



## Study to infer out any co existing relationship between haemoglobin level and bone mineral density in pregnant: A prospective study

Dr. Mahaveer Meena<sup>1</sup>, Dr. Sunita Meena<sup>2\*</sup>, Dr. Saksham Sharma<sup>3</sup>, Dr. P Jhanwar<sup>4</sup>

<sup>1</sup> Assistant Professor, Department of Orthopaedics, S.R.G. Hospital and Jhalawar Medical College, Jhalawar, Rajasthan, India

<sup>2</sup> P.G. Resident, Department of Physiology, S.R.G. Hospital and Jhalawar Medical College, Jhalawar, Rajasthan, India

<sup>3</sup> P.G. Resident, Department of Orthopaedics, S.R.G. Hospital and Jhalawar Medical College, Jhalawar, Rajasthan, India

<sup>4</sup> Principal, Department of Orthopaedics, S.R.G. Hospital and Jhalawar Medical College, Jhalawar, Rajasthan, India

### Abstract

Bone mineral density (BMD) is the amount of bone mineral in bone tissue and its measurement is used in clinical medicine as an indirect indicator of osteoporosis and fracture risk. Anemia is a commonly encountered clinical condition with iron deficiency anemia being more common in females especially pregnant. This study aims to predict the hypothesis that there exists a directly proportional relation between haemoglobin level and bone mineral density. This study was conducted as an interdepartmental exercise done by Department of Orthopaedics and Physiology of SRG Hospital and Jhalawar Medical College, Jhalawar (Raj.). Total of 100 patients were included in the study 50 acting as control (hb levels above 9gm %) and rest as test (hb levels between 9-7gm%). Decreased bone mineral density and its association with haemoglobin levels is proven in various studies, our study though have a small sample size but it predicts a directly proportional relation between haemoglobin levels and T-Score.

**Keywords:** bone mineral density, anemia, osteoporosis

### 1. Introduction

Bone mineral density (BMD) is the amount of bone mineral in bone tissue the concept is of mass of minerals per volume of bone although clinically it is measured by proxy according to optical density per square centimetre of bone surface upon imaging <sup>[1]</sup>, bone density measurement is used in clinical medicine as an indirect indicator of osteoporosis and fracture risk

Physiology: Bone is a connective tissue which is in active or dynamic state, as it continuously remodels itself to adapt to the influence of growth and change in mechanical load, to maintain mineral haemostasis and to regulate the marrow environment. bone tissue is composed of type I collagen, organic components like fibronectin, osteonectin etc and inorganic phase mainly of Calcium and phosphate (hydroxyapatite,  $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ) <sup>[2]</sup>.

Bone modelling is defined as a process in which bone is removed from one site and deposited at other during growth <sup>[3]</sup>, while once the skeleton is mature, regeneration continues to maintain skeleton integrity by removing the foci of damaged bone and replacing it with new, this process is called bone remodelling <sup>[4]</sup>.

Bone remodelling occurs in 4 phases: activation, resorption, reversal and formation <sup>[5, 6]</sup>, the activation phase consists of differentiation of osteoclast precursor into osteoclast and their activation<sup>5</sup>, under the influence of 2 cytokinin's, macrophage colony stimulating factor (M-CSF) and receptor activator of NF-  $\kappa$ B ligand (RANKL), s activated osteoclast begins the resorption phase by adhering to bone and resorbing it by

acidification and proteolysis of bone matrix.

After resorption is the reversal phase in which the osteoclast transits into osteoblast, there is osteoclast apoptosis and osteoblast maturation, once the osteoblast are mature they lay down the osteoid which is eventually mineralised making the stage of formation.

The main mechanism underlying osteopenia and the osteoporosis involves abnormal bone remodelling, an imbalance in bone turnover between osteoclast which creates an excessively deep cavity and osteoblast which refits the normal resorption cavity <sup>[7, 8]</sup>.

Anemia is a commonly encountered clinical condition with iron deficiency anemia (microcytic) being more common in females especially pregnant.

### Probable role of iron in bone metabolism

1. Iron participates in collagen synthesis which is major component of bone structure the physiology involved is, for conversion of procollagen into collagen, hydroxylation of prolyl and lysyl for which iron as a cofactor is needed <sup>[9, 10]</sup>.
2. Iron via cytochrome P450 is essential in vitamin D metabolism which inturn regulates bone metabolism<sup>11</sup>.
3. Another mechanism is hypoxia, which occurs in anemia and is a major stimulator of bone resorption inducing osteoclast genesis which later is followed by osteoblast genesis <sup>[12, 13]</sup>.

This study aims to predict the hypothesis that there exists a

directly proportional relation between haemoglobin level and bone mineral density.

## 2. Material and method

This study was conducted as an interdepartmental exercise done by department of orthopaedics and physiology of SRG Hospital and Jhalawar Medical College, Jhalawar (Raj.). The study was done as a OPD process, bone mineral density was measured using ultrasound BMD machine at mid- tibia shin, left side was chosen in all to eliminate side biasing.

Total of 100 patients were included in the study 50 acting as control and rest as test, the exclusion criteria was:

1. Early pregnancy (< 6 weeks gestation)
2. Multi gravida (> 3 gravida)
3. Twin pregnancy
4. Associated co-morbidities (like eclampsia, Diabetes, hypo/hyperthyroidism etc)
5. Severe anemia (< 7 gm% hb level)

The study group was broadly divided into 2 groups, those with

Hb levels <9 gm% labelled as test and those with level  $\geq$  9 gm% labelled as control.

The division of the broad group was in accordance to WHO guidelines which grades mild anemic (pregnant) with haemoglobin level between 9 gm% to 10.9 gm% and moderate anemic (pregnant) with haemoglobin level between 7 gm% to 8.9 gm%.

The T-Score evaluation of bone mineral density is inferred out as:

- Above -1: Normal
- 1.1 to -2.4: Osteopenia
- Below -2.5: Osteoporosis

## 3. Results

On comparing the 2 groups with sample size of 50 each a positive correlation between haemoglobin levels and T-Score(BMD Score) can be inferred out, as out of 50 test patients 45 had T-Score levels below the normal range.

**Table 1:** Test Group Hb Levels and T-Score

S.no.	Name	w/o	Age	Trimester	Gravida	hb (gm%)	T-score
1	kiran	sanjay	23	3	2	8	-1.8
2	laxmi	purilal	24	3	3	8	-2
3	kiran	hemraj	25	3	3	7.2	-2.5
4	khushboo	rahul	22	3	1	8.9	-1.3
5	santosh	balu	25	3	1	8.6	-1.4
6	rijwana	firoj	25	2	2	7	-2.8
7	yashmin	said	24	3	1	8.7	-1.3
8	babli	vishnu	23	3	1	8.8	-1.5
9	sona	rajesh	25	3	2	8.2	-1.4
10	radha	gopal	25	3	4	7.8	-2.2
11	prembai	lakhan	23	2	2	8.2	-1.6
12	anita	dinesh	30	3	1	8.2	-1.7
13	meena	shekhar	22	1	1	8.8	-1.3
14	chandvi	rasik	30	2	3	8.9	-1.1
15	kavita	vijay	26	3	3	8	-1.4
16	lalita	prem	28	3	3	8.2	-1.3
17	narang	bheru	25	3	3	7.4	-1.8
18	manju	govind	22	2	1	7.4	-3.5
19	jyoti	kishor	26	2	2	8.4	-1.8
20	kavita	pappulal	20	3	1	8	-1.9
21	pooja	arvind	21	3	1	8.6	-0.6
22	kavita	dolatram	28	3	3	7.4	-0.9
23	neetu	ashok	25	2	2	8	-0.4
24	arti	shyam	24	3	2	7.2	-3
25	archana	lalchand	25	3	1	7.2	-2.5
26	shivi	shubham	24	2	2	8.4	-1.7
27	muskan	rohit	22	2	2	8.2	-1.9
28	sangeeta	jeetu	28	2	3	8	-1.8
29	neelu	arvind	29	3	4	8.8	-0.5
30	golu	kunal	32	1	2	8.6	-1.6
31	khushboo	shielendra	34	3	2	8.1	-1.8
32	pavitra	rishabh	20	2	2	8.1	-1.7
33	ronak	sunisha	25	2	2	8.9	-1.4
34	mehjabin	salim	26	3	1	7.6	-2.4
35	lalita	mahaveer	22	3	1	7.9	-2.5
36	shajiya	wasim	21	3	3	8.2	-1.9
37	neeta	arpit	27	3	1	8.4	-1.8
38	ruksar	irfan	29	2	1	7.8	-3
39	sunita	manish	24	2	1	7.6	-2.6
40	divya	aditya	24	2	1	8.2	-1.8
41	laxmi	saurabh	26	3	2	8.3	-1.7
42	sahiba	pappulal	22	3	2	8.8	-0.3

43	arti	lalit	30	2	2	8.4	-1.6
44	anjali	devesh	29	2	3	8.7	-1.7
45	diksha	arvind	27	2	1	7.8	-1.9
46	manisha	rajesh	25	2	3	7.4	-2.5
47	meenu	vinod	25	3	2	7.6	-2.4
48	anita	rajendra	24	3	1	8	-1.9
49	bulbul	yashpal	28	2	1	7.8	-2.5
50	dhapu	balikshan	26	2	1	8	-1.9

Whereas out of 50 control patients 47 had T-Score levels within the normal range.

**Table 2:** Control Group Hb level And T-Score

s.no	Name	w/o	Age	Trimester	Gravida	hb (gm%)	T-Score
1	pooja	balkishan	26	3	1	10.1	-0.9
2	pinky	mahaveer	23	2	2	10.8	-0.3
3	deepika	dinesh	32	3	2	9.7	-0.2
4	shintu	dheraj	25	3	1	9.5	0
5	sugna	kashiram	35	3	1	9.4	-0.9
6	shabina	munna	29	3	2	9.5	-0.8
7	parveen	asfaq	33	2	4	10.8	-0.2
8	bhagwati	rambabu	23	3	1	9.8	-0.5
9	mangi	balchand	22	3	1	10.2	-0.4
10	neeta	rajesh	32	2	3	10	-0.1
11	pooja	kamlesh	24	2	2	9.2	-0.2
12	pooja	sitaram	22	3	1	9.8	-2.3
13	kamlesh	surendra	29	3	1	9.2	-1.9
14	sharda	bardhulal	22	3	2	9.3	-0.7
15	Raji	chandraprakash	25	3	2	9.1	-0.6
16	Jyoti	jitendra	21	3	1	10.2	-0.4
17	anita	rajendra	24	3	2	10.2	-0.3
18	geeta	naresh	29	2	3	10	0
19	radha	koshal	20	3	1	9.3	-0.9
20	kavita	sitaram	29	2	2	10.8	0
21	kavita	murlidhar	20	2	1	10.3	-0.8
22	savitri	indrajeet	22	1	1	9.4	-0.8
23	rekha	shivnarayan	38	2	2	10	-0.5
24	anuradha	arvind	26	2	2	10	-0.9
25	padma	meghpal	30	3	2	10.2	-0.2
26	divya	sudhir	32	3	3	10	-0.1
27	pooja	pulkit	28	2	2	9.6	-0.8
28	sangeeta	rajendra	25	2	1	9.8	-0.6
29	shivani	prashant	24	2	1	10.8	-0.2
30	Iram	arif	28	2	3	10.5	-0.4
31	megha	ramswaroop	25	2	2	10.7	-0.3
32	neha	badrilal	26	2	2	9.6	-0.9
33	sanju	rakesh	24	2	2	9.9	-0.7
34	Arti	manoj	28	2	2	10.9	0
35	neha	satish	22	3	1	10.2	-0.4
36	sanjana	arvind	22	1	1	10.1	-0.2
37	komal	rahul	29	3	1	10	-0.3
38	sajya	shrinath	31	3	1	9.5	-0.8
39	sunita	mahendra	30	3	3	9.4	-0.4
40	nandini	navin	35	3	3	9.3	-1.4
41	alfiza	israil	28	2	2	9.8	-0.9
42	pooja	mahesh	27	2	3	10.9	-0.4
43	disha	pankaj	25	2	1	9.7	-0.2
44	manisha	ramesh	26	3	2	10	0
45	pooja	jeetendra	29	3	2	10	-0.5
46	nisha	keshav	23	3	1	9	-0.9
47	tanzim	alfez	22	3	1	10.4	-0.1
48	teena	rahul	21	2	1	10.8	-0.4
49	minakshi	ramchandra	28	2	3	9.7	-0.8
50	aafaina	faizan	24	3	1	9.2	-0.8

Another trend which was also observed was that out of 50 test patients 14 had Hb level between 7 to 7.9 gm% and 11 among them had T-score in the range of osteoporosis.

#### 4. Discussion

Osteoporosis i.e. decreased bone mineral density, is often a subject of interest and various mechanisms causing it or associated with it are subjected to multiple studies by various authors, one of this being its association with anemia.

Till date a number of studies relating anemia with osteoporosis are done for example: study of Korkmaz U et.al.<sup>14</sup> done over postmenopausal Turkish women found out a positive correlation between anemia and osteoporosis,

A nationwide population based study done in Taiwan by Mei-Lien Pan et.al.<sup>[15]</sup> concluded that iron deficiency anemia is a significant and independent risk factor for osteoporosis, in our study we hypothesised that chronic hypoxia due to long term anemia causes decreased bone mineral density which is similar to that studied by Fuzimoto H et.al.<sup>[16]</sup>, Karadag F et.al.<sup>[17]</sup> Laudisio A et al.<sup>[18]</sup> which also concluded the same.

Similar to our study, study by Yun Hwan OH et.al.<sup>19</sup> found that haemoglobin and anemia status were associated with bone mineral density scores.

Laura Toxqui et al.<sup>[20]</sup> gave a hypothesis stating chronic iron deficiency as an emerging risk factor for osteoporosis and concluded that apart from in vitro and animal studies the main work should be done in human prospective studies, haematologic and bone parameters should be determined in different population like woman at child bearing, elderly etc, our study aims to prove the hypothesis justified in child bearing woman

#### 5. Conclusion

Osteoporosis or decreased bone mineral density and its association with haemoglobin levels is proven in various studies but none of these studies were done exclusively in pregnant females, our study though have a small sample size but it predicts a directly proportional relation between haemoglobin levels and T-Score, a larger sample size can be further studied to confirm it, biasing of including females from a defined geographical area, none with severe anemia, excluding other parameters like BMI, Gravida etc is also to be looked for in further studies.

#### 6. References

1. Bone + density at the US National Library of Medicine, Medical Subject Headings
2. Proff P, Romer P. The molecular mechanism behind bone remodelling: A review. *Clin. Oral Investig.* 2009; 13:355-362.
3. Manolagas SC. Birth and death of bone cells: Basic regulatory mechanisms and implications for the pathogenesis and treatment of osteoporosis. *Endocr. Rev.* 2000; 21:115-137. [PubMed]
4. Boyce BF, Rosenberg E, De Papp AE, Duong le T. The osteoclast, bone remodelling and treatment of metabolic bone disease. *Eur. J. Clin. Invest.* 2012; 42:1332-1341. [PubMed]
5. Kular J, Tickner J, Chim SM, Xu J. An overview of the regulation of bone remodelling at the cellular level. *Clin.*

6. Reynaga-Montecinos B, Zeni N. Biochemical markers of bone remodelling. Clinical utility. *Acta Bioquím. Clín. Latinoam.* 2009; 43:177-193. (in Spanish)
7. Riggs BL, Melton LJ. III The prevention and treatment of osteoporosis. *N. Engl. J. Med.* 1992; 327:620-627. [PubMed]
8. Voskaridou E, Terpos E. New insights into the pathophysiology and management of osteoporosis in patients with beta thalassemia. *Br. J. Haematol.* 2004; 127:127-139. doi: 10.1111/j.1365-2141.2004.05143.x.
9. Gorres KL, Raines RT. Prolyl 4-hydroxylase. *Crit. Rev. Biochem. Mol. Biol.* 2010; 45:106-124. [PMC free article] [PubMed]
10. Tuderman L, Myllyla R, Kivirikko KI. Mechanism of the prolyl hydroxylase reaction. 1. Role of co-substrates. *Eur. J. Biochem.* 1977; 80:341-348.
11. Pikuleva IA, Waterman MR. Cytochromes P450: Roles in diseases. *J. Biol. Chem.* 2013; 288:17091-17098.
12. Arnet TR, Gibbons DC, Utting JC, Orriss IR, Hoebertz A, Rosendaal M, Meghji S. Hypoxia is a major stimulator of osteoclast formation and bone resorption. *J. Cell. Physiol.* 2003; 196:2-8. [PubMed]
13. Shiozawa Y, Jung Y, Ziegler AM, Pedersen EA, Wang J, Wang Z, et al. Erythropoietin couples hematopoiesis with bone formation. *PLoS ONE.* 2010; 5:e10853.
14. Korkmaz U, Korkmaz N, Yazici S, et al. Anemia as a risk factor for low Bone mineral density in postmenopausal Turkish women. *Eur J. Intern Med* 2012; 23(2):154-158.
15. Mei-Lien Pan, Li Ru Chen, Hsia- Mei Tsao, Kuo Huchen. Iron deficiency anemia as a risk factor for osteoporosis in Taiwan: a nationwide population based study. *Nutrients.* 2017; 9(6):616.
16. Fujimoto H, Fujimoto K, Veda A, et al. Hypoxia is a risk factor for bone mass loss. *J Bone Miner Metab.* 1999; 17:211-216.
17. Karaday F, Ciddag O, Yurekli Y, et al. Should COPD patient be routinely evaluated for bone ineral density. *J Bone Miner Metab.* 2003; 21:242-246.
18. Laudisio A, Marzetti E, Antonica L, et al. Association of left ventricular failure with bone mineral density in older women: a population based study. *Calcif Tissue Int.* 2008; 82:27-33.
19. Yun Hwan OH. Ji Hyun Moon and Belonz Cho. Association between haemoglobin levels and bone mineral density in Korean adults. *J. Bone Metab.* 2017; 24(3):161-173.
20. Laura Toxqui M, Pilar Vaquero. Chronic iron deficiency as an emerging risk factor for osteoporosis: a hypothesis. *Nutrients.* 2015; 7(4):2324-2344.