RESEARCH ARTICLE

The accuracy and precision of plain CT chest for diagnosis of anaemia

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Abstract

Objective: To determine the accuracy and precision of anaemia diagnosis with plain computed tomography of chest by keeping complete blood count as the gold standard.

Method: The cohort study was conducted from January 1 to December 31, 2020, at Dow University of Health Sciences, Karachi, and comprised patients attending the hospital regardless of gender or age. The subjects underwent complete blood count and high-resolution computed tomography scan of chest with 7-day interval. On the basis of haematology, the subjects were divided into anaemic group A and control group B. Blood attenuation measurements and visual perception of the inter-ventricular septum was done blinded to haemoglobin values. Region of interest attenuation cursor was placed within the right ventricular chamber and left ventricular chamber. Quantitative diagnosis of anaemia on computed tomography was done with Hounsfield unit <35 in a chamber. Qualitative computed tomography diagnosis of anaemia was equivalent to inter-ventricular septum visualisation. Accuracy and precision was calculated. Data was analysed using SPSS 17.

Results: Of the 124 subjects, 62(50%) were males and 62(50%) were females. The overall mean age was 51.45±17.3 years (range: 8-96 years). On the basis of haematology, 74(59.6%) subjects were in group A and 50(40.3%) were in group B. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of chest computed tomography for quantitative diagnosis of anaemia were 48.6%, 76.5%, 76.5%, 50.6% and 60.5% respectively. The corresponding values for qualitative diagnosis of anaemia were 55.4%, 88.0%, 87.2%, 57.1%, and 68.5%.

Conclusion: There was a high positive predictive value for quantitative diagnosis of anaemia on chest computed tomography with low diagnostic accuracy and moderate reliability.

Keywords: Computed tomography, Plain CT, Haemoglobin, Anaemia. (JPMA 74: 1593; 2024)

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Introduction

Haemoglobin (Hb) is the iron-containing oxygen-transport metallo-protein in erythrocytes comprising 2 alpha and 2 globin chains. The display of different shades of grey on computed tomography (CT) is due to variable densities of tissues in the human body. Blood displays a specific density range of 30-40 on CT not because of its iron (Fe+2) content, but because of its elongated protein chains.[1] In Pakistan, the prevalence of anaemia among ever-married women aged 15-44 years is reported to be 26% in urban areas and 47% in rural Areas.[2] Plain high-resolution CT (HRCT) of chest is a non-contrast examination recommended by clinicians and pulmonologists to evaluate the cause of respiratory symptoms; for example, shortness of breath (SOB), cough, haemoptysis etc. It is an examination with thin section acquisition protocol having two windows: the lung window for pulmonary parenchymal assessment, and the soft tissue window for gross mediastinal abnormalities and calcifications. CT displays the density of body tissues according to various shades of grey, varying from white to black. The human eye can appreciate only a few shades, but CT scanner can assess more than a thousand levels. It depicts minute differences in blood density/attenuation, which is due to the Hb concentration (conc.).[3]

In 2013, Bruni SG et al.[4] found a positive correlation between attenuation values of cranial venous drainage and anaemia, concluding that for every 1 Hounsfield unit (HU) increase in average torcular attenuation, also known as the confluence of sinuses, the Hb level increased 1.63g/L.

By measuring HU attenuation values, the reporting radiologist can alert the physician about anaemia and can add more value to the diagnostic exam.

The current study was planned to determine the accuracy and precision of anaemia diagnosis with plain CT chest by keeping complete blood count (CBC) as the gold standard.

Materials and Methods

The retrospective cohort study was conducted from January 1 to December 31, 2020, at Dow University of Health Sciences (DUHS), Ojha campus, Karachi after IRB approval- IRB-2743/DUHS Approval 2022/1096, and comprised patients who attended the hospital regardless of gender or age. Principal Investigator extracted the data from HMIS in December 2022. Patients who underwent

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transfusion and who were hydrated via intravenous (IV) route were excluded, and so were those having incomplete information, blurring artefacts on CT. The subjects underwent CBC and HRCT scan of chest with 7-day interval. Hb and haematocrit (Hct) levels were recorded. CBC data was automatically analysed using a haematology analyser (Sysmex XN-3000TM).

The reference range for Hb was 12.0-15.0g/dl, and for Hct it was 36-46%. The diagnosis of anaemia in men was based on Hb <13.0g/dl, and in women, it was <12g/dl.[5] The anaemia was classified into mild >11-<12g/dl, moderate >8.0-<11.0g/dl and severe <8.0g/dl. On the basis of haematology, the subjects were divided into anaemic group A and control group B. HRCT chest was done at 16- and 128-slice scanner (Siemens 16 slice, Germany, Hitachi 16 slice, Japan and GE 128 slice scanner, USA) with standard CT protocol. Consecutive non probability sampling technique was applied. Retrospective Data was extracted via Excel match function for health management information systems (HMIS) picture archiving and communication system (PACS) database for CBC and HRCT records.

Using a digital imaging and communications in medicine (DICOM) workstation, quantitative assessment of blood attenuation/ HU measurements was done by a radiologist blinded to CBC data. Region of interest (ROI) attenuation cursor with 2-2.5cm^2 was placed within right ventricular chamber (RVC), left ventricular chamber (LVC) in soft tissue window settings (WW: 350; WL: 30) on axial CT sections. The arbitrary cut-off value selected for anaemia prediction at CT was <35HU, which was equivalent to CT quantitative diagnosis. The inter-ventricular septum (IVS) visualization was equivalent to qualitative diagnosis (Figure 1).

Average attenuation values were calculated for RVC and LVC.

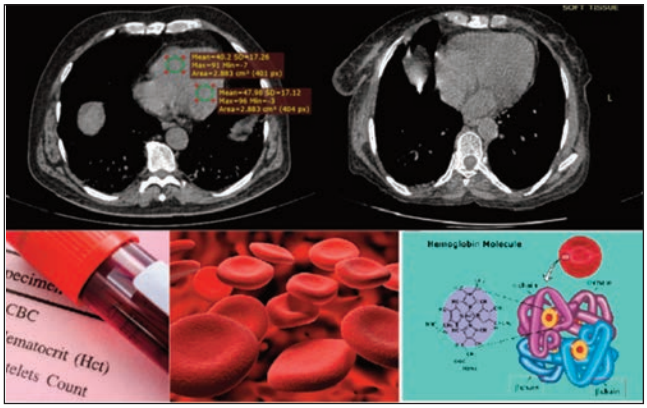

Figure-1: Top row: Axial plain computed tomography (CT) chest demonstrating region of interest (ROI) attenuation cursor over the blood poles. Inter-ventricular septum (IVS) was visualised in anaemic patients. Bottom row: Laboratory work and haemoglobin (Hb) structure.

After approval from the institutional ethics review board, the sample size of at least 536 patients was calculated using PASS 15 based on one-sample sensitivity and specificity test with 95% confidence interval (CI), sensitivity 76%, specificity 81%, and disease prevalence 26%.[6]

Data was analysed using SPSS 17. Chi-square test was used to assess the association between the variables. The sensitivity, specificity, diagnostic accuracy, positive predictive value (PPV), negative predictive value (NPV), receiver operating characteristics (ROC) curve for CT diagnosis of anaemia was calculated, as per the Standards for Reporting of Diagnostic Accuracy Studies (STARD) 2015 guidelines).[7] Pearson correlation was used to assess the correlation between the attenuation values and Hb concentration. Intra-observer reliability for HU measurements in RV and LV was assessed using Cohens' Kappa and intra-class correlation (ICC) coefficient for precision. P<0.05 was considered significant.

Results

Of the 124 subjects, 62(50%) were males and 62(50%) were females. The overall mean age was 51.45±17.3 years (range: 8-96 years). On the basis of haematology, 74 (59.6%) subjects were in group A and 50 (40.3%) were in group B. Among those with anaemia, 10.8% were severely anaemic.

The mean blood HU measurement in group B was 42.2±7.37 (range: 26-67) and it was 35.5±8.9 (range: 16-53) in group A. ICC coefficient for HU attenuation values was 0.74 with 95% CI (Kappa: 0.531; p<0.001).

There was no correlation of Hb conc. with RVC blood HU values (r=-0.08), and there was a small correlation of Hb with LVC blood HU values (r=-0.34).

The sensitivity, specificity, PPV, NPV and diagnostic accuracy of chest CT for quantitative diagnosis of anaemia were 48.6%, 76.5%, 76.5%, 50.6% and 60.5% respectively (Table-1). The corresponding values for qualitative

Table-1: Diagnostic accuracy of plain computed tomography (CT) findings for quantitative diagnosis of anaemia with haematology as the gold standard (n=124).

Anaemia (CT diagnosis)	**Anaemia** (Lab diagnosis)		***p*-value**	**Sensitivity**	48.6%	36.85- 60.56% CI
	Positive	**No**	0.003	**Specificity**	76.5%	64.04- 88.47% CI
Positive	36	11		**PPV**	76.5%	64.88- 85.29% CI
No	38	39		**NPV**	50.6%	44.02- 57.25% CI
Total 124	74	50		**Diagnostic accuracy**	60.5%	51.31- 69.14% CI

Gender	**Anaemic Subjects (n)**	**Sensitivity %**	**Specificity %**	**Diagnostic Accuracy %**
Male	42	76	62.7	67.6
Female	35	77	37	51.6

PPV: Positive predictive value, NPV: Negative predictive value, CI: Confidence interval; ***p*-value is significant at 0.005 levels;** Diagnostic accuracy: (True positive [TP] + True negative [TN] / TP+ False positive [FP] + TN + False negative [FN]) * 100; Sensitivity = (TP/ TP + FN) * 100; Specificity = (TN /TN + FP)* 100; PPV = (TP/ TP + FP) * 100; NPV = (TN /TN + FN)* 100.

Table-2: Diagnostic accuracy of plain computed tomography (CT) findings for qualitative diagnosis of anaemia with haematology as the gold standard (n=124).

Visualization of IVS	Anaemia (n= 74)	Control group (n=50)	*p*-value*			
Total sample population (n=124)			<0.001	**Sensitivity**	55.4%	43.39- 66.98% CI
				Specificity	88.0%	75.69- 95.47% CI
Positive (n= 47)	41 (TP)	6 (FP)		**PPV**	87.2%	75.84- 93.70% CI
Negative (n= 77)	33 (FN)	44 (TN)		**NPV**	57.1%	50.35- 63.68% CI
Total	74	50		**Diagnostic accuracy**	68.5%	59.60- 76.59% CI

PPV: Positive predictive value, NPV: Negative predictive value, CI: Confidence interval, TP: True positive, TN: True negative, FP: False positive, FN: False negative; **p*-value is significant at 0.005 levels.

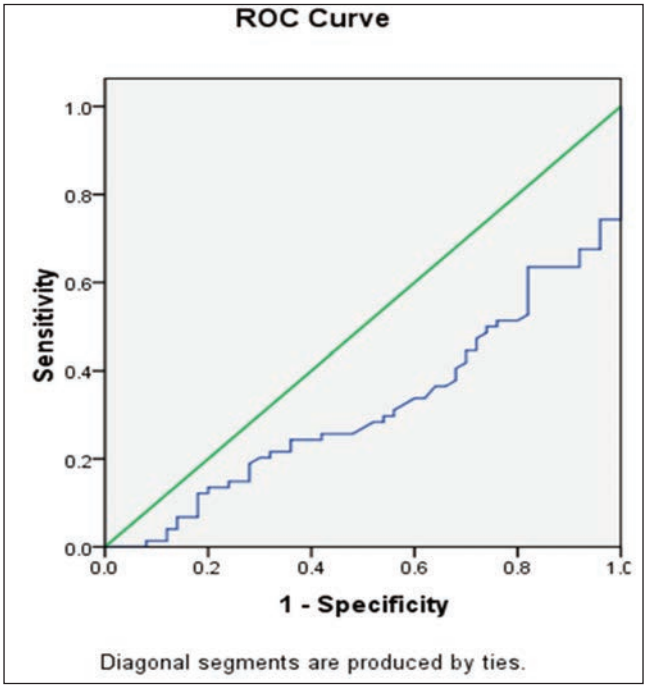

Figure-2: TReceiver operating characteristics (ROC) area under the curve (AUC) for computed tomography (CT) diagnosis of anaemia. The AUC value was 0.312 while for perfect diagnostic accuracy, it needed to be close to 1.0.

diagnosis of anaemia were 55.4%, 88.0%, 87.2%, 57.1%, and 68.5% (Table-2).

IVS was visualised in 47(37.9%) subjects. A significant association between anaemia and IVS visualisation was observed in group A compared to group B ($p<0.001$).

The ROC curve was skewed toward the left side and AUC was 0.312. The exact cut-off attenuation value was 32HU with true positive (TP) rate up to 61.8% for quantitative anaemia prediction. ROC analysis ranked a random positive example higher than a random negative example <50% of the time (Figure 2).

Discussion

The linkage between CT blood density and Hb has been reported in the literature by a variety of qualitative and quantitative means. Patil NG et al. in 2017 found a good correlation with (r=0.63_ between aortic CT HU values and Hb levels.[8] A.J. Collins et al.[9] in 2001 studied patients undergoing CBC and plain CT within 3 days by putting ROI cursors at IVC and aorta. They found a significant positive correlation between Hb-IVC and Hb-aorta attenuation value with (r=0.57 and r=0.64, respectively), whereas the present study noted comparatively lower values (r=0.08 and r=0.34 for Hb-RV and Hb-LV, respectively).

E. Di Giandomenico et al[10] studied quantitative blood assessment at aorta and IVC, and correlated with Hb, RBC count and Hct. High positive correlation was found in vitro and in vivo for HU-Hb (r=0.76), for Hb-RBC (r=0.68), and for Hb-Hct (r=0.75). They found an attenuation cut-off for anaemic-normal blood difference as 33HU for females and 36HU for males. The attenuation coefficient was selected as 35HU in the present study.

E.M. Kamel et al.[11] examined aortic CT attenuation values and Hb levels and reported good correlation (r=0.60), with anaemia threshold of ≤35HU, while the sensitivity and specificity values of aortic CT HU were 84% and 94%, respectively. Zhou QQ et al.[12] in 2003 found high accuracy of plain CT chest for severe anaemia in 317 patients, with sensitivity and specificity up to 94.7% and 83.6% in males, and 82.4% and 84.6% in females, whereas it was fine and low for moderate and mild anaemia respectively. This study had good intra- and inter-observer reliability (ICC=0.99). Title R.S. et al.[6] assessed observer performance for anaemia quantitatively and qualitatively on thoracic CT. Again, there was a good correlation between HU and Hb level (r=0.72). The anaemia threshold was <35HU, with 76% sensitivity and 81% specificity. Inter-observer agreement was poor (kappa=0.09-0.21). HU measurements performed better than subjective reviewer analyses for anaemia diagnosis.

Lan H. et al.[13] placed ROI cursors in the LV cavity, thoracic and abdominal aortic lumens, inferior vena cava, and IVS, and found that the difference in CT attenuation between LV and IVS was the best quantitative method for anaemia diagnosis. Foster M. et al.[14] also concluded that anaemia should be suggested when IVS is visible on plain CT chest.

Fino-Velásquez L. et al.[15] was also convinced that plain CT chest is a useful diagnostic tool for anaemia. The lumen of mediastinal vessels were analysed in 130 CT that showed high accuracy; aortic ring and the IVS sign proved specific signs for anaemia detection.[14] Doppman JL et al.[16] also emphasised IVS visualisation as a sign of anaemia, similar to the present study.

Y. Sato et al.[17] previously conducted a CT study in 113 subjects comparable to the present study regarding the

qualitative and quantitative diagnoses of anaemia. They divided subjects into groups according to the visualisation of cardiac muscle, and found significant differences between the groups with Hb-HU correlation attenuation value 0.76.

In 2012, Jung C et al.[18] emphasised documentation of anaemia at CT pulmonary angiography (CTPA) studies since it can increase risks of morbidity and mortality. HU measurements, made by two observers showed high intra- and inter-rater agreement (ICC>0.98 and ICC>0.96), whereas in the present study, it was 0.74. Their study showed linear positive correlation between Hb-HU values and high sensitivity (men 80.4%, women 91.3%) and specificity (men 84.0%, women 84.9%). In the present study, it was 76%, 62.7%, and 77%, 37% respectively.

Attenuation values at virtual non-contrast (VNC) dual-energy CT (DECT) produced images similar to plain CT images in nearly all tissues. In contrast to conventional CT, where one X-ray tube is used to create images, DECT/Spectral CT uses two separate X-ray energy spectra with different attenuation with image generation via subtraction of iodine from contrast images.[19,20]

Zopfs et al.[21] in 2020 examined LV and descending thoracic aortic lumen at VNC- DECT chest, and found significant HU differences among healthy and those with mild, moderate and severe anaemia, and found a moderate correlation between Hb and HU measurements (r^2=0.54).

Dehydration can cause falsely high Hct and Hb with possibly false interpretation of anaemia.[22] According to present clinical experience, patients are referred by clinicians for CT chest after correction of acute conditions. The major drawback found in nearly all the anaemia studies done compared to CBC, including the present study, is that there exists an overlapping grey zone of CT HU values ranging 30-40 compared to the exact cut-off value of Hb in CBC in a significant number of patients, which causes reduced diagnostic accuracy. It was evident in a study in which all 13 CT scans with Hb range 7.6-10.2gm/dl were anaemia-positive, all 14 CT scans with Hb range 12.9-16.0gm/dl were anaemia-negative, while only 47% of 23 scans with Hb ranging 10.5-12.8gm/dl were anaemia-positive.[23] Low AUC was also the unfortunate outcome. The possibility of using this tool in a busy department also needs to be assessed, keeping in view the widespread availability of CBC.

The current study, to the best of our knowledge, is the first of its kind in Pakistan. However, the study has its limitations as conclusions were extrapolated from a small sample size when repeat analysis over a longer time period could have provided better evidence. As against a required sample size of 536, the current study had 124 subjects. A small sample is justified considering the low-resource setting in which the study was conducted. Besides, studies with small size are also published in international journals.[6,10]

Conclusion

Overall, the quantitative diagnosis of anaemia on plain CT chest had high PPV, low diagnostic accuracy and moderate reliability.

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MH: Design, data analysis and interpretation.
AS, NN: Revision and final approval.