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ORIGINAL RESEARCH

Hemoglobin Estimation using Hounsfield Unit Measurements on the Single Nonenhanced Computed Tomography Abdomen Scan and Its Correlation with Biochemically derived Hemoglobin

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ABSTRACT

Aim:

- To find the correlation of Hounsfield unit (HU) values with biochemically derived values of hemoglobin (Hb).
- To postulate new radiological formula for the estimation of Hb.
- To evaluate interventricular septum (IVS) and its attenuation difference with the ventricle for diagnosis of anemia.
- Accurate Hb estimation in emergency set-up (including trauma) for patient requiring computed tomography (CT) scan.

Materials and methods: A total of 200 random adult patients who had undergone CT abdomen-chest were enrolled in the study: 52% males, mean age 30 ± 15 SD, and 48% females, mean age 30 ± 14 SD. The two groups were then subdivided into anemic and normal subjects, 10 gm/dL being taken as the borderline values for males and females.

Blood density (HU) was measured after defining three regions of interest (ROI) on the aorta, inferior vena cava (IVC), and left ventricle (LV). Visualization/nonvisualization of the IVS distinct from blood density of LV was also assessed.

Results: Correlation between HU and Hb concentration was seen *in vivo* (r = 0.73, $p < 0.001$). When the mean density value was 42 HU in our sample, the expected Hb value was 12.6 gm/dL (± 1.5 SD).

A significant difference of blood attenuation values was present between normal subjects and anemic patients ($p < 0.001$). This difference identifies the cut-off density value, below which the patient is sure to be anemic: the value is different for males and females (33 HU for females and 36 HU for males).

- A formula for Hb estimation by using HU values has been figured out.
- Visualization of the IVS in non-enhanced computed tomography is an indirect marker of anemia (99% confidence).
- Hb estimation by CT before biochemical reports arrived proved beneficial to the patient in acute trauma setting.

Discussion and conclusion: It is an observational study in which a new formula for estimation of Hb can be given radiologically and in emergency set-up (including trauma), and CT scan may guide an accurate value of Hb estimation before biochemical results are revealed.

Keywords: Hemoglobin, Hounsfield unit, Non-enhanced computed tomography.

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INTRODUCTION

The HU scale is a linear transformation of the original linear attenuation coefficient measurement into one in which the radiodensity of distilled water at standard pressure and temperature (STP) is defined as zero HU, while the radio density of air at STP is defined as –1000 HU. The HU values are calculated on CT images and are approximately fixed for all tissues in the body.

The HU values change with varying density of the organ or fluid. A change of every single HU represents a change of 0.1% of the attenuation coefficient of water since the attenuation coefficient of air is almost zero. This variability of the HU values depends on the density of the fluid and can be used for correlation of the different body fluids like blood, ascitic fluid, pleural fluid, etc. The contrast resolution of current CT scanners can detect differences in contrast less than 5 HU (<0.5%).

Patients undergo CT, particularly in the acute situation who often lack an accompanying hematologic laboratory values at the time of imaging. Of these, the diagnostic significance is the Hb level, a low value that can be associated with a considerable number of abnormalities. The capacity to identify anemia as an incidental finding on CT has the potential to significantly influence patient management and outcome.[2]

On noncontrast CTs, the attenuation coefficient of *in vitro* blood relates primarily to the concentration of erythrocytes and Hb—globin moiety, with minimal contribution from the Hb iron content.[3] By comparing the degree of intravascular attenuation with that of the adjacent vessel wall, many radiologists can correctly diagnose patients who are anemic by subjective (visual) inspection alone.[4]

Furthermore, objective analyses (with HU measurements) of thoracic and abdominal CTs are able to differentiate between healthy subjects and anemic patients.[5-10] Density measurements play a crucial role in the diagnosis and management of certain disease processes. Computed tomography density measurements of intravascular blood by Di Giandomendico et al[6] showed a significant difference in HU values between healthy subjects and anemic patients. This study identified the cut-off density values of 33 HU for women and 36 HU for men, below which the diagnosis of anemia could be made with 99% confidence.

Despite the presence of evidence of the efficacy of objective attenuation measurements in the assessment of anemia, it is observed that the diagnosis of anemia is rendered by many reviewers based on visual inspection and that objective measurement is seldom performed for confirmation.[6] Furthermore, studies of the accuracy of objective measurements have also been scarce, and sample sizes of these studies have been small.

Experienced radiologists are able to visually appreciate minor variations in attenuation between adjacent tissues on CT images. The measured attenuation value is always reproducible physical density measurement, which is readily obtainable from a standard CT examination. A correlation between attenuation value and plasma Hb may permit the identification of anemia at CT examination.[7]

During interpretation of noncontrast CT scans of the chest or abdomen performed for other indications, some radiologists may comment on the density of the blood within the various vessels and cardiac chambers. It is assumed by many radiologists that we can usually diagnose anemia (Hb<10 gm/dL) in patients simply by comparing the attenuation of blood in noncontrast studies with the adjacent vessel wall or myocardium.

A study by Powell et al[11] revealed that in the low-Hb state, the right and left ventricular cavities become clearly visible in canine hearts, thus making it possible to distinguish readily walls, the papillary muscles, the major trabeculae, and the aorta. Conventional wisdom and anecdotal clinical experience support these findings; however, their validity in *in vivo* human heart has not, to our knowledge, been studied extensively till date.

AIMS AND OBJECTIVES

- To find the correlation of HU values with biochemically derived values of Hb (Tables 1, 2 and 3).
- To postulate a new radiological formula for the estimation of Hb.
- To evaluate the IVS and its attenuation difference with the ventricle for diagnosis of anemia.
- Accurate Hb estimation in emergency set-up (including trauma) for patients requiring CT scan.

MATERIALS AND METHODS

Study Design

This is a noninterventional retrospective observational study. The study included both men and women.

Duration of Study

12 months.

Study Setting

The CT Scan Department, Department of Radiology, Seth G.S. Medical College and KEM Hospital, Parel, Mumbai. The study was carried out over the given duration with the approval of the Institutional Ethics Committee, Seth G.S. Medical College and KEM Hospital.

Approximate Subjects

The total number of patients was 200. Out of all the patients referred to us, the patients who met the inclusion criteria were evaluated and patients in whom CT scan abdomen was done for other purpose as requested by the referring clinician. Patient had to never undergo CT scan specifically for this study purpose. It included both outpatients and inpatients.

Inclusion Criteria

All patients of age more than 20; patients having registration at this institute; patients in whom CT abdomen scan was indicated; and patients with a history of abdominal trauma were also included.

Exclusion Criteria

Patient not willing for the study; age less than 20 years.

Study Procedure

All studies were performed on a PHILIPS 64 slice Brilliance CT unit.

The CT data were obtained with following parameters: Field of view: 350 mm; thickness: 2 mm; increment 1 mm; filter standard B window 60 window W 360 matrix 512. An age-based standard low-dose [Kv-120Mas/slice-220] CT protocol was used. During CT, patients were told to hold their breath. Only unenhanced scan was done without using contrast. Scanning was performed from lower thoracic level to the pubic symphysis in patients. The CT was performed in the craniocaudal direction. The CT was performed during quiet breathing in patients who cannot hold their breath.

Before the scan, essential clinical history was obtained along with the Hb values of those patients in whom serum Hb test was done for other purpose. Blood collection was not done specifically for the study purpose. The method used for Hb estimation used in our institute is fully automated cell counter method, which uses the principle of cyanmethemoglobin. The principle behind this method lies in the conversion of Hb to cyanmethemoglobin by the addition of potassium cyanide and ferricyanide whose absorbance is measured in a photoelectric calorimeter at 540 nm against a standard solution. The Electronic Recording Machine, Accounting which gives three part differential is used in our institute.

Blood density was quantified by measuring CT attenuation values (HU) by means of ROIs of 3 mm^2 drawn over LV at its maximum diameter, aorta, and IVC at the level of gastroesophageal (GE) junction separately. For each individual patient, presence or absence of dense IVS against the hypodense left ventricular cavity was determined (Tables 4 and 5).

Table 1: Correlation between HU values and biochemically derived Hb of LV, aorta, and IVC in total population (n = 200)

		Correlation coefficient, r	*Sig.*	*95% CI*
n = 200	LV	0.816	p<0.0001	0.764
				0.857
	Aorta	0.752	p<0.0001	0.685
				0.806
	IVC	0.812	p<0.0001	0.759
				0.854

Table 2: Correlation between HU values and biochemically derived Hb of LV, aorta, and IVC in males (n = 116)

		Correlation coefficient, r	*Sig.*	*95% CI*
n = 116	LV	0.844	p<0.0001	0.783
				0.889
	Aorta	0.761	p<0.0001	0.672
				0.828
	IVC	0.836	p<0.0001	0.772
				0.883

Table 3: Correlation between HU values and biochemically derived Hb of LV, aorta, and IVC in females (n = 84)

		Correlation coefficient, r	*Sig.*	*95% CI*
Females, n = 84	LV	0.739	p<0.0001	0.624
				0.823
	Aorta	0.72	p<0.0001	0.598
				0.809
	IVC	0.746	p<0.0001	0.633
				0.827

DISCUSSION

Our study included 200 patients in whom CT scan abdomen was done for some other purpose. Scanning was performed from lower thoracic level to the pubic symphysis in patients. The CT was performed in the craniocaudal direction and was performed during quiet breathing in patients who could not hold their breath.

Table 4: Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of LV, aorta, and IVC for the diagnosis of anemia in total population (n = 200)

	n = 200					
	LV		*Aorta*		*IVC*	
Correlation coefficient, r	0.816		0.752		0.812	
Sig.	p<0.0001		p<0.0001		p<0.0001	
95% CI	0.764	0.857	0.685	0.806	0.759	0.854
	LV		*Aorta*		*IVC*	
	A	34	A	49	A	51
	B	62	B	47	B	45
	C	0	C	2	C	2
	D	104	D	102	D	102
	N	200		200		200
Sensitivity		100.0		96.1		96.2
Specificity		62.7		68.5		69.4
Positive predictive value		35.4		51.0		53.1
Negative predictive value		100.0		98.1		98.1
Accuracy		69.0		75.5		76.5

Table 5: Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of LV, aorta, and IVC for the diagnosis of anemia in males (n = 116)

	Males (n = 116)					
	LV		*Aorta*		*IVC*	
Correlation coefficient, r	0.844		0.761		0.836	
Sig.	p<0.0001		p<0.0001		p<0.0001	
95% CI	0.764	0.857	0.685	0.806	0.759	0.854
	LV		*Aorta*		*IVC*	
	A	18	A	23	A	27
	B	29	B	24	B	20
	C	0	C	1	C	0
	D	69	D	68	D	69
	N	116		116		116
Sensitivity		100.0		95.8		100.0
Specificity		70.4		73.9		77.5
Positive predictive value		38.3		48.9		57.4
Negative predictive value		100.0		98.6		100.0
Accuracy		75.0		78.4		82.8

Table 6: Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of LV, aorta, and IVC for the diagnosis of anemia in females (n = 84)

Females (n = 84)						
	LV		*Aorta*		*IVC*	
Correlation coefficient, r	0.739		0.72		0.746	
Sig.	p < 0.0001		p < 0.0001		p < 0.0001	
95% CI	0.764	0.857	0.685	0.806	0.759	0.854
	LV		*Aorta*		*IVC*	
	A	16	A	26	A	24
	B	33	B	23	B	25
	C	0	C	1	C	2
	D	35	D	34	D	33
	N	84		84		84
Sensitivity		100.0		96.3		92.3
Specificity		51.5		59.6		56.9
Positive predictive value		32.7		53.1		49.0
Negative predictive value		100.0		97.1		94.3
Accuracy		60.7		71.4		67.9

Table 7: Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of IVS sign for the diagnosis of anemia in total population (n = 200), males (n = 116), and females (n = 84)

IVS sign						
	All (n = 200)		*Males (n = 116)*		*Females (n = 84)*	
	A	38	A	19	A	19
	B	60	B	28	B	30
	C	0	C	0	C	0
	D	102	D	69	D	35
	N	200		116		84
Sensitivity		100.0		100		100
Specificity		63.0		71.1		53.8
Positive predictive value		38.8		40.4		38.8
Negative predictive value		100.0		100		100
Accuracy		70.0		75.9		64.3

Table 8: Frequency table of IVS sign

		Frequency	*%*	*Valid %*	*Cumulative %*
Valid	Y	38	19.0	19.0	19.0
	N	162	81.0	81.0	100.0
	Total	200	100.0	100.0	

Before the scan, essential clinical history was obtained along with the Hb values of those patients in whom serum Hb test was done for other purposes.

Out of the sample study of 200, sex distribution was: 116 males comprising 58% and 84 females comprising 42%; random selection was done to avoid gender bias and all those meeting inclusion criteria were included (Tables 6 and 7). Age group range for population in the study was from 20 to 86 years with a mean age of 42 years. Majority of patients comprising the sample population were in between 30 and 60 years of approximately 60% of the study population, possibly due to the underlying referral system of patients to the Department of Radiology in our institute over the given duration of study.

Blood density was quantified by measuring CT attenuation values (HU) by means of ROIs of 3 mm^2 drawn over the LV at its maximum diameter, aorta, and IVC at the level of GE junction separately. For each individual patient, presence or absence of dense IVS against the hypodense left ventricular cavity was determined (Table 8).

Using statistical analysis, correlation of Hb with HU values of IVC, aorta, and LV was determined separately (Table 9), and correlation coefficient r value and p value for significance with confidence interval (CI) were obtained and the results are summarized in Table 10. Title et al,[4] in a similar study, performed using unenhanced CT thorax and showed that correlation coefficient for the analysis of attenuation values in LV (HU) *vs* Hb was 0.72. Separating data by sex revealed correlation coefficient of 0.81 for men *vs* 0.52 for women.

Collins et al,[7] in a study of noncontrast CT of thorax or abdomen, showed that correlation coefficient for the analysis of aortic, IVC attenuation value, and Hb was stronger with "r" value of 0.64 and 0.58, respectively. The cut-off value of 11 gm/dL was taken for diagnosis of anemia. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were determined for all diagnostic statistics for correlation of Hb with HU values separately for LV, aorta, and IVC for diagnosis of anemia (Table 11).

In our study population of 200, for diagnosing anemia using CT attenuation values (HU), LV was most sensitive, however, not specific and accurate as aorta and IVC. Overall, IVC was sensitive, specific, and had higher diagnostic accuracy compared with LV and aorta. The IVS sign being positive or negative was determined by identifying IVS as relatively

Table 9: Formula to assess Hb based on HU values of LV, aorta, and IVC

Formula to assess Hb based on biological parameters			
Parameters	*All*	*Males*	*Females*
LV	−2.214 + 0.355 × LV	−2.329 + 0.341 × LV	−1.417 + 0.310 × LV
Aorta	−0.411 + 0.292 × Aorta	−1.117 + 0.311 × Aorta	0.963 + 0.252 × Aorta
IVC	0.275 + 0.271 × IVC	0.042 + 0.280 × IVC	1.137 + 0.244 × IVC

Table 10: Correlation coefficient, significance, and 95% CI in total 200 population, males, and females

Correlation of HU vs biochemically derived Hb			
Parameters	*All*	*Males*	*Females*
LV	0.816	0.844	0.739
Aorta	0.752	0.761	0.72
IVC	0.812	0.836	0.746
IVS	0.651	0.642	0.685

Table 11: Sensitivity, specificity, accuracy of LV, aorta, and IVC in the diagnosis of anemia in total population, males, and females

Parameter	*Sensitivity (%)*	*Specificity (%)*	*Accuracy (%)*
LV	100	62.7	69
Aorta	96.1	68.5	75.5
IVC	96.2	69.4	76.5

Table 12: Sensitivity, specificity, PPV, NPV, and accuracy of IVS sign in the diagnosis of anemia in total population, males, and females

	IVS sign					
	All (n = 200)		*Males (n = 116)*		*Females (n = 84)*	
	A	38	A	19	A	19
	B	60	B	28	B	30
	C	0	C	0	C	0
	D	102	D	69	D	35
	N	200		116		84
Sensitivity	100.0		100		100	
Specificity	63.0		71.1		53.8	
Positive predictive value	38.8		40.4		38.8	
Negative predictive value	100.0		100		100	
Accuracy	70.0		75.9		64.3	

hyperdense structure as compared with the hypodense ventricular cavity in patients suffering from anemia.

Correlation between IVS sign and anemia was done and statistically it showed significant correlation with correlation coefficient of 0.651. Out of 200 sample population, 102 people were negative for IVS sign and were nonanemic and 38 had IVS sign positive and were anemic; 60 had IVS sign positive but were nonanemic and none had IVS sign negative but were anemic.

Thus, the IVS sign has a sensitivity of 100%, specificity of 63% with diagnostic accuracy of 70%. There was mild alteration with regard to the sex of the population. Results are tabulated in Table 12. Title et al,[4] using unenhanced CT thorax quantitatively, attempted to identify anemic from nonanemic patients, keeping the threshold Hb as 10 gm/dL for differentiating anemia from nonanemia and using HU values of LV which showed sensitivity of 72% and specificity of 83%.

However, Title et al[4] attempted qualitative analysis using visualization of images. It was done by three reviewers with a five-point scale, which included IVS sign to classify patients as anemic, indeterminate, and nonanemic. In our study, for the first time, we tried to investigate and derive Hb level from the available data of CT attenuation values (HU) of IVC, aorta, and LV.

However, the degree of correlation is not that strong enough to provide accurate Hb value; however, the possible value and to greater extent the presence and absence of anemia could be identified. Formulas were deduced with our data for evaluating Hb using HU values of IVC, aorta, and LV separately. The formula for males and females was separate, which can help to classify anemic from nonanemic.

Limitations

There were several potential limitations of this study. These include the radiodensity inconsistencies and artifacts like nonideal geometry, scattered radiation, beam hardening, metal artifacts, partial reconstruction, and exo-masses hindering in obtaining ROI in the aorta, IVC, which are closer to the bone, and use of different energy for scanning as HU depends on μ and μ depends on the energy provided in the form of kiloelectronvolt. There were subjective variations in assessing IVS by visualization, as it varies from observer to observer, i.e., interobserver variation.

SUMMARY AND CONCLUSION

Prevalence of anemia has been recently shown to be more common in Indian population. Despite this fact, anemia remains a neglected and undertreated diagnosis. Consequently, every effort must be done to identify and treat anemia as early as possible to avoid many unnecessary comorbidities. We studied 200 people who underwent CT scan for some other purpose and had got their Hb levels, and we found that our results demonstrate a significant correlation between the biochemically derived Hb assay and the CT attenuation values of LV, aorta, and IVC.

In addition, we have defined subgroups of anemic and nonanemic patients, and shown that IVS sign which, although subjective, is of great importance in differentiating them. We found that IVC attenuation values were of high diagnostic accuracy in correlation with Hb values for the diagnosis of anemia. This allows the accurate pinpointing of anemia at unenhanced CT examination, and we conclude that this readily available information may provide a valuable adjunct in the interpretation of such examinations.

In some metabolic diseases such as secondary hemochromatosis and glycogen storage disease, excess cardiac iron or glycogen would result in a relative increase in the interventricular density despite normal Hb levels giving false-positive results.

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