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Original Article

Radiology Section

# Role of Unenhanced Computed Tomography of the Chest in the Prediction of Anaemia: A Cross-sectional Study

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## ABSTRACT

**Introduction:** Anaemia is a common clinical condition. The detection of incidental findings on unenhanced Computed Tomography (CT) that predict the presence of anaemia may play a pivotal role in early diagnosis, treatment and prognosis.

**Aim:** To assess the role of unenhanced CT thorax in predicting anaemia by determining the sensitivity and specificity of the Interventricular Septum Sign (IVS) and Aortic Rim Sign (ARS) in the prediction of anaemia.

**Materials and Methods:** This was a cross-sectional study conducted on 300 patients who underwent High-resolution Computed Tomography (HRCT) of the thorax using a 128-slice CT scanner in the Department of Radiology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India, Nizams Institute of Medical Sciences, Hyderabad, from July 2022 to September 2022. An estimation of haemoglobin levels was performed from a peripheral blood sample within 24 hours of the scan and the diagnosis of anaemia was made based on World Health Organisation (WHO) guidelines of haemoglobin values according to age and gender. On imaging, the following parameters were analysed: the variables considered for each patient included age and gender, the presence or absence of ARS, the presence or absence of an IVS and the Hounsfield Units (HU) values of seven selected Regions of Interest (ROI) on each examination. Three ROIs were placed in the Left Ventricular (LV) cavity, three on the IVS and a single ROI was placed in the aorta at the same level. Mean, percentage, frequency and standard deviation were calculated. The Chi-square test was applied for statistical analysis and a p-value of <0.05 was considered significant.

**Results:** Out of the total sample size of 300, 188 were males and 112 were females with the mean age of 47.16±19.77 years. The mean haemoglobin percentage in the study was 11.62±2.25 gm%. Approximately 195 (65%) out of 300 patients were found to be anaemic based on blood reports. Among them, the majority were diagnosed with moderate anaemia 109 (36.3%), followed by mild anaemia 76 (25.3%) and severe anaemia 10 (3.3%), respectively. The sensitivity of the dense IVS was 100% for severe anaemia, 75.6% for moderate anaemia and 55.3% for mild anaemia. In comparison, the aortic rim sign showed a sensitivity of 100% for severe anaemia, 86.5% for moderate anaemia and 67.69% for mild anaemia, with a specificity of 88.57%.

**Conclusion:** The presence of an IVS on an unenhanced CT predicts the likelihood of underlying anaemia and suggests the need for further evaluation and timely management.


**Keywords:** Anaemia evaluation, Aortic rim sign, Haemoglobin, Interventricular septum sign

## INTRODUCTION

The CT scans of the chest and other parts of the body often reveal incidental findings, one of which can be anaemia. While anaemia is typically diagnosed through blood tests that measure plasma haemoglobin levels, identifying incidental signs of anaemia on CT scans can be crucial, especially in emergencies. This capability is important because it allows for timely and effective management of the patient, thereby enhancing clinical outcomes [1]. Historically, anaemia has been detected on CT using signs such as the "aortic ring sign"-where a hyperdense aortic wall is seen against a relatively hypoattenuating aortic blood pool - or the "i.v. septum sign," where the dense myocardium or interventricular (i.v.) septum is visible on a non contrast CT against the hypodense Left Ventricular (LV) cavity [2,3]. While these signs are reliable indicators of severe anaemia, they are observer-dependent, leading to significant interobserver variability [3]. Researchers have debated the most reliable indicators, with some focusing on the CT attenuation of the abdominal aorta and others on the attenuation differences between the LV cavity and the i.v. septum [4]. However, there is potential for misdiagnosis. Research has shown that even when haemoglobin levels are normal, a false increase in i.v. density on CT can occur due to elevated iron or glycogen content, as seen in conditions like hemochromatosis and glycogen storage diseases [2]. Similarly, while the presence of a hyperdense aortic wall has been used to diagnose anaemia, this sign can be confounded by existing calcified atherosclerotic plaques [3,5].

Objective analysis offers a more accurate and reliable method for diagnosing anaemia. This approach involves measuring the density of blood in large vessels or cardiac chambers on unenhanced CT using Hounsfield Units (HU), effectively distinguishing between anaemic and non anaemic individuals [4]. Supporting this, a study by Di Giandomenico E et al., showed significant differences in blood attenuation values between healthy subjects and anaemic patients through CT density measurements of intravascular blood [6]. With this background, the present study was conducted with aim to demonstrate the association between the Hounsfield values of the IVS on unenhanced CT and haemoglobin values from peripheral blood examinations and to evaluate the sensitivity and specificity of the IVS and ARS in predicting anaemia.

## MATERIALS AND METHODS

This cross-sectional study involved the random selection of 300 patients who underwent HRCT of the thorax using a 128-slice CT scanner in the Department of Radiology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India, from July 2022 to September 2022.

**Inclusion and Exclusion criteria:** The study included any patient who had undergone a non enhanced CT of the thorax for any reason. However, patients with a prior diagnosis of anaemia or those who had received blood transfusions for anaemia were excluded from the study.

### Study Procedure

An estimation of haemoglobin levels was performed using a peripheral blood sample collected within 24 hours of the scan and the diagnosis of anaemia was made based on the World Health Organisation (WHO) guidelines for haemoglobin values according to age and gender [Table/Fig-1] [7,8].

| Population | Non anaemia (g/L) | Mild anaemia (g/L) | Moderate anaemia (g/L) | Severe anaemia (g/L) |
|---|---|---|---|---|
| Children 6-59 months of age | 110 or higher | 100-109 | 70-99 | Lower than 70 |
| Children 5-11 years of age | 115 or higher | 110-114 | 80-109 | Lower than 80 |
| Children 12-14 years of age | 120 or higher | 110-119 | 80-109 | Lower than 80 |
| Non-pregnant women (15 years of age and above) | 120 or higher | 110-119 | 80-109 | Lower than 80 |
| Pregnant women | 110 or higher | 100-109 | 70-99 | Lower than 70 |
| Men (15 years of age and above) | 130 or higher | 110-129 | 80-109 | Lower than 80 |

**[Table/Fig-1]:** WHO guidelines of haemoglobin values (g/L) as per age and gender [7,8].

The study was conducted using a 128-slice CT scanner with the following technical parameters: a kVp of 120, an effective mAs of 130 during inspiration and 170 during expiration, a rotation time of 0.5 seconds, an average acquisition time ranging from 3.5 to 4.5 seconds with a pitch value of 0.90. The scan direction was craniocaudal, with the patient in a supine position.

For each patient, the variables considered included age and gender, the presence or absence of the ARS (hyperattenuating aortic wall against a relatively hypoattenuating aortic lumen) and the presence or absence of the IVS (hyperdense IVS visualised against a hypodense LV cavity on an unenhanced CT). Additionally, HU values were recorded for seven selected ROIs during each examination.

The ROIs were obtained from a single scan plane at the mid-cardiac level, with each ROI measuring less than 25 square millimetres. Three ROIs were placed in the LV cavity, three on the IVS and one in the aorta at the same level. If the IVS was not visualised, it was assigned the average attenuation value corresponding to the LV cavity.

Image analysis: All CT examinations were analysed by a single assessor in the Radiology Department, who was unaware of the patients' serum haemoglobin levels at the time of data collection. For interpretation, a soft tissue window setting was used for all patients (WW: 200 HU; WL: 75 HU). A circular ROI of less than 0.25 $cm^2$ was applied consistently throughout the study.

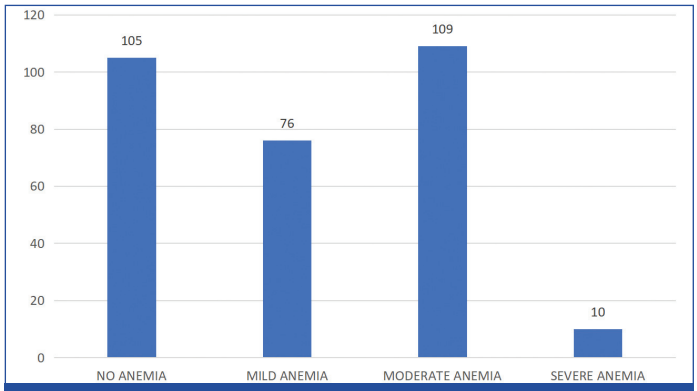
Cases were classified as true positive if both CT findings and haemoglobin estimation correctly indicated anaemia. True negative cases were those where both CT findings and haemoglobin levels correctly indicated the absence of anaemia. False positive cases had CT findings suggestive of anaemia, but haemoglobin levels indicated no anaemia. Conversely, false negative cases were those where CT findings did not indicate anaemia, but haemoglobin levels confirmed its presence.

## STATISTICAL ANALYSIS

The data were analysed using the Statistical Package for Social Sciences (SPSS) software, version 21.0. Categorical variables were analysed using the Chi-square test. Receiver Operating Characteristic (ROC) curves were generated and the Area Under the Curve (AUC) was calculated for both the ARS and the IVS. A p-value of less than 0.05 was considered statistically significant.

## RESULTS

Out of 300 participants in the study, 195 were suffering from anaemia, with the majority diagnosed with moderate anaemia (n=109), followed by mild anaemia (n=76) and severe anaemia (n=10) [Table/Fig-2].




**[Table/Fig-2]:** Distribution of anaemia.

The age distribution of the study participants [Table/Fig-3], with a mean age of 47.16±19.77 years, showed that the majority fell within the 31-50 years age group, accounting for 40.7% (122 individuals) of the total.

| Age (years) | Frequency | Percentage |
|---|---|---|
| <30 | 51 | 17.0% |
| 31-50 | 122 | 40.7% |
| 51-70 | 104 | 34.7% |
| >70 | 23 | 7.7% |
| Total | 300 | 100% |

**[Table/Fig-3]:** Age distribution of participants.

The mean Hb levels showed a difference between age groups. Participants aged ≥50 years (n=140) had a mean haemoglobin level of 11.2±2.17 g/dL, while those under 50 years (n=160) had a higher mean haemoglobin level of 11.9±2.27 g/dL and this observation was statistically significant (p=0.02). Out of the total sample size of 300 participants, 188 were males and 112 were females. The overall mean Hb level in the study was 11.62±2.25 g/dL. Males had a higher mean haemoglobin level of 12.05±2.33 g/dL, while females had a significantly lower mean haemoglobin level of 10.89±1.90 g/dL. Specifically, 44.6% of females had moderate anaemia and 5.4% had severe anaemia, compared to 31.4% of males with moderate anaemia and 2.1% with severe anaemia [Table/Fig-4].

| Parameters | No anaemia | Mild anaemia | Moderate anaemia | Severe anaemia | Total |
|---|---|---|---|---|---|
| Male | 70 (37.2%) | 55 (29.3%) | 59 (31.4%) | 4 (2.1%) | 188 (100%) |
| Female | 35 (31.3%) | 21 (18.8%) | 50 (44.6%) | 6 (5.4%) | 112 (100%) |
| Total | 105 (35.0%) | 76 (25.3%) | 109 (36.3%) | 10 (3.3%) | 300 (100%) |

**[Table/Fig-4]:** Gender disparity in the distribution of anaemia severity within the study population.

As the severity of anaemia increased, the proportion of patients with ARS also rose markedly (p<0.00001). Specifically, among those with ARS, 8.3% had no anaemia, 20.1% had mild anaemia, 64.6% had moderate anaemia and 6.9% had severe anaemia. The study also found that 12 patients with no anaemia had a falsely positive ARS, while 63 patients (47 with mild anaemia and 16 with moderate anaemia) had falsely negative ARS [Table/Fig-5]. The analysis of the IVS in relation to anaemia [Table/Fig-6] demonstrated a significant association between anaemia severity and the presence of IVS on CT (p<0.00001). Specifically, among patients with a positive IVS, 6.1% had no anaemia, 15.7% had mild anaemia, 69.6% had moderate anaemia and 8.7% had severe anaemia.

Additionally, seven patients with IVS were identified as false positives, while 87 were false negatives, including 58 with mild anaemia and 29 with moderate anaemia. This indicated that as anaemia severity increased, the likelihood of detecting IVS also increased.

| Aortic Rim Sign (ARS) | No anaemia | Mild anaemia | Moderate anaemia | Severe anaemia | Total |
|---|---|---|---|---|---|
| Present | 12 (8.3%) | 29 (20.1%) | 93 (64.6%) | 10 (6.9%) | 144 (100.0%) |
| Absent | 93 (59.6%) | 47 (30.1%) | 16 (10.3%) | 0 | 156 (100%) |
| Total | 105 (35.0%) | 76 (25.3%) | 109 (36.3%) | 10 (3.3%) | 300 |
| Chi-square value ($\chi^2$) | 130.87 | | | | |
| p-value | <0.00001 ($3.51\times10^{-28}$) | | | | |

**[Table/Fig-5]:** Analysis of the Aortic Rim Sign (ARS) in relation to anaemia severity.

| Interventricular Septum Sign (IVS) | No anaemia | Mild anaemia | Moderate anaemia | Severe anaemia | Total |
|---|---|---|---|---|---|
| Present | 7 (6.1%) | 18 (15.7%) | 80 (69.6%) | 10 (8.7%) | 115 (100.0%) |
| Absent | 98 (53.0%) | 58 (31.4%) | 29 (15.7%) | 0 | 185 (100%) |
| Total | 105 (35.0%) | 76 (25.3%) | 109 (36.3%) | 10 (3.3%) | 300 |
| Chi-square value ($\chi^2$) | 124.21 | | | | |
| p-value | <0.00001 ($9.56\times10^{-27}$) | | | | |

**[Table/Fig-6]:** Analysis of the Interventricular Septum Sign (IVS) in relation to anaemia severity.

The odds ratio for the IVS was 17.38, with a 95% confidence interval ranging from 7.67 to 39.34, indicating a strong association with anaemia (p-value <0.001) [Table/Fig-7].

| Factor | Odds ratio | Lower value with 95% confidence interval | Upper value with 95% confidence interval |
|---|---|---|---|
| Aortic Rim Sign (ARS) | 16.23 | 8.29 | 31.79 |
| Interventricular septum sign (IVS) | 17.38 | 7.67 | 39.34 |

**[Table/Fig-7]:** Analysis of odds ratios in the associations between ARS and IVS with anaemia.

The ARS demonstrated varying diagnostic performance for different severities of anaemia [Table/Fig-8]. For mild anaemia, the sign had a sensitivity of 67.69% and a specificity of 88.57%.

| Statistics | Mild anaemia | Moderate anaemia | Severe anaemia |
|---|---|---|---|
| Sensitivity | 67.69% (60.64% to 74.20%) | 86.55% (79.09% to 92.12%) | 100.00% (69.15% to 100.00%) |
| Specificity | 88.57% (80.89% to 93.95%) | 77.35% (70.55% to 83.23%) | 53.79% (47.87% to 59.64%) |
| Positive likelihood ratio | 5.92 (3.45 to 10.18) | 3.82 (2.89 to 5.05) | 2.16 (1.91 to 2.45) |
| Negative likelihood ratio | 0.36 (0.29 to 0.45) | 0.17 (0.11 to 0.28) | 0.00 |
| Disease prevalence | 65.00% (59.31% to 70.39%) | 39.67% (34.09% to 45.45%) | 3.33% (1.61% to 6.04%) |
| Positive predictive value | 91.67% (86.49% to 94.97%) | 71.53% (65.54% to 76.84%) | 6.94% (6.18% to 7.79%) |
| Negative predictive value | 59.62% (54.36% to 64.66%) | 89.74% (84.64% to 93.29%) | 100.00% |

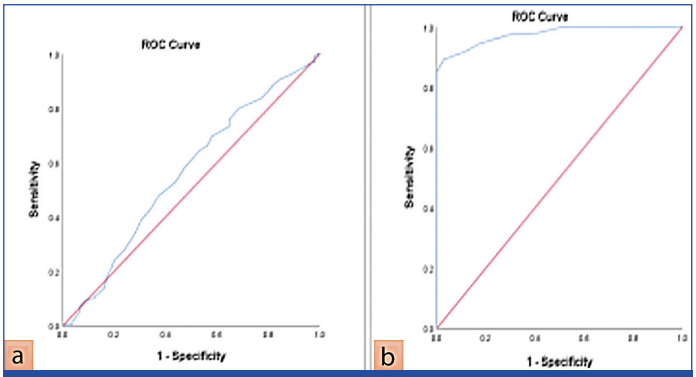
**[Table/Fig-8]:** Diagnostic performance of Aortic Rim Sign (ARS) for different severities of anaemia.

The IVS showed varying diagnostic capabilities for different levels of anaemia [Table/Fig-9]. For mild anaemia, it had a sensitivity of 55.38% and a high specificity of 93.33%. For severe anaemia, the sign achieved a perfect sensitivity of 100.00%, but with a lower specificity of 63.79%. Overall, the IVS was highly sensitive for severe anaemia but varied in its diagnostic performance for mild and moderate anaemia.

**ROC curve analysis:** In comparison to the aortic ring sign, the ROC curve analysis revealed that the hyperdense IVS sign had a significantly larger AUC, indicating better diagnostic performance [Table/Fig-10a,b]. The AUC for the IVS sign was 0.978 (standard error: 0.006, asymptotic significance: 0.000), with a 95% confidence interval ranging from 0.966 to 0.991. In contrast, the aortic ring sign had an AUC of 0.559 (standard error: 0.036, asymptotic significance: 0.094), with a 95% confidence interval between 0.489 and 0.629. The cut-off value for the IVS sign was determined to be 38.5 HU, whereas for the aortic ring sign, it was 39.5 HU [Table/Fig-11]. This analysis highlighted the superior diagnostic ability of the hyperdense IVS sign compared to the aortic ring sign. One representative case is illustrated in [Table/Fig-12a,b].

| Statistics | Mild anaemia | Moderate anaemia | Severe anaemia |
|---|---|---|---|
| Sensitivity | 55.38% (48.11% to 62.49%) | 75.63% (66.91% to 83.03%) | 100.00% (69.15% to 100.00%) |
| Specificity | 93.33% (86.75% to 97.28%) | 86.19% (80.29% to 90.86%) | 63.79% (57.97% to 69.33%) |
| Positive likelihood ratio | 8.31 (4.02 to 17.18) | 5.48 (3.75 to 7.99) | 2.76 (2.37 to 3.22) |
| Negative likelihood ratio | 0.48 (0.41 to 0.56) | 0.28 (0.20 to 0.39) | 0.00 |
| Disease prevalence | 65.00% (59.31% to 70.39%) | 39.67% (34.09% to 45.45%) | 3.33% (1.61% to 6.04%) |
| Positive predictive value | 93.91% (88.18% to 96.96%) | 78.26% (71.16% to 84.01%) | 8.70% (7.56% to 9.99%) |
| Negative predictive value | 52.97% (48.86% to 57.04%) | 84.32% (79.59% to 88.13%) | 100.00% |

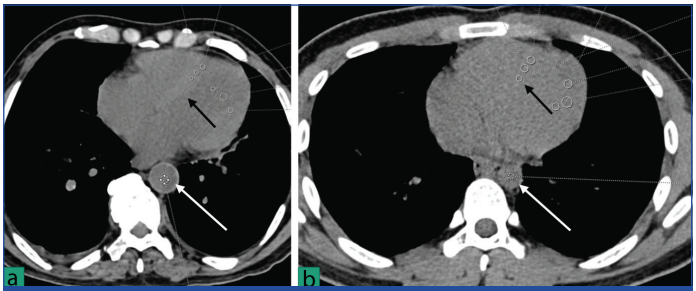
**[Table/Fig-9]:** Diagnostic performance of Interventricular Septum Sign (IVS) for different severities of anaemia.




**[Table/Fig-10]:** ROC curve analysis for: a) Aortic Rim Sign (ARS); and b) Interventricular Septum Sign (IVS).

| Test variable | Area | Standard error (a) | Asymptotic Sig (b) | Lower boundary (95% CI) | Upper boundary (95% CI) |
|---|---|---|---|---|---|
| IVS HU | 0.978 | 0.006 | 0.000 | 0.966 | 0.991 |
| AORTA HU | 0.559 | 0.036 | 0.094 | 0.489 | 0.629 |

**[Table/Fig-11]:** ROC curve analysis.




**[Table/Fig-12]:** a) Unenhanced CT thorax of a 79-year-old male patient with severe anaemia (haemoglobin level 8.0 g/dL), shows aortic ring sign (white arrow) and inter ventricular septum sign (black arrow); b) Unenhanced CT thorax of a 19-year-old male patient with normal haemoglobin levels-15.2 g/dL showing normal appearance of aortic wall (white arrow) and normal appearance of myocardium (black arrow).

## DISCUSSION

The present study, involving 300 participants, identified moderate anaemia as the most prevalent, affecting 109 individuals. The mean age of the participants was 47.16 years, with noticeable gender disparities in haemoglobin levels and anaemia severity. These findings

align with those of Wazzan M et al., who also noted significant gender differences, with males exhibiting higher haemoglobin levels and densities in the aortic and inferior vena cava compared to females [9]. In the present study, the IVS demonstrated a sensitivity of 100% for severe anaemia, 75.6% for moderate anaemia and 55.3% for mild anaemia, with a specificity of 93.3%. Conversely, the ARS exhibited a sensitivity of 100% for severe anaemia, 86.5% for moderate anaemia and 67.69% for mild anaemia, but with a lower specificity of 88.57%. The lower specificity of the ARS could be attributed to faint atherosclerotic wall calcifications in the aorta, which may have impacted its accuracy.

The ROC curve analysis showed a significantly larger AUC for the IVS sign (0.978) compared to the ARS (0.559), indicating superior diagnostic performance. This contrasts with the findings of Iuga A et al., who reported higher specificity for the ARS (98%) compared to the IVS (92%), with moderate sensitivities (42% for ARS and 60% for IVS) [10]. The ROC thresholds identified in the present study were 38.5 HU for the IVS sign and 39.5 HU for the ARS, which differ from those reported by Iuga A et al., where the best thresholds were ≤36.5 HU for LV cavity attenuation values and slightly varied by gender [10]. Foster M et al., found that the IVS sign had a sensitivity of 75.4% and a specificity of 90.3% for anaemia detection using unenhanced CT, with an overall accuracy of 80% [4]. These findings align with the present study results, which show high sensitivity for the IVS sign, particularly for severe anaemia; however, the present study reported slightly different sensitivity and specificity values. In comparison to Lan H et al., who emphasised the superiority of the attenuation difference between the IVS and the LV cavity for predicting anaemia over the LV cavity alone, our study's results support this observation [11]. The IVS sign's high sensitivity in our study further corroborates its utility in anaemia detection. On the other hand, Kamel EM et al., concluded that the ARS had higher sensitivity compared to the IVS sign in predicting anaemia, although the IVS sign was more specific [3]. This highlights a nuanced difference from the present study, where the IVS sign demonstrated superior performance overall, particularly in terms of sensitivity for severe anaemia. Overall, the present study findings underscore the strong diagnostic potential of the IVS sign, especially in identifying severe anaemia. While variations in cut-off values and performance metrics across studies highlight the need for further research, the present study contributes valuable insights into the diagnostic capabilities of CT imaging for anaemia detection. Standardisation and validation across diverse populations and settings remain essential to enhance diagnostic accuracy and clinical utility.

### Limitation(s)

As an operator-dependent investigation, it was vulnerable to errors arising from interobserver variability, which could compromise the consistency and accuracy of the findings. Additionally, the potential for false negative results was significant, particularly among patients with mild anaemia, where the diagnostic indicators might not be as apparent. Furthermore, the possibility of false positive results was noted, as the presence of hyperdense IVS could lead to misinterpretation in the diagnosis of anaemia, thereby affecting the overall diagnostic precision.

## CONCLUSION(S)

The specificity of the IVS is higher compared to the ARS, while the latter is more sensitive. In emergency settings and cases of trauma, the mere presence of the IVS can help predict the presence of anaemia due to blood loss, which can aid in timely intervention and improve outcomes.

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**PLAGIARISM CHECKING METHODS:** [Jain H et al.]

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- Manual Googling: Oct 03, 2024
- iThenticate Software: Oct 05, 2024 (15%)

**ETYMOLOGY:** Author Origin

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