Original Article

FNAC-Based Evaluation of Thyroid Lesions: Significance of Hematological and Biochemical Parameters in Untreated Hyperthyroid Patients

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ABSTRACT

Objective: To assess thyroid lesions and biochemical alterations in untreated hyperthyroid patients.
Study Design: Hospital based observational cross-sectional study
Place and Duration of Study: This study was conducted at the MINAR Cancer Hospital, Multan from January 2023 to December 2024.
Methods: A total of 1,000 thyroid disorder patients were enrolled at MINAR Cancer Hospital, South Punjab, Pakistan. Clinical evaluation and thyroid function tests (TFTs) identified 272 hyperthyroid patients, 325 euthyroid controls, and 403 with other thyroid disorders. FNAC was performed in 403 cases and categorized using the Bethesda system. Thyroid scans showed predominantly low radioiodine uptake, enabling stratification into hyperthyroid and FNAC groups. Hematological indices, including WBC, RBC parameters, platelet count, and MPV, were assessed. Statistical analyses employed One-way ANOVA, Student's t-test, Chi-square, Pearson, and Spearman correlations, with $p<0.05$ considered significant.
Results: FNAC analysis showed 35.60% of patients with colloid nodule (Bethesda II), 18.18% with follicular neoplasm (Bethesda IV), 23.07% suspicious for malignancy (Bethesda V), and 18.8% malignant (Bethesda VI). Malignancy was more frequent in patients above 45 years, while residence near the hospital had no effect on malignancy distribution. Hematological findings in untreated hyperthyroid patients revealed significant changes in RBC ($p=0.004$), MPV ($p=0.000$), and platelet count ($p=0.000$). Correlation analysis demonstrated negative associations of T4 with HGB, HCT, MCV, and MCH, and a positive association of MPV with T4 across different subgroups.
Conclusion: FNAC classifies thyroid lesions cytologically, while hematological and biochemical parameters reveal systemic changes, aiding diagnosis and treatment planning independently.
Key Words: Thyroid lesions, FNAC, Thyroid function tests (TFTs), Hematological parameters, Untreated hyperthyroidism

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INTRODUCTION

The thyroid gland derives its name from the Greek word thyreos (shield) due to its resemblance to armor. It secretes hormones that regulate metabolic functions such as energy expenditure, lipid and glucose metabolism, thermoregulation, and basal metabolic rate[1]. Thyroid hormone production is regulated by the hypothalamic pituitary thyroid axis through thyroid-stimulating hormone (TSH)[2]. The thyroid predominantly releases thyroxine (T4, ~85%), while a smaller proportion is secreted as triiodothyronine (T3, ~15%). Structural or functional abnormalities in thyroid growth can lead to various thyroid disorders[3].

Fine-needle aspiration cytology (FNAC) is the key diagnostic tool for Bethesda Category II thyroid nodules, including colloid nodules and Hashimoto's thyroiditis, with a malignancy risk of 0–3%. It shows colloid, follicular cells, lymphocytes, or Hurtles cells, ensuring accurate benign diagnosis, guiding follow-up, reducing unnecessary surgery, and complementing ultrasound findings. FNAC also identifies dense lymphoid infiltrates with occasional oncocytic cells,

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aiding diagnosis of Hashimoto's thyroiditis (Bethesda II/III)[4].

FNAC helps to diagnose Bethesda Category IV thyroid lesions (15–30% malignancy risk), showing hypercellularity, micro follicles, scant colloid. Though 85% accurate, it cannot assess invasion; thus, diagnostic lobectomy and molecular testing refine management. FNAC is also valuable in Bethesda Category V (60–75% malignancy risk), detecting suspicious nuclear or architectural features of carcinoma. Though not definitive, it guides surgical excision, integrates with ultrasound, and shows >90% predictive value for papillary subtypes[5]. In Bethesda Category VI (97–99% malignancy risk), FNAC confirms thyroid cancer with classic nuclear features, enabling prompt total thyroidectomy, radioiodine therapy, staging, and follow-up, achieving up to 98% sensitivity in papillary carcinoma[6].

Hyperthyroidism is a hypermetabolic condition characterized by increased energy expenditure, weight loss, enhanced lipid and glucose metabolism, and altered cholesterol levels. It may also accelerate growth in children and patients with Turner syndrome[3]. Complete blood count (CBC) is a key hematological test performed with automated analyzers, measuring parameters such as white blood cells (WBC), red blood cells (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular values, platelet (PLT) count, and mean platelet volume (MPV). WBCs play a crucial role in host defense[7].

In Graves' disease, WBC counts may remain low, whereas hyperthyroid patients generally show higher leukocyte counts due to increases in corpuscles, granulocytes, and mononuclear cells[8]. RBCs transport oxygen, and thyroid dysfunction influences RBC levels; hypothyroidism is often associated with reduced blood cell counts, while hyperthyroidism may cause relative increases[9]. Thyroid hormone imbalance and iron deficiency can also alter erythrocyte distribution width, sometimes resulting in pernicious anemia. Platelets, an important CBC component, may also be affected in hyperthyroidism, with increased platelet count and reduced lifespan being reported. Thyroid disorders are more common in females, and thyroid hormones influence multiple systems, including the coagulation fibrinolytic pathway. MPV and platelet distribution width (PDW) are therefore considered important markers in assessing platelet function in thyroid disease. Moreover, both hypothyroidism and hyperthyroidism have emerged as significant endocrine factors influencing the clinical course and prognosis of COVID-19.[10,11].

Our study underscores the pivotal role of FNAC in thyroid evaluation, emphasizing its diagnostic yield across Bethesda categories, while also integrating hematological and biochemical parameters in hyperthyroid patients.

METHODS

Laboratory Measurements: Patients visited the nuclear medicine department & diagnostic section of MINAR Cancer Hospital, Multan for diagnostic and therapeutic purposes, and completed a structured form concerning demographic characteristics. Samples were taken in K2-EDTA vials (BD-Vacutainer for TFT'S & CBC analysis)[12,13], after the approval of a local ethical committee of MINAR cancer hospital (Pakistan Atomic Energy **Commission, Ref .No.M-3(13)/2018),** and informed consent of participants. T3, T4,FT3,FT4 and TSH were measured with an electrochemiluminescence immunoassay (Hitachi Modular E411; Roche Diagnostics, Mannheim, Germany), routine hematology testing was performed on the MEK9100 Celltac G Hematology Analyzer. Microscopy was performed through Olympus CX-43.

Statistical Analysis: Statistical analyses were performed using SPSS version 24.0 (SPSS Inc., Chicago, IL, USA). Differences between hyperthyroid patients and the euthyroid control group, as well as between malignant and non-malignant cases, were evaluated using the independent t-test or the Mann Whitney U test, depending on data normality as assessed by the Kolmogorov Smirnov and Shapiro Wilk tests. A significance level of $P < 0.05$ was considered statistically significant. The chi-square test was applied to examine the influence of demographic variables on diagnosis, while correlations between thyroid function tests (TFTs) and complete blood count (CBC) parameters were assessed using Pearson and Spearman correlation analyses.

RESULTS

A total of 1000 patients with thyroid disorders were included in the study. Among them, 597 patients were newly diagnosed and untreated, comprising 272 hyperthyroid patients and 325 euthyroid controls, with ages ranging from 1 to 80 years (mean age 35.02 ± 12.86). FNAC-based categorization according to the Bethesda system showed that 35.60% were colloid nodules (Category II), 18.18% were follicular neoplasms (Category IV), 23.07% were suspicious for malignancy (Category V), 9.79% were malignant (Category VI), and 9.09% were papillary thyroid carcinoma (Category VI), while lymphocytic or granulomatous thyroiditis and oncocytic changes accounted for less than 2% as indicated in figure 1.

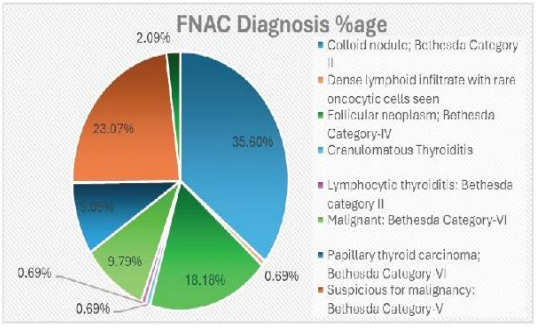
Significant differences were observed between hyperthyroid patients and the euthyroid control group for thyroid function tests, including T3, T4, and TSH (all p=0.000), as well as hematological parameters such as RBC (p=0.004), MPV (p=0.000), and PLT (p=0.000) as indicated in table 1.

Table No.1: Comprehensive Results of TFT'S and CBC parameters

Parameters	Hyperthyroid group	Euthyroid (Control group)	P-value
T3 nmol/L	4.41±2.90	1.98±0.51	[b] **0.000★**
T4 nmol/L	197.8±100.3	111.81±26.14	[b] **0.000★**
TSH µIU/ml	0.06±0.19	1.03±0.81	[b] **0.000★**
WBC×10^3/µL	8.85±3.53	8.97±2.44	[b] 0.269
RBC× 10^6/µL	5.21±0.67	4.50±0.56	[b] **0.004★**
HGB g/dl	12.90±2.32	12.69±1.78	[b] 0.238
HCT%	41.09±6.32	39.62±5.05	[a] 0.076
MCV fL	79.18±10.73	79.80±10.25	[b] 0.404
MCH pg	25.09±3.67	25.59±3.69	[b] 0.100
MCHC g/dl	31.38±3.42	32.04±2.18	[b] 0.156
PLT×10^3/µL	302.74±103.70	350.10±114.16	[b] **0.000★**
RDW%	13.48±1.69	13.09±2.01	[b] 0.045
PCT%	0.23±0.06	0.24±0.09	[b] 0.511
MPV fL	7.92±1.19	7.10±1.54	[b] **0.000★**
PDW%	17.65± 0.96	17.50±1.18	[b] 0.415

[a] Independent t-test, [b] Mann-Witney U Wilcoxon test, ★significant result,

A.



B.

S NO	Diagnosis Through FNAC	%age
1	Colloid nodule; Bethesda Category-II	35.60 %
2	Dense lymphoid infiltrate with rare oncocytic cells seen	0.69%
3	Follicular neoplasm; Bethesda Category-IV	18.18 %
4	Granulomatous Thyroiditis	0.69%
5	Lymphocytic thyroiditis: Bethesda category II	0.69%
6	Malignant: Bethesda Category-VI	9.79%
7	Papillary thyroid carcinoma; Bethesda Category-VI	9.09%
8	Suspicious for malignancy: Bethesda Category-V	23.07 %
9	Suspicious for Papillary thyroid carcinoma: Bethesda Category-V	2.09%

C.

Variable	Benign (mean ± SD)	Malignant (mean ± SD)	t-statistic	p-value
Age	41.3 ± 13.4	50.8 ± 14.6	-3.45	**0.001**
FT3	3.41 ± 12.1	2.53 ± 0.63	0.62	0.54
FT4	1.47 ± 0.55	1.34 ± 0.32	1.36	0.18
TSH	10.5 ± 23.7	11.8 ± 27.1	-0.28	0.78
CEA	5.9 ± 8.1	6.4 ± 9.2	-0.21	0.83

D.

S No	Marker	Colloid nodule; Bethesda Category-II	Follicular neoplasm: Bethesda Category- IV	Suspicious for Malignancy: Bethesda Category-V	Malignant: Bethesda Category-VI	Papillary thyroid carcinoma: Bethesda Category-VI	F-statistic	p-value
1	FT3	7.82±17.51	2.55±0.35	2.64± 0.39	2.65±0.30	-	0.198	0.94
2	FT4	1.40±0.58	1 ±0.1	1.10±0.37	1.45±0.15	1.19±0.09	0.635	0.62
3	TSH	5.94±21.70	1.77 ±1.63	12.14±29.89	17.80±38.66	1.95±1.47	0.501	0.74
4	T3	7.60± 17.61	3.09± 1.08	1.44 ± 0.61	1.70 ± 0.00	1.69± 0.34	3.221	**0.04**
5	T4	-	95.2±39.43	112.24±28.51	104.13±53.13	82.40±8.76	-	-

Figure No.1: A & B FNAC diagnosis percentage, C: Difference between benign and malignant parameters, D: Bethesda category parameters differences

Correlation analysis revealed that, in untreated hyperthyroid patients, T4 was negatively associated with hemoglobin (r=-0.30, p=0.004), hematocrit (r=-0.23, p=0.03), mean corpuscular volume (r=-0.27, p=0.01), and mean corpuscular hemoglobin (r=-0.34, p=0.001), while it showed a positive correlation with mean platelet volume (r=0.23, p=0.03). T3 was negatively correlated with WBC (r=-0.22, p=0.04) and MCH (r=-0.23, p=0.03) overall, whereas gender-specific results indicated a positive association of T3 with MPV in females (r=0.30, p=0.01) and a negative association with MCH in males (r=-0.28, p=0.02) as indicated in table 2.

Age-based analysis further highlighted specific associations. In patients younger than 18 years, TSH was negatively correlated with WBC (r=-0.89, p=0.04), while in young adults (18–35 years), it was negatively correlated with RBC (r=-0.43, p=0.01). In the adult group (36–55 years), MPV was strongly positively associated with T3 (r=0.48, p=0.001), and WBC was negatively associated with T3 (r=-0.38, p=0.01). Moreover, all RBC-related parameters (HGB, HCT,

MCV, and MCH) were negatively correlated with T4, while MPV showed a positive association with T4 (r=0.33, p=0.02). In patients aged 56 years and above, T3 demonstrated a highly significant positive correlation with MCV (r=1.0) as indicated in table 3.

When benign and malignant cases were compared, age was significantly higher in malignant patients (50.8 ± 14.6) compared to benign ones (41.3 ± 13.4) (p=0.001). However, FT3, FT4, TSH, and CEA levels did not show significant differences between the two groups. One-way ANOVA across Bethesda categories revealed that only T3 levels varied significantly (p=0.04), whereas other thyroid function tests did not show notable variation as indicated in figure 1.

Overall, the findings indicate that hyperthyroidism exerts significant effects on thyroid function and hematological parameters, particularly RBC indices and platelet markers. T4 was consistently associated with reduced RBC parameters, while T3 was strongly linked with platelet activity (MPV) and WBC regulation. Age-specific differences suggest that thyroid dysfunction affects hematological parameters more prominently in young adults and middle-aged individuals. Furthermore, FNAC results demonstrated that advanced age is an important risk factor for malignancy, while biochemical markers (FT3, FT4, TSH, and CEA) alone were insufficient to distinguish benign from malignant thyroid disease.

Table No.2: Correlation Table [a] Pearson correlation, [b] Spearman correlation, ★significant result.

Categories	Overall Results			Gender-Based Results(Males)			Gender-Based Results(Females)		
Parameters	T3 nmol/L	T4 nmol/L	TSH µIU/ml	T3 nmol/L	T4 nmol/L	TSH µIU/ml	T3 nmol/L	T4 nmol/L	TSH µIU/ml
WBC 10^3/µL	**-0.22(0.04)** [b]★	-0.15(0.14) [b]	-0.13(0.21) [b]	-0.22(0.38) [b]	-0.28(0.26) [b]	-0.14(0.55) [b]	-0.22(0.06) [b]	-0.13(0.26) [b]	-0.12(0.28) [b]
RBC 10^6/µL	0.05(0.61) [b]	-0.06(0.61) [b]	-0.05(0.62) [b]	0.12(0.64) [b]	0.28(0.25) [b]	0.04(0.85) [b]	0.07(0.56) [b]	-0.06(0.59) [b]	-0.11(0.34) [b]
HGB g/dl	-0.14(0.18) [b]	**-0.30(0.00)** [b]★	0.02(0.86) [b]	-0.14(0.58) [b]	-0.23(0.36) [b]	0.16(0.50) [b]	-0.14(0.26) [b]	-0.24(0.05)	-0.05(0.66) [b]
HCT%	-0.08(0.47) [b]	**-0.23(0.03)** [b]★	0.01(0.95) [b]	-0.07(0.78) [b]	-0.18(0.46) [b]	0.22(0.36) [b]	-0.06(0.64) [b]	-0.16(0.18) [b]	-0.09(0.45) [b]
MCV fL	-0.17(0.12) [b]	**-0.27(0.01)** [b]★	0.10(0.33) [b]	-0.27(0.29) [b]	**-0.53(0.02)** [b]★	0.21(0.39) [b]	-0.13(0.27) [b]	-0.17(0.14) [b]	0.06(0.60) [b]
MCH pg	**-0.23(0.03)** [b]★	**-0.34(0.00)** [b]★	0.15(0.16) [b]	-0.24(0.35) [b]	-0.46(0.05)	0.23(0.34) [b]	-0.22(0.06) [b]	**-0.28(0.02)** [b]★	0.11(0.33) [b]
MCHC g/dl	-0.12(0.34) [b]	-0.14(0.17) [b]	0.05(0.61) [b]	-0.04(0.89) [b]	-0.06(0.78) [b]	0.05(0.84) [b]	-0.11(0.39) [b]	-0.13(0.25) [b]	0.06(0.62) [b]
PLT10^3/µL	-0.15(0.15) [b]	-0.10(0.33) [b]	0.02(0.84) [b]	0.04(0.88) [b]	-0.10(0.68) [b]	0.02(0.93) [b]	-0.20(0.09) [b]	-0.19(0.11) [b]	0.05(0.63) [b]
RDW%	0.15(0.15) [b]	0.17(0.09) [b]	-0.17(0.09) [b]	-0.09(0.72) [b]	-0.03(0.91) [b]	0.03(0.88) [b]	0.19(0.10) [b]	0.23(0.06) [b]	-0.23(0.05)
PCT%	-0.00(0.97) [b]	-0.02(0.83) [b]	-0.01(0.88) [b]	0.25(0.34) [b]	0.11(0.64) [b]	-0.15(0.54) [b]	-0.06(0.59) [b]	-0.14(0.22) [b]	0.06(0.60) [b]
MPV fL	0.31(0.00) [b]	**0.23(0.03)** [b]★	-0.08(0.45) [b]	0.35(0.17) [b]	0.48(0.05)	-0.44(0.06) [b]	**0.30(0.01)** [b]★	0.17(0.13) [b]	-0.00(0.98) [b]
PDW%	0.14(0.19) [b]	0.05(0.61) [b]	-0.02(0.81) [b]	-0.17(0.52) [b]	0.12(0.61) [b]	0.04(0.86) [b]	0.21(0.08) [b]	0.08(0.48) [b]	-0.05(0.61) [b]

Table No.3: Correlation Table [a] Pearson correlation, [b] Spearman correlation, ★significant result, °P-value was calculated by Spearman, Level of significance P<0.05

Category	Age Wise Results (<18y)			Young Adult Age : 18-35 y			Adult: 36-55 y			Senior:56 Y and up		
Para-meters	T3 nmol/L	T4 nmol/L	TSH µIU/ml	T3 nmol/L	T4 nmol/L	TSH µIU/ml	T3 nmol/L	T4 nmol/L	TSH µIU/ml	T3 nmol/L	T4 nmol/L	TSH µIU/ml
WBC 10^3/µL	0.61 (0.39)[a]	0.39 (0.61)[a]	**-0.89 (0.04)** [b]★	0.19(0.27) [b]	0.19 (0.25) [b]	-0.10 (0.53) [b]	**-0.38 (0.01)** [b]★	-0.20 (0.16) [b]	-0.06 (0.67) [b]	0.20 (0.80) [b]	0.40 (0.60) [b]	-0.26 (0.74)[b]
RBC 10^6/µL	-0.01 (0.99)[a]	0.18 (0.81)[a]	0.44 (0.45) [b]	-0.00 (0.96) [b]	0.11 (0.51) [b]	**-0.43 (0.01)** [b]★	-0.05 (0.75) [b]	-0.05 (0.72) [b]	-0.01 (0.93) [b]	-0.20 (0.80) [b]	-0.40 (0.60) [b]	-0.77 (0.22)[b]
HGB g/dl	0.03 (0.97)[a]	-0.15 (0.85)[a]	-0.78 (0.12) [b]	0.31 (0.08) [b]	0.30 (0.08) [b]	-0.23 (0.18) [b]	-0.17 (0.25) [b]	**-0.31 (0.03** [b]**)** ★	0.01 (0.96) [b]	-0.20 (0.80)	-0.40 (0.60) [b]	-0.77 (0.22)[b]
HCT%	0.01 (0.99)[a]	-0.08 (0.92)[a]	-0.34 (0.57) [b]	0.28 (0.11) [b]	0.29 (0.09) [b]	-0.12 (0.49) [b]	-0.21 (0.16) [b]	**-0.34 (0.02)** [b]★	0.01 (0.96) [b]	-0.20 (0.80)	-0.40 (0.60) [b]	-0.77 (0.22)[b]
MCV fL	0.01 (0.99)[a]	-0.25 (0.75)[a]	-0.78 (0.12) [b]	0.29 (0.10) [b]	0.17 (0.32) [b]	0.13 (0.45) [b]	-0.18 (0.23) [b]	**-0.32 (0.03)** [b]★	0.04 (0.79) [b]	**1.0**[b] ★	0.80 (0.20) [b]	0.77 (0.22)[b]
MCH pg	0.03 (0.97)[a]	-0.23 (0.77)[a]	-0.78 (0.12) [b]	0.31 (0.07) [b]	0.18 (0.30) [b]	0.04 (0.83) [b]	-0.14 (0.36) [b]	**-0.29 (0.04)** [b]★	0.06 (0.66) [b]	0.80 (0.20) [b]	0.40 (0.60) [b]	0.77 (0.22)[b]
MCHC g/dl	0.03 (0.97)[a]	-0.22 (0.78)[a]	-0.80 (0.10) [b]	0.08 (0.62) [b]	0.08 (0.61) [b]	-0.08 (0.63) [b]	-0.07 (0.63) [b]	-0.12 (0.41) [b]	0.06 (0.69) [b]	0.00 (1.00) [b]	-0.60 (0.40) [b]	-0.26 (0.74)[b]
PLT10^3/µL	-0.07 (0.93)[a]	-0.26 (0.74)[a]	-0.11 (0.86) [b]	-0.28 (0.10) [b]	-0.19 (0.26) [b]	0.15 (0.37) [b]	-0.25 (0.09) [b]	-0.18 (0.21) [b]	0.12 (0.39) [b]	0.20 (0.80) [b]	0.40 (0.60) [b]	-0.26 (0.74)[b]
RDW%	0.52 (0.48)[a]	0.71 (0.28)[a]	0.22 (0.72) [b]	-0.18 (0.31) [b]	-0.09 (0.59) [b]	0.05 (0.77) [b]	0.10 (0.50) [b]	0.21 (0.15) [b]	-0.15 (0.30) [b]	-0.20 (0.80) [b]	-0.40 (0.60) [b]	-0.77 (0.22)[b]
PCT%	-0. 08 (0.92)[a]	-0.09 (0.90)[a]	0.22 (0.72) [b]	-0.20 (0.31) [b]	-0.07 (0.67) [b]	0.22 (0.21) [b]	-0.08 (0.57) [b]	-0.09 (0.54) [b]	0.17 (0.23) [b]	0.40 (0.60) [b]	0.80 (0.20) [b]	0.25 (0.74)[b]
MPV fL	-0.05 (0.95)[a]	0.21 (0.79)[a]	0.34 (0.57) [b]	0.08 (0.64) [b]	0.04 (0.82) [b]	0.06 (0.74) [b]	**0.48 (0.001)** [b]★	**0.33 (0.02)** [b]★	0.05 (0.71) [b]	-0.40 (0.60) [b]	-0.20 (0.80) [b]	0.26 (0.74)[b]
PDW%	0.42 (0.59)[a]	0.51 (0.49)[a]	-0.22 (0.72) [b]	-0.24 (0.17) [b]	-0.23 (0.19 [b])	-0.03 (0.85) [b]	0.24 (0.10) [b]	0.07 (0.63) [b]	0.03 (0.82) [b]	-0.60 (0.40) [b]	0.00 (1.00) [b]	-0.26 (0.74)[b]

DISCUSSION

Thyroid hormones (TH) continue to be recognized as central regulators of metabolism, growth, and hematopoiesis. Recent large-scale studies reinforce the association between thyroid dysfunction and alterations in blood parameters. For instance, a pooled analysis from the Thyroid Studies Collaboration (42,162 individuals) found that both overt hyperthyroidism and hypothyroidism are associated with increased odds of anemia, with lower hemoglobin among those with abnormal thyroid status compared to euthyroid persons[14]. In the Asir region of Saudi Arabia, a cross-sectional study of nearly 10,000 subjects also demonstrated that thyroid abnormalities are strongly linked with anemia, with the prevalence varying by age and gender[15].

In our study of 1000 patients (597 untreated for thyroid disorder vs. euthyroid controls), we similarly observed that hyperthyroid patients exhibit decreased platelet counts (PLT) and increased mean platelet volume (MPV)[16]. These findings align with recent evidence that MPV is elevated in hyperthyroidism and may reflect a hypermetabolic, prothrombotic state. Although fewer recent studies specifically examine MPV in hyperthyroid patients, the gender-based subgroup in our data (adult females) showed a strong positive correlation between T3 and MPV, which is consistent with the role of TH in influencing platelet activation.

Red blood cell (RBC) indices also showed consistent associations: T4 negatively correlated with HGB, HCT, MCV, and MCH, especially in the 36-55 years age group as indicated by previous work[17]. This is supported by local data from Karachi (Ziauddin University) where hyperthyroid patients had significantly lower hemoglobin and hematocrit compared to euthyroid controls[18]. Similarly, studies like "Impact of thyroid dysfunction on red cell indices in Sahiwal" (2022) found changes in MCV and overall red cell indices in thyroid disorders, reinforcing our age-wise observed effects[19].

Our examination of white blood cell (WBC) counts revealed that T3 had a negative correlation with WBC in adults aged 36-55, and TSH had negative association with WBC in the under-18 group. While less commonly reported in recent literature, these findings may tie into broader observations of immune modulation in thyroid disease. Recent investigations (e.g., Saudi and UK Biobank data) show that thyroid dysfunction correlates with systemic inflammation and immune changes, though precise WBC-TH relationships are still under study[20].

A novel and clinically important finding in our cohort was the age-stratified effect: the adult group (36-55 y) showed more pronounced negative associations between T4 and RBC indices, whereas in seniors (≥56 y) we observed a strongly significant positive correlation of T3 with MCV. This suggests that the hematologic impact of TH varies across lifespan, potentially due to shifts in bone marrow responsiveness, co-morbidities, and nutritional status in older age.

We also integrated FNAC (fine-needle aspiration cytology) results from thyroid nodules to assess malignancy risk vis-à-vis hematological / hormonal profiles. Our data confirmed that malignant FNAC (Bethesda VI) cases were significantly older than benign ones, supporting the well-known finding that advancing age is a risk factor for thyroid malignancy. However, as seen in more recent literature (e.g., studies of Bethesda Category III nodules), cytological categories (including those with indeterminate cytology) may carry varying malignancy risk, and integrating age, ultrasound features, and possibly hormone / hematology data strengthens diagnostic stratification[21].

Taken together, our results reinforce that in untreated hyperthyroid patients, T4 is strongly associated with suppression of red cell parameters, while T3 corresponds more to platelet activity and WBC changes, with distinct gender and age patterns. The FNAC data add value: while biochemical markers alone (FT3, FT4, TSH, CEA) often do not reliably differentiate benign vs malignant thyroid disease, the combination of age, cytological findings, and hematological indices may help in risk stratification, especially in indeterminate cases (Bethesda III).

CONCLUSION

In conclusion, our findings demonstrate that hyperthyroidism significantly alters hematological parameters, with T4 strongly linked to suppression of RBC indices and T3 associated with both platelet activity and leukocyte regulation. The observed age- and gender-specific patterns provide important insights for individualized patient management. FNAC results underscore that while cytology remains the gold standard for diagnosis, integration with TFTs and hematological indices may enhance risk stratification, particularly for malignancy. Future studies should explore the utility of combining hematological markers with molecular and cytological data to develop more robust diagnostic and prognostic tools in thyroid disease.

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