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## Electrocardiographic Changes Associated with Moderate Anemia in Young Adults

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### Abstract

**Introduction:** Anemia is one of the most prevalent nutritional disorders worldwide, particularly among young women of reproductive age. By reducing oxygen delivery to vital organs, anemia may alter cardiac electrical activity, though its effects on electrocardiographic (ECG) parameters in moderate anemia remain incompletely characterized. This cross-sectional pilot study aimed to evaluate ECG changes associated with moderate anemia in university students aged 18-30 years at the University of Karachi, Pakistan.

**Methods:** Thirty participants were enrolled; 15 were anemic ( $Hb < 12$  g/dL) and 15 non-anemic controls ( $Hb \geq 12$  g/dL). A 12-lead ECG was performed and nine parameters were compared using the Mann-Whitney U test.

**Results:** Of the ECG parameters assessed, only P-wave amplitude showed a statistically significant difference, with higher values in the anemic group than in the non-anemic group ( $p=0.020$ ). No statistically significant differences were found in P-wave duration, PR interval, QRS duration, ST segment duration, T-wave amplitude, or any QTc indices (QT, QTcH, QTcB, QTcF).

**Conclusion:** In this pilot study, only P-wave amplitude was the ECG variable which showed statistical differences between cohorts in the study reported here. However, while useful, these findings should be considered only of preliminary nature as additional studies are necessary to confirm this association.

**Keywords:** Anemia, cardiac electrophysiology, cross-sectional study, electrocardiography, hemoglobin, P wave amplitude, young adults

### 1. Introduction

Anemia ranks as the most widespread illness, particularly in India. While it is estimated that 9% of individuals are affected by anemia in highly developed nations, the figure rises to 43% in less developed countries<sup>1</sup>. Anemia is among the most prevalent nutritional issues globally and a significant contributor to both disability and mortality<sup>2</sup>. Anemia is a medical condition characterized by reduced level of RBC in blood. In anemia, hemoglobin (Hb) level and RBC count are lower than normal for a particular age group. A normal value is defined as the statistical range that encompasses 95% of the values found within the general population<sup>3</sup>. Anemia is identified as a separate risk factor for heart related issues, where even slight reductions in Hb levels increase the chances of cardiovascular incidents and death<sup>4</sup>. The risk of cardiovascular disease shows a complex connection with Hb levels, whether they are high or low<sup>5-8</sup>. A

Hb level of less than 13 g/dL in adult men and less than 12 g/dL in non-pregnant adult women is considered as anemia by the World Health Organization (WHO)<sup>9</sup>. The heart begins compensatory measures, such as raising cardiac output and lowering circulation time, in order to increase oxygen transport to tissues and make up for the reduced oxygen supply<sup>10</sup>. However, these adaptations remain in place as long as anemia persists, putting constant strain on the cardiovascular system. Cardiac abnormalities are caused by these heart changes.

Electrocardiography (ECG) is an essential diagnostic instrument for evaluating cardiac electrical activity and identifying modifications linked to anemia. Because anemia decreases the oxygen delivery to the myocardium, it can cause changes in heart rate, repolarization abnormalities, and, in extreme cases, ischemic-like alterations. Due to the wide range (10-80%) of reported rates of electrocardiographic abnormalities in anemia, different studies have come to contradictory

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conclusions about the link between ECG alteration and illness<sup>11,12</sup>. Prior research indicated that anemia might cause moderate atrioventricular (AV) conduction abnormalities, T waves flattening, and reduction in QRS amplitude<sup>13</sup>. However, recent research hasn't always supported these results. These studies have shown that anemic individuals experience frequent non-specific alteration in their ST-T wave<sup>14</sup>. In this study we aimed to identify the ECG changes related to moderate anemia among students in the University of Karachi.

## 2. Methods

The study was carried out at the Department of Physiology, University of Karachi for approximately two weeks (4 September, 2025 to 30 September, 2025). The sample included undergraduate university students aged 18-25 years. This age group was chosen to guarantee that age-related physiological, cardiovascular, and hematological differences would not affect the results. Convenience sampling recruited participants from outside the university, including 30 students (15 anemic students with Hb<12 g/dL and 15 healthy controls with Hb≥12 g/dL). Female and male participants were equally distributed in the sample. Individuals suffering from known chronic, cardiovascular, or metabolic diseases, as well as any other conditions that could affect hematological parameters or the electrical activity of the heart were excluded from the sampling process as these factors could interfere with the accuracy of the results.

This research is classified as exploratory case-control study with a total of 30 participants, divided into 15 moderate anemic individuals and 15 individuals without anemia. The experiment was conducted according to the ethical standards of research conducted using human subjects. Ethical clearance was obtained from the Departmental Research Committee (DRC), University of Karachi (Approval Number: DRC-24/2025). Before commencing the study, the participants were informed about the objective, procedure, benefits, and risks involved in the study. Verbal and written informed consent were obtained from each participant. Confidentiality and privacy of the participants were maintained throughout the study. All data collected were only used for the purpose of the study. Before undertaking laboratory and ECG work, participants had to provide demographic and clinical data. This data comprised age, sex, height, weight, and relevant medical history. Measurements were taken using calibrated instruments for precision. Participants had to fill out a questionnaire to determine the signs usually associated with anemia. The procedure was carried out using a standard 12-lead ECG machine. Before the ECG procedure, the participants spent 5 minutes lying down flat on their back to ensure that external factors, such as a physical activity or emotional tension, did not impact the electrical activity of the heart. Skin preparation procedures were performed to ensure proper electrode connection and reduce possible recording errors. Standard anatomical landmarks were followed when connecting electrodes to the limb leads (I, II, III, aVR, aVL and aVF) and chest precordial leads (V1-V6). ECG was measured during the period of stationary state. During the measurement, the following parameters were observed and registered: heart rate, time taken by P wave, value of PR interval, duration of QRS wave and ST interval and form of T wave. The complete blood count (CBC), was performed simultaneously using venous blood samples. The blood was collected under strict aseptic conditions using sterile disposable syringes. To analyze blood samples, they were transported on the same day to the hospital laboratory. Simple tests were conducted in the laboratory to interpret the different blood components such as RBC count and WBC count. The tests were also used to determine the health status of the subjects with reference to anemia. Among all of the individuals who were evaluated for the blood tests, only anemic patients were studied in detail. The anemia was diagnosed using the Hb cut-off figures. Subjects with normal Hb levels were excluded from the study.

Demographic and clinical information were acquired using the strictly fixed forms.

## 3. Results

The demographic and hematological characteristics of the study participants were evaluated to describe the baseline comparability of the anemic and non-anemic groups and to characterize their hematological status. Table 1 summarizes age, sex, Hb concentration, RBC count, hematocrit, and red-cell indices, along with the corresponding statistical comparisons between the two groups. The baseline demographic and hematological data reveal that the two groups are similar with regard to age and sex. There are significant differences in case of Hb ( $p<0.001$ ), RBC count ( $p=0.001$ ) and HCT levels ( $p=0.001$ ). However, there were no significant differences in MCV, MCH, and MCHC values ( $p>0.05$ ).

**Table 1:** Demographic and hematological characteristics of anemic and non-anemic groups

| Parameter                   | Anemic (n=15) | Non-Anemic (n=15) | p-value |
|-----------------------------|---------------|-------------------|---------|
| Age (years)                 | 21.80 ± 1.42  | 23.53 ± 3.76      | 0.238   |
| Sex (F/M)                   | 15/0          | 12/3              | —       |
| Hb (g/dL)                   | 10.27 ± 1.86  | 12.57 ± 0.37      | <0.001* |
| RBC (× 10 <sup>12</sup> /L) | 3.97 ± 0.37   | 4.64 ± 0.47       | 0.001*  |
| HCT (%)                     | 28.68 ± 5.42  | 36.35 ± 4.99      | 0.001*  |
| MCV (fL)                    | 75.17 ± 10.94 | 79.71 ± 6.96      | 0.300   |
| MCH (pg)                    | 25.00 ± 3.52  | 27.09 ± 2.65      | 0.093   |
| MCHC (g/dL)                 | 34.35 ± 3.30  | 34.94 ± 3.59      | 0.561   |

\* Statistically significant at  $p<0.05$ . Values are presented as mean±SD. Mann-Whitney U test was used to calculate p-values. Hb: hemoglobin; RBC: red blood cell count; HCT: hematocrit; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration

To assess the potential cardiac electrical effects associated with anemia, electrocardiographic parameters were compared between participants in the anemic and non-anemic groups. Table 2 presents the comparative analysis of selected ECG waveforms and intervals, including P-wave, QRS, ST-segment, and QT/QTc parameters, together with the statistical tests used to determine differences between the two groups.

**Table 2:** Comparison of electrocardiographic parameters between anemic and non-anemic groups

| ECG Wave   | Variable          | Anemic Mean ± SD (n=15) | Non-Anemic Mean ± SD (n=15) | Statistical Test and Distribution | Test Statistic | p-value |
|------------|-------------------|-------------------------|-----------------------------|-----------------------------------|----------------|---------|
| T wave     | T wave amplitude  | 0.191 ± 0.035 mV        | 0.203 ± 0.018 mV            | Mann-Whitney U; not normal        | U=92.50        | 0.305   |
| P wave     | P duration        | 99.6 ± 13.2 ms          | 92.5 ± 14.2 ms              |                                   | U=76.50        | 0.114   |
|            | P amplitude       | 0.183 ± 0.035 mV        | 0.152 ± 0.051 mV            |                                   | U=58.50        | 0.020*  |
|            | PR interval       | 123.3 ± 10.5 ms         | 125.3 ± 11.9 ms             |                                   | U=103.00       | 0.644   |
|            | QRS duration      | 58.7 ± 20.7 ms          | 48.0 ± 16.6 ms              |                                   | U=82.50        | 0.128   |
| ST segment | ST segment        | 130.7 ± 83.5 ms         | 100.0 ± 22.7 ms             | Independent t-test; normal        | U=84.00        | 0.203   |
| QTc        | QT interval       | 352.9 ± 20.5 ms         | 325.6 ± 68.9 ms             |                                   | t=1.225        | 0.231   |
| QTc        | QTcH (Hodges)     | 399.5 ± 16.9 ms         | 395.1 ± 16.9 ms             |                                   | t=0.442        | 0.662   |
| QTc        | QTcB (Bazett)     | 422.9 ± 21.9 ms         | 416.7 ± 20.3 ms             |                                   | t=0.804        | 0.428   |
| QTc        | QTcF (Fridericia) | 397.8 ± 18.0 ms         | 391.4 ± 18.5 ms             |                                   | t=1.345        | 0.189   |

\*Statistically significant at  $p<0.05$ . Hb: hemoglobin; U: Mann-Whitney U statistic; t: independent samples t-test. Values are mean ± SD or median (IQR). Only P-wave amplitude showed a significant difference between groups ( $p=0.020$ ); all other parameters were non-significant ( $p>0.05$ ).

The normality of the ECG measurements was verified by the Shapiro-Wilk test for each measurement and was found to be normal. The two groups of individuals (moderately anemic vs non-anemic) were compared using independent samples t-test on variables with a normal distribution and Mann-Whitney U-test on variables with an abnormal distribution.  $P < 0.05$  was considered statistically significant.

The results of the T wave showed that the T-wave peak was not significantly different between the anemic and non-anemic groups ( $p = 0.305$ ), which indicates that moderate anemia does not significantly affect the T wave which is representative of the repolarization of the ventricle.

The results for the P wave indicate that there is no statistical difference between the P-wave duration ( $p = 0.114$ ) or PR-interval ( $p = 0.644$ ). The P-wave amplitude was significantly higher for the anemic vs non-anemic groups ( $p = 0.020$ ). Thus, moderate anemia is considerably associated with an increase in P-wave amplitude. The QRS duration was not statistically significant between the anemic and non-anemic individuals ( $p = 0.128$ ). The ST segment was not statistically significant between the two groups ( $p = 0.203$ ). QTc indices were normally distributed, as were the QT intervals that were analyzed using independent samples t-test. There was no statistical difference in the measurements for QTc intervals: QT ( $p = 0.231$ ), QTcH/Hodges ( $p = 0.662$ ), QTcB/Bazett ( $p = 0.428$ ), QTcF/Fridericia ( $p = 0.189$ ).

Of the ECG parameters measured, only the P-wave amplitude was found to have a statistically significant relationship with moderate anemia ( $p = 0.020$ ). The other ECG parameters did not show any significant difference between the two groups. There was also a clear difference in mean Hb between anemic ( $10.27 \pm 1.86$  g/dL) and non-anemic ( $12.57 \pm 0.37$  g/dL) subjects, further confirming the difference between the groups.

## 4. Discussion

The oxygen-carrying capacity of blood is reduced by anemia due to the mismatch between the oxygen demand and supply of the myocardial muscle. As a compensatory response to reduced oxygen availability, the body activates several cardiovascular mechanisms, including increased heart rate, raised cardiac output, and alterations of atrial and ventricular electrical activity, which may cause indirect variations in ECG parameters.

In this study, no statistically significant differences were observed between the two groups for most ECG parameters. However, P-wave amplitude was significantly greater in the anemic group compared to the non-anemic group ( $p = 0.020$ ).

The rationale behind the selective implication of the atria in moderate anemia is based on well-established physiological principles. Anemia causes an overall reduction in oxygen transport in the body, resulting in sympathetic activation and increased return of blood to the heart, preload, and stretching of the atria. The stretching of the atria leads to increased amplitude of the P wave by extension of the wavefront of depolarization of the atria. In contrast, other parameters such as the duration of the QRS complex, ST segment, and QTc are insufficiently affected to reach statistical significance. Thus, the idea of selective changes in the atria does not violate any principle and seems to fit the theory of atrial capacitive adaptation before any significant changes occur in the ventricles. However, given the small sample size, the risk of getting a false positive finding is present and cannot be ignored.

Shashikala et al. (2014)<sup>15</sup> conducted a cross-sectional study examining the relationship between Hb concentration and ECG findings in 100 anemic patients. Patients with severe anemia (Hb 0-5 g/dL), predominantly showed ECG abnormalities including left ventricular hypertrophy, T-wave changes, and ST segment depression, with the frequency of abnormalities increasing as Hb concentration fell. In the

present study, participants had moderate anemia. Therefore, the absence of significant abnormalities in T wave, QRS, and ST segment parameters suggests that a Hb-dependent threshold exists beyond which overt ECG changes become apparent.

In our study, there were no statistically significant differences in T wave amplitude, QRS duration, ST segment, PR interval, or any of the QTc indices between groups. This is consistent with Biradar et al. (2020)<sup>16</sup>, who found that ECG abnormalities could be reversed by correcting the anemia. Traditional findings such as decreased QRS amplitude, T-wave flattening, and mild atrioventricular conduction disturbances are not universally present, and non-specific ST and T-wave abnormalities reported across studies do not consistently correlate with anemia severity.

Regarding QTc, Kwon et al. (2020)<sup>17</sup> undertook a large-scale analysis of QTc prolongation and ECG abnormalities in patients presenting with severe anemia and found significant associations with prolonged QTc interval, decreased QRS amplitude, T-wave inversion, and right axis deviation. The absence of significant QTc prolongation or repolarization disturbances in our study likely reflects the moderate degree of anemia in our participants, with more severe myocardial hypoxia being required to produce these changes.

Simsek et al. (2010)<sup>18</sup> reported that P-wave duration and dispersion in patients with iron deficiency anemia were significantly greater than in healthy controls, supporting the notion that atrial conduction is affected by anemia. This effect was attributed to a reduction in atrial conduction velocity caused by tissue hypoxia and diastolic dysfunction secondary to myocardial ischemia. Although the present study focused on P-wave amplitude rather than dispersion, the underlying physiological mechanism i.e., atrial stretch and autonomic activation in response to reduced oxygen delivery, appears consistent across both findings.

Most recently, Yildiz et al. (2025)<sup>19</sup> evaluated the morphology-voltage-P-wave duration (MVP) score in 241 patients with iron deficiency anemia compared to 204 healthy controls and reported that the total MVP score was significantly higher in the anemic group ( $p < 0.001$ ). This difference was attributed to sympathetic nervous system activation, increased heart rate, and atrial stretching as physiological responses to chronic hypoxia. The significantly increased P-wave amplitude observed in the present study is consistent with these findings and further supports the concept that mild-to-moderate anemia produces measurable changes in atrial depolarization forces.

The sensitivity of P-wave amplitude as an early marker of cardiac involvement in moderate anemia appears to manifest at a much earlier stage than the more overt repolarization and conduction changes seen only at extreme levels of anemia. Because P-wave amplitude can be measured on a standard 12-lead ECG machine, it may provide a low-cost, non-invasive means of screening for early cardiac involvement in moderate anemia.

## 5. Limitations of the Study

The major limitation of this study is the relatively small sample size, which may restrict the applicability of the findings. As an exploratory study, the results should be interpreted carefully and future studies with sufficient sample size are recommended to confirm these observations.

## 6. Conclusion

This pilot cross-sectional study found that the anemic cohort had a significantly higher value of P-wave amplitude than the non-anemic group, while all other parameters on the ECG did not exhibit significant differences. The findings of the research must be interpreted with caution, as the small sample size does not allow for statistical power and generalization. It appears that P-wave amplitude can be seen as an early indicator of adaptation to moderate anemia, but this information must be confirmed in further investigations

involving more numerous representative samples of participants.

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### Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of the article.

### Disclosure of AI Use

No AI tool was used in the preparation of the manuscript.

### Authors' Contributions

DK was responsible for conceptualization of the study, data collection, laboratory procedures, ECG interpretation, data analysis and compilation, documentation, graphical representation, and drafting and finalization of the manuscript. MN was the principal investigator and was responsible for supervision of the study, methodology designing, and critically reviewing the manuscript. MJA was the co-supervisor, providing academic guidance throughout the study, as well as assisting in ECG interpretation and analysis, and critically reviewing the manuscript. ZK was responsible for reviewing and final preparation of manuscript. Both supervisors contributed equally to the supervision and academic support of this research work. All contributors reviewed and approved the final manuscript.

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