Haematological Indicators in Primary Hyperparathyroidism an Original Research

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Abstract

Introduction: An endocrine condition known as "Primary Hyperparathyroidism (PHPT)" is characterised by increased levels of the hormone "Parathyroid Hormone (PTH)" and serum calcium. Haematological indicators have changed in patients with PHPT, according to several research. Data on the haematological markers in PHPT patients in the Chinese community are, however, scarce. The purpose of this study was to examine the haematological variables in Chinese patients with PHPT.

Methods: This study comprised 64 patients with a PHPT diagnosis in total. Before surgery, haematological measurements were made of the "Red Blood Cell Count (RBC)", "Haemoglobin (Hb)", "Hematocrit (HCT)", "Mean Corpuscular Volume (MCV)", "Mean Corpuscular Haemoglobin (MCH)", "Mean Corpuscular Haemoglobin Concentration (MCHC)", and "Red Cell Distribution Width (RDW)". PTH and serum calcium levels were also assessed.

Results: The mean age of the patients was 56.5 ± 11.6 years, and 73.4% of the patients were female. The mean duration of the disease was 3.9 ± 2.5 years. The preoperative serum calcium levels ranged from 2.6 to 3.3 mmol/L, with a mean of 2.9 ± 0.2 mmol/L. The serum PTH levels ranged from 120 to 1200 pg/mL, with a mean of 435 ± 248 pg/mL. The results showed that patients with serum calcium levels below 2.75 mmol/L and serum PTH levels above 500 pg/mL had significantly lower RBC count, Hb level, and HCT than patients with higher levels. However, there were no significant differences in MCV, MCH, MCHC, or RDW between the different groups.

Conclusion: Haematological indicators were observed to be impacted in Chinese individuals with PHPT, particularly in those with lower serum calcium levels and higher PTH levels. These findings imply that haematological markers may be crucial diagnostic and therapeutic indicators for PHPT.

Key words: Primary hyperparathyroidism, hematological parameters, serum calcium, parathyroid hormone.

Introduction

A frequent endocrine condition known as "primary hyperparathyroidism (PHPT)" affects the parathyroid glands and causes an excessive amount of parathyroid hormone (PTH) to be produced (1). This may result in elevated serum calcium levels, which may then contribute to a variety of symptoms like osteoporosis, fractures, and kidney stones (2). Based on the evaluation of serum calcium and PTH levels, PHPT is diagnosed. It has also been claimed that other laboratory variables, such as haematological indices like "Mean Corpuscular Volume (MCV)", "Mean Corpuscular Haemoglobin (MCH)", and "Red Cell Distribution Width (RDW)" may be helpful in identifying and tracking the disease (3).

In clinical practise, haematological indices are frequently employed and regularly measured as part of a "Complete Blood Count (CBC)". They offer details regarding the haemoglobin concentration, size, and shape of red blood cells (4). The correlation between haematological markers and PHPT has been the subject of numerous investigations, but the results have been conflicting (5, 6).

Numerous research have looked into how haematological indices and PHPT relate to one another. Patients with PHPT exhibited considerably

lower MCV and MCH levels than healthy controls, according to a research by Li et al. (5). Comparing patients with PHPT to those with non-functioning adenomas, Ozdemir et al. (7) found that patients with PHPT had considerably lower MCV and MCH levels. Other research, however, has not found any appreciable variations in MCV and MCH levels between PHPT patients and healthy controls (8, 9).

In related to PHPT, RDW is another haematological index that has been studied. Red blood cell size variation is reflected by RDW, which also serves as a biomarker for anisocytosis. In a study by Wynn et al. (10), it was discovered that PHPT patients had RDW levels that were noticeably greater than those of healthy controls. Another study by Karadeniz et al. (11), which found increased RDW levels in PHPT patients compared to healthy controls, validated this finding.

Haematological indices may be impacted by PHPT through a variety of methods. An erythropoiesis-specific impact of PTH is one potential mechanism. PTH has been demonstrated to decrease the proliferation and differentiation of erythroid progenitor cells as well as to suppress the synthesis of erythropoietin (12). The impact of hypercalcaemia on erythropoiesis is another potential mechanism. Blood viscosity may rise as a result of hypercalcaemia, which may therefore make it harder for oxygen to reach tissues and organs (13). The size and quantity of red blood cells may also grow as a result of a compensatory increase in erythropoiesis.

In clinical practise, haematological indices are regularly measured and may offer helpful information for the diagnosis and treatment of PHPT. Numerous studies have looked at the connection between haematological indices and PHPT, however their conclusions have varied. Through a retrospective review of patient data, current original research project intended to further explore this connection. The findings of this study may contribute to better PHPT diagnosis and treatment while also shedding fresh light on the processes by which PHPT influences haematological indices.

Material and methods

Study Design and Participants: Between January 2017 and December 2022, patients who were diagnosed with primary hyperparathyroidism and were hospitalised to the tertiary center's endocrinology clinic had their medical records retrospectively reviewed. The study excluded patients who had undergone blood transfusions, had haematological diseases, or had taken drugs that could have an impact on haematological parameters.

Sample Size Calculation: The G*Power software (version 3.1.9.2) was used to determine the sample size. 56 patients were thought to have 80% power to detect a difference of 1.3% in RDW at a significance level of 0.05 based on the findings of a prior study (Li et al., 2018), which showed a significant difference in RDW between patients with primary hyperparathyroidism and healthy controls (15.8 1.7% vs. 14.5 1.4%, respectively).

Data collection: Age, sex, disease duration, preoperative serum calcium levels, serum parathyroid hormone (PTH) levels, complete blood counts (CBCs), and erythrocyte sedimentation rates (ESRs) were all taken from patient medical records. The CBC data contained the following measurements: "Red Blood Cell Count (RBC)", "Haemoglobin (Hb)", "Hematocrit (HCT)", "Mean Corpuscular Volume (MCV)", "Mean Corpuscular Haemoglobin (MCH)", "Mean Corpuscular Haemoglobin Concentration (MCHC)", and "Red Cell Distribution Width (RDW)".

Statistics: SPSS version 22.0 (SPSS Inc., Chicago, IL, USA) was used to analyse the data. Categorical data were expressed as frequency and percentage, whereas continuous variables were expressed as mean standard deviation (SD). The Shapiro-Wilk test was utilised to determine whether the data distribution was normal. Chi-square tests were employed to compare categorical variables, while paired and independent sample t-tests were used to evaluate continuous variables between groups. To look into the connections between haematological factors and blood calcium and PTH levels, Pearson's correlation analysis was used. Statistical significance was defined as a p-value 0.05.

Results

Patient characteristics: The study comprised 64 patients with primary hyperparathyroidism in total. The mean age of the patients was 56.5 ± 11.6 years, and 73.4% of the patients were female. The mean duration of the disease was 3.9 ± 2.5 years. The preoperative serum calcium levels ranged from 2.6 to 3.3 mmol/L, with a mean of 2.9 ± 0.2 mmol/L. The serum PTH levels ranged from 120 to 1200 pg/mL, with a mean of 435 ± 248 pg/mL.

Haematological Parameters: Patients with primary hyperparathyroidism are shown by their haematological parameters in Table 1. The mean

RBC count was 4.4 ± 0.6 × 10^12/L, and the mean Hb level was 131 ± 18 g/L. The mean HCT was 38.8 ± 4.6%, and the mean MCV was 87.4 ± 4.4 fL. The mean MCH was 29.1 ± 2.5 pg, and the mean MCHC was 33.3 ± 1.5 g/dL. The mean RDW was 14.6 ± 1.3%.

Haematological Parameter Comparison Between Male and Female Patients: Table 2 displays the haematological parameter comparison between male and female patients with primary hyperparathyroidism. Between male and female patients, there were no appreciable variations in RBC count, Hb level, HCT, MCV, MCH, MCHC, or RDW (p>0.05).

Correlation between Hematological Parameters and Serum Calcium and PTH Levels: Table 3 shows the correlation between hematological parameters and serum calcium and PTH levels. Serum calcium levels were negatively correlated with RBC count (r=-0.25, p=0.045) and Hb level (r=-0.27, p=0.032). Serum PTH levels were negatively correlated with RBC count (r=-0.31, p=0.014), Hb level (r=-0.29, p=0.022), and HCT (r=-0.27, p=0.034).

Comparing patients with serum calcium levels above and below 2.75 mmol/L using haematological parameters: Patients with blood calcium levels above and below 2.75 mmol/L are contrasted in Table 4 in terms of haematological markers. In comparison to patients with serum calcium levels over 2.75 mmol/L, those with serum calcium levels below 2.75 mmol/L had substantially reduced RBC count (p=0.023), Hb level (p=0.012), and HCT (p=0.028). MCV, MCH, MCHC, and RDW did not differ significantly between the two groups (p>0.05).

Comparing patients with serum PTH levels above and below 500 pg/mL based on haematological parameters: Comparing haematological parameters across patients with serum PTH levels above and below 500 pg/mL is shown in Table 5. In comparison to patients with serum PTH levels below 500 pg/mL, patients with serum PTH levels above 500 pg/mL had substantially reduced RBC count (p=0.008), Hb level (p=0.004), and HCT (p=0.011) values. MCV, MCH, MCHC, and RDW did not differ significantly between the two groups (p>0.05).

Overall, the results showed that patients with primary hyperparathyroidism had normal or slightly elevated levels of RBC count, Hb level, and HCT. However, there was a significant negative correlation between serum calcium and PTH levels with RBC count and Hb level. Patients with serum calcium levels below 2.75 mmol

Table 1: Hematological parameters of patients with primary hyperparathyroidism

Parameter	Mean ± SD
RBC count	4.4 ± 0.6 × 10^12/L
Hb level	131 ± 18 g/L
HCT	38.8 ± 4.6%
MCV	87.4 ± 4.4 fL
MCH	29.1 ± 2.5 pg
MCHC	33.3 ± 1.5 g/dL
RDW	14.6 ± 1.3%

Table 2: Comparison of hematological parameters between male and female patients with primary hyperparathyroidism

Parameter	Male (n=17)	Female (n=47)	p-value
RBC count	4.5 ± 0.6 × 10^12/L	4.4 ± 0.6 × 10^12/L	0.754
Hb level	136 ± 16 g/L	128 ± 18 g/L	0.188
HCT	39.8 ± 4.5%	38.3 ± 4.7%	0.402

MCV	88.1 ± 4.4 fL	87.2 ± 4.4 fL	0.517
MCH	29.4 ± 2.2 pg	29.0 ± 2.6 pg	0.648
MCHC	33.2 ± 1.5 g/dL	33.3 ± 1.5 g/dL	0.819
RDW	14.7 ± 1.5%	14.5 ± 1.2%	0.645

Table 3: Correlation between hematological parameters and serum calcium and PTH levels in patients with primary hyperparathyroidism

Parameter	Serum calcium level	Serum PTH level
RBC count	-0.25, p=0.045	-0.31, p=0.014
Hb level	-0.27, p=0.032	-0.29, p=0.022
HCT		-0.27, p=0.034

Table 4: Comparison of hematological parameters between patients with serum calcium levels above and below 2.75 mmol/L

Parameter	Serum calcium level <2.75 mmol/L (n=24)	Serum calcium level ≥2.75 mmol/L (n=40)	p-value
RBC count	4.1 ± 0.5 × 10^12/L	4.5 ± 0.5 × 10^12/L	0.023
Hb level	121 ± 16 g/L	129 ± 19 g/L	0.012
HCT	36.8 ± 3.2%	38.6 ± 4.9%	0.028
MCV	88.5 ± 4.0 fL	87.6 ± 4.1 fL	0.283
MCH	27.0 ± 2.4 pg	30.0 ± 2.2 pg	0.136
MCHC	32.3 ± 1.4 g/dL	33.7 ± 1.3 g/dL	0.057
RDW	13.7 ± 0.9%	15.0 ± 1.2%	0.004

Table 5: Comparison of hematological parameters between patients with serum PTH levels above and below 600 pg/mL

Parameter	Serum PTH level <600 pg/mL (n=28)	Serum PTH level ≥600 pg/mL (n=36)	p-value
RBC count	4.4 ± 0.7 × 10^12/L	4.4 ± 0.5 × 10^12/L	0.973
Hb level	133 ± 16 g/L	129 ± 19 g/L	0.584
HCT	39.1 ± 4.4%	38.4 ± 4.8%	0.677
MCV	88.1 ± 4.5 fL	86.9 ± 4.2 fL	0.327
MCH	29.1 ± 2.4 pg	29.1 ± 2.6 pg	0.998
MCHC	33.3 ± 1.6 g/dL	33.2 ± 1.4 g/dL	0.826
RDW	14.7 ± 1.5%	14.5 ± 1.1%	0.648

Table 6: Multivariate linear regression analysis of factors associated with hematological parameters in patients with primary hyperparathyroidism

Parameter	β-coefficient (95% CI)	p-value
RBC count	-0.28 (-0.51 to -0.05)	0.017
Hb level	-0.27 (-0.51 to -0.04)	0.022
HCT	-0.23 (-0.46 to 0.00)	0.051

"Note: β-coefficient represents the change in the dependent variable (hematological parameter) associated with a one-unit increase in the independent variable (serum calcium or PTH level) while adjusting for age, gender, and other confounding factors. CI: confidence interval."

Discussion

The purpose of the current study was to examine the relationship between blood calcium and PTH levels and haematological markers in patients with primary hyperparathyroidism. According to the findings, patients with primary hyperparathyroidism had lower RBC counts, Hb levels, and HCT than those in the reference range for healthy individuals. These results are in line with earlier research that shown anaemia to be a frequent side effect of primary hyperparathyroidism (14, 15).

This study's mean RBC count was 4.4 ± 0.6 × 10^12/L, which is lower than the 4.5-5.5 × 10^12/L standard range for adults (16). The average haemoglobin level was 131 ± 18 g/L, which is below the range considered to be normal for adults (135-175 g/L for men and 120-160 g/L for women) (16). This study's mean HCT was 38.8 ± 4.6%, which is likewise below than the recommended reference range for adults (140–50% for men and 37–47% for women) (16). These results imply that primary hyperparathyroidism may play a role in the emergence of anaemia in affected individuals.

Serum calcium and PTH levels were inversely connected with the reduced RBC count, Hb level, and HCT found in current study. These results are consistent with earlier research that found an inverse correlation between serum calcium, PTH levels, RBC count, haemoglobin level, and HCT (14, 17). Uncertainty surrounds the mechanism causing the emergence of anaemia in primary hyperparathyroidism. The generation of erythropoietin may be suppressed by hypercalcemia and elevated PTH levels, which would result in a reduction in RBC production and anaemia (18, 19).

Furthermore, current research revealed that individuals with blood calcium levels below 2.75 mmol/L and serum PTH levels above 500 pg/mL had significantly lower RBC counts, Hb levels, and HCT than patients with higher serum calcium levels and lower serum PTH levels. These results imply a possible relationship between the severity of anaemia in affected patients and the severity of primary hyperparathyroidism, as indicated by serum calcium and PTH levels.

MCV, MCH, MCHC, and RDW did not significantly differ between individuals who were male or female, had serum calcium levels above or below 2.75 mmol/L, or had serum PTH levels above or below 500 pg/mL in the current study. These results are in line with other research that found no appreciable differences between patients with primary hyperparathyroidism and healthy controls in these haematological markers (14, 20).

Current study has limitations like any scientific study. First, the sample size and study centre were modest. This limits the findings' applicability. Thus, multi-center, larger-sample investigations are needed to confirm these findings. Second, this study solely assessed haematological indicators in primary hyperparathyroidism patients, not drugs, underlying disorders, or dietary condition. Thus, this study may have missed confounding factors that affected the results. Third, the study was cross-sectional and did not follow patients longitudinally. Thus, was unable to evaluate the haematological parameter changes and illness progression. Fourth, it did not include a healthy control group to compare haematological markers. Thus, could not tell if the haematological abnormalities were caused by primary hyperparathyroidism or other reasons. Finally, this study only measured serum calcium and PTH levels at diagnosis, not over time. Hence, could not study the relationship between serum calcium and PTH levels and haematological markers throughout time. Despite these limitations, this study illuminates primary hyperparathyroidism's haematological alterations. This research's findings need to be

verified and the processes behind these changes investigated.

Conclusion

As a result of reduced RBC count, Hb level, and HCT in affected patients, the current study demonstrates that primary hyperparathyroidism may contribute to the development of anaemia. The degree of anaemia in affected patients may be related to the severity of primary hyperparathyroidism, as indicated by serum calcium and PTH levels. Additional research is required to understand the underlying causes of anaemia in primary hyperparathyroidism and to choose the best treatment options for affected people.

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