.60
▪ Subclinical hypothyroidism (n=30)*	19 (70.37)	11 (100)	-	5 (83.33)	7 (87.50)	8 (72.73)	6 (75)	3 (75)	1 (100)	7.60
▪ Primary hyperthyroidism (n=1)*	1 (3.70)	-	-	-	-	1 (9.09)	-	-	-	-
▪ Subclinical hyperthyroidism (n=1)*	1 (3.70)	-	-	-	1 (12.50)	-	-	-	-	-

T2DM=type 2 diabetes mellitus, ^percent calculation based on total patients with T2DM, *percent calculation based on subtotal patients with dyslipidemia or thyroid dysfunction Significant biomarkers in patients with and without T2DM

Serum HbA1c level in patients with T2DM was 7.95%±1.51 (p<01), whereas it was 5.76%±0.50 in controls. BMI was significantly higher in T2DM patients (26.02 kg/m2±3.94) (p=09) compared to non-T2DM patients (24.98 kg/m2±4.10). The serum levels of lipid biomarkers and thyroid function tests in patients with and without T2DM. The odds ratio of having high HBA1c, increased BMI, hypercholesterolemia, hypertriglyceridemia, low HDL, undesirable LDL cholesterol, low T3, low T4 and high TSH was 64.7 (95% CI; 34.01-122.67), 1.16 (95% CI;0.78-1.72), 1.04 (95% CI; 0.68-1.59), 6.4 (95% CI;4.12-9.94), 1.24 (95% CI;0.84-1.84), 1.19 (95% CI;0.81-1.76), 1.58 (95% CI;0.95-2.64), 1.93 (95% CI;1.30-2.87) and 48.45 (95% CI;11.64-200.25) respectively (Table 3).

Table 3: Biomarkers among T2DM patients and controls(n=413).

Laboratory parameters		Groups		p-value
		Case(n=202)	Controls(n=211)	
HbA1c	%	7.95±1.51	5.76±0.50	<01*
BMI	kg/m^2	26.02±3.94	24.98±4.10	09*
Lipid profile	TC (mg/dl)	174.25±47.43	169.51±54.99	0.350
	TGC (mg/dl)	179.33±102.02	120.07±35.63	<01*
	HDL (mg/dl)	42.22±13.95	43.27±11.15	0.397
	LDL (mg/dl)	97.43±37.86	95±28.72	0.462
Thyroid function tests	T3 (pg/ml)	2.74±0.54	2.65±0.33	0.051
	T4 (pg/ml)	12±2.61	12.78±1.91	01*
	TSH (µIU/ml)	3.19±2.72	2.03±1.08	<01*

BMI=body mass index, TC=total cholesterol, TGC=triglycerides, HDL=high-density lipoprotein, LDL=low-density lipoprotein, TSH=thyroid-stimulating hormone, T3=free triiodothyronine, T4=free thyroxine, *statistically significant at 95% confidence interval

Discussion

T2DM is a major global health issue, linked to thyroid hormone dysfunction that affects lipid metabolism and causes dyslipidemia.[3,16] While most research has focused on type 1 diabetes due to its autoimmune nature,[2] few studies have explored this relationship in T2DM patients.

In this study, the prevalence of T2DM was 8.12%, lower than the 10% reported in a systematic review and meta-analysis in Nepal.[11] The prevalence of T2DM in Nepal increased from 7.75% in 2010-15 to 11.24% in 2015–2020. with a similar rise in India from 7.10% in 2009 to 8.90% in 2019.[11,17] The median age of T2DM patients in this study was 51 years, higher than in some studies (48.30 years), but lower than others (>57 years).[18-20] Herein, the majority of patients were middle-aged (40–59 years) (48.51%), followed by the elderly (>60 years) (29.21%) and young adults (20–39 years) (22.28%). T2DM was more common in males with a male-to-female ratio of 1.53:1, contrasting with studies showing higher incidence in females (1:1.30) or equal incidence in both genders.[8,21]

Managing diabetes involves monitoring HbA1c levels, as the risk of coronary heart disease increases linearly with HbA1c levels above 6%.[5] This study found an elevated HbA1c level of 7.95% in T2DM patients compared to those without T2DM, consistent with other research.[5,9] Such high HbA1c indicates poorer glycemic control, often due to excessive glycosylation from high glucose levels.[9] Ogbonna et al. reported that 51% of T2DM patients did not meet glycemic goals, a finding supported by similar studies.[8,18] In this study, early adulthood (20–39 years) and elderly (≥60 years) patients had higher median HbA1c (7.60%) compared to middle-aged adults (7.30%). Females also had a higher median HbA1c (7.55%) than males (7.40%), potentially due to issues like poor medication adherence and financial constraints.[8]

In this study, the mean BMI of T2DM patients was 26.02 kg/m², lower than the 27.40 kg/m² reported in a Turkish meta-analysis.[22] Most T2DM patients were overweight (41.09%), with a smaller proportion obese (17.33%). This aligns with findings that T2DM is more common among overweight individuals compared to the obese. Hara et al. reiterated that the Asian population tends to develop diabetes at lower obesity (23–27.5 kg/m^2) rates than their white counterparts (≥ 27.5 kg/m^2) due to higher physiological markers for insulin resistance. The study found that females with T2DM had higher rates of overweight (43.75% vs. 39.34%) and obesity (23.75% vs. 13.11%) than males, contrary to a Japanese study showing higher rates among males. Unlike several studies where HbA1c (7.30-7.50%) increased with BMI, this study observed a slight decrease in mean HbA1c with higher BMI.[6]

Thyroid function is critical for regulating metabolic parameters and influencing cardiovascular disease (CVD) risk.[9] This study found a prevalence of thyroid dysfunction at 18.81%, lower than the 35.41% reported in a previous Nepalese study and the 23.33–28.50% found in other Asian studies of T2DM patients.[3,4,23] Herein, the most common thyroid disorder among T2DM patients was subclinical hypothyroidism (14.85%), followed by primary hypothyroidism (2.97%), with a small percentage having subclinical or primary hyperthyroidism (0.50%). The findings of Bajpai et al.[4] also indicate a higher incidence of subclinical hypothyroidism (16.70%), followed by hypothyroidism (5%) and hyperthyroidism (1.60%). In this study, females were more affected by

thyroid dysfunction (100%) than males (22.13%), consistent with studies from India, Saudi Arabia, and Greece.[23-25] While both males experienced hypothyroidism and hyperthyroidism, females were only affected by subclinical hypothyroidism. T2DM patients had significantly lower free T4 levels (12 pg/ml vs. 12.78 pg/ml) and higher free TSH levels (3.19 µIU/ml vs. 2.03 µIU/ml) compared to controls, indicating impaired thyroid function. Pangajam et al. also reported similar findings. This impairment may be due to reduced iodide uptake or chronic hyperglycemia affecting T4 to T3 conversion.[8,10] The study also noted that thyroid disorders were more common in T2DM patients with a BMI >25 kg/m², aligning with other research linking higher BMI with increased prevalence of thyroid disorders.[2,25]

The study found that 54.95% of T2DM patients had dyslipidemia, characterized by elevated triglycerides (92.79%) and total cholesterol (9.91%), and decreased HDL (15.32%). Numerous studies from India have shown a high prevalence of dyslipidemia in T2DM patients (62-63.30%). These studies also reported higher levels of triglycerides and cholesterol, as well as HDL.[2,4] In comparison to non-diabetic subjects, T2DM patients had higher total cholesterol (174.25 vs. 169.51 mg/dl) ($p>0.05$), triglycerides (179.33 vs. 120.07 mg/dl) ($p<01$), and LDL (97.43 vs. 95 mg/dl) ($p>0.05$) levels, attributed to decreased lipoprotein lipase activity (induced by lowering of thyroid hormone levels) and impaired lipoprotein clearance.[10] HDL levels ($p>05$) were lower in T2DM patients, possibly due to insulin resistance increasing free fatty acid flux.[26] Several studies have also reported similar patterns.[1,16] In this study, the prevalence of dyslipidemia was higher in T2DM males compared to females, which contrasts with some studies that report higher rates in T2DM females, but was in agreement with findings from research conducted in Pakistan.[1,27,28]

The study acknowledges several limitations. Firstly, as a hospital-based study with a small sample size, the findings cannot be generalized without further research involving a larger, population-based sample with age- and sex-matched participants. Secondly, a more sensitive chemiluminescent immunoassay method could have provided more accurate results for thyroid and lipid biomarkers. Additionally, the study did not assess hypothyroidism or hyperthyroidism secondary to pituitary disease. Despite these limitations, this study recommends maintaining blood glucose levels within the reference range for T2DM patients and suggests screening for lipid profiles and thyroid function tests every three months to prevent complications.

Conclusions

This study found that T2DM prevalence was low in the paramilitary hospital, with higher rates observed in males and individuals aged 50-59. Dyslipidemia was more common than thyroid dysfunction among T2DM patients, with most thyroid dysfunctions related to subclinical hypothyroidism. Dyslipidemia was more prevalent in males, while hypothyroidism was more frequent in females. Adults were more prone to dyslipidemia, while the elderly were more susceptible to thyroid dysfunction. T2DM patients had higher levels of HbA1c, BMI, triglycerides, and TSH, but lower free T4 levels compared to those without T2DM.

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Conflict of Interest

The authors declare no competing interest.
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Author's Contribution and ORCID iDs

Dr. Mahendra Raj Shrestha
Conceptualization, Methodology, Literature review, Data analysis, Drafting.

: https://orcid.org/ 0000-0002-8292-5757

Dr. Apurba Shrestha
Methodology, Literature review, Data analysis, Manuscript review

: https://orcid.org/0009-0002-6990-625X

Dinesh Singh Bhat
Literature review, Data acquisition, Drafting

: https://orcid.org/0009-0004-7128-6066

Dr. Rajendra Maharjan
Data analysis, Manuscript editing

: https://orcid.org/0000-0001-9399-9383

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Bios

Dr. Mahendra Raj Shrestha is an Associate Professor and consultant pathologist at Nepal APF Hospital, Kathmandu, Nepal. He serves as Chairperson, IRC of Nepal APF Hospital. His research focus on anatomical pathology, cytopathology, and clinical pathology.

Email: mahendrapath@gmail.com

Dr. Apurba Shrestha is an Assistant Professor and consultant physician at Nepal APF Hospital, Kathmandu, Nepal. His research focus on metabolic disorder, infectious disease and non-communicable disease.

Email: shresthaapurba@gmail.com

Mr. Dinesh Singh Bhat is a laboratory technologist at Nepal APF Hospital, Kathmandu, Nepal. His research focus on biochemistry, immunology, microbiology and hematology.

Email: dinesinsp@gmail.com

Dr. Rajendra Maharjan is a consultant pathologist at Nepal APF Hospital, Kathmandu, Nepal. He is also serving as editor in Medical Journal of Armed Police Force Nepal (MJAPFN) and Journal of Pathology Nepal(JPN). His research focus on anatomical pathology, cytopathology, and clinical pathology.

Email: docryanm10@gmail.com