

## Age Related Change in Morphometric Study of Normal Lumbar Intervertebral Disc by MRI in A Tertiary Hospital of Bangladesh

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### Abstract

**Background:** Magnetic resonance imaging is the most widely used method of specifically assessing intervertebral disc degeneration. The present study was aimed to evaluate morphology of lumbar intervertebral disc at different vertebral level in relation to age of normal individuals of Bangladeshi population of Chattogram district.

**Materials and methods:** This cross-sectional observational study was conducted in the Department of Anatomy, Chittagong Medical College, Chattogram, during the period April 2021 to March 2022 upon 50 male and 50 female by dividing them into five age groups according to decade. For statistical analysis ANOVA test was done and p-value was considered significant if it was <0.05 at 95% level of confidence. For significant ANOVA test post hoc was done.

**Results:** The age of the respondents ranged from 30-79 years with the mean  $\pm$  SD was 43.50 $\pm$ 12.61 year. The mean of SL and IL compared with different age group which was highly significant (p <0.01). ADH, MDH and PDH were observed to differ among different age group but statistically was not significant (p > 0.05) when ANOVA test was performed.

**Conclusion:** The morphometry of lumbar intervertebral disc might be considered during the surgical reconstruction for the treatment of lumbar spine diseases and for the medical manufacturers to make proper surgical devices for the Bangladeshi population.

**Key words:** Age; Lumbar intervertebral disc; MRI; Spinal column.

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### Introduction

The vertebral column possesses a considerable degree of flexibility due to presence of intervertebral discs.<sup>1</sup> The lumbar spine has a larger mobile segment in the sagittal plane.<sup>2</sup> It is a vital and dynamic structure which lies between the vertebrae and consists of annulus fibrosus, nucleus pulposus and end plates.<sup>3</sup> This particular construction of Intervertebral Disc (IVD) with stands the high loads acting on the spine during everyday life, while giving mobility to the vertebral column.<sup>4</sup> The structure, form and function of the human lumbar spine change inevitably as we become aged/older. In turn, this results in a gradual change in the shape of the lumbar discs and together with biochemical and histological change, reduces spinal posture, flexibility and compliance as well as the lumbar region's capacity to withstand sustained loading.<sup>5</sup>

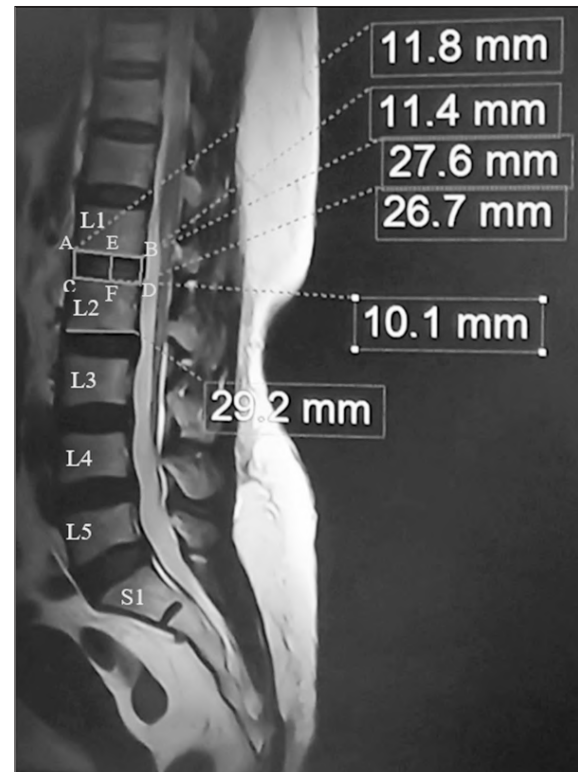
Around the age of 25, the spinal column is completely developed, and thereafter, the spinal elements begin a progressive degeneration process that accelerates around the age of 50. After the age of 50, the degeneration of the spinal column accelerates with the increasing appearance of osteophytes, lipping, and microporosity.<sup>6</sup> Men have disc degeneration approximately a decade earlier than women, in the second decade of life. In general, young and middle-aged males tend to have more severe age-matched disc degeneration. Two recent population-based investigations revealed that although young and middle-aged males are more likely than women to have lumbar disc degeneration, this pattern is reversed in older people, with women often having more severe lumbar disc degeneration than men.<sup>7</sup> The reduction of lumbar Intervertebral Disc Height (IDH) is the key point of intervertebral disc degeneration.<sup>8</sup> Most human aged 30 and more show degenerative changes in the intervertebral discs.<sup>9</sup> MRI is non invasive and provides diverse information about soft tissues of lumbar area thorough pictures of sagittal and axial planes.<sup>10</sup>

The geometry of the Artificial Intervertebral Disc (AID) is crucial for its development because it helps prevent the vertebral column's form from changing and the movement of the AID within the vertebral column.<sup>11</sup>

### Materials and methods

This cross sectional observational study with some analytical component was carried out in the Department of Anatomy of Chittagong Medical College, Chattogram during the period April 2021 to March 2022. Data were collected from the Department of Radiology and Imaging, Chittagong Medical College and Hospital, Chattogram. Approval was taken from Ethical Review Committee of Chittagong Medical College. Subjects were selected from patients attending at Radiology and Imaging Department of Chittagong Medical College Hospital (CMCH) according to enrollment criteria. MRI scans were performed with high field 1.5 Tesla Magnetic resonance system (Hitachi, Japan) with HMS Spine Coil. After reporting the MRI as normal scan by the expert radiologist the subject was contacted. The participants' ages ranged between 30 -79 years and were divided into 5 groups according to decade, such as of age 30-39 years, 40-49 years, 50-59 years, 60-69 years and 70-79 years. Age was recorded according to NID/birth certificate. Subjects having bone deformity such as, acromegaly, dwarfism etc. and tribal people were excluded. The results were summarized in the following order: After taking demographic data, some morphometric data measured from the T2 weighted sagittal lumbar MRI scan- all data were recorded and analyzed statistically. It involves the measurement of Superior Length (SL) of intervertebral disc, Inferior Length (IL) of intervertebral disc, Anterior Disc Height (ADH) Midpoint Disc Height (MDH) and Posterior Disc Height (PDH). Superior length of the disc was measured as the distance between anterior end and posterior end of the inferior border of corresponding upper vertebrae of the relevant intervertebral disc, measured in mm.<sup>12</sup> Inferior length of the disc was measured as the distance between anterior end and posterior end of the superior border of corresponding lower vertebrae of the relevant intervertebral disc measured in mm.<sup>12</sup> Anterior Disc Height (ADH) was taken as the distance between the extreme anterior margins

of the two adjacent vertebral endplates of the relevant intervertebral disc, measured in mm.<sup>13</sup> Midpoint Disc Height (MDH) was taken as the distance between the midpoints of the two adjacent vertebral endplates of the relevant intervertebral disc measured in mm.<sup>13</sup> Posterior Disc Height (PDH) was measured as the distance between the extreme posterior margins of the two adjacent vertebral endplates of relevant intervertebral disc, measured in mm<sup>13</sup> (Figure 1).



**Figure 1** Lumbar MRI showing measurement of SL, IL, ADH, MDH and PDH. SL (A -B), IL (C-D), ADH (A-C), MDH (E-F), PDH (B-D)

All collected data were entered into computer and analyzed by SPSS (Statistical Package for Social Science) version-25 software program. Comparison between numerical variables was found out by the ANOVA test and post hoc test was done for significant ANOVA finding.

### Results

The age of the respondents ranged from 30-79 years with the mean  $\pm$  SD age of  $43.50 \pm 12.61$  years. Age was distributed according to decade. There were 46 (46%), 21 (21%), 18 (18%), 8 (8%)

and 7 (7%) participants in age group of 30-39 years, 40-49 years, 50-59 years, 60-69 years and 70-79 years respectively. There were 50 males and 50 females. The mean age  $\pm$  SD of males was  $43.56 \pm 12.34$  years whereas a  $43.44 \pm 13.01$  year was in females.

In the level of L3-L4 SL increased with advancing age. In the other levels SL increased from 30-39 years to 50-59 years, then decreased in 60-69 years followed by an increase in 70-79 years. In all level IL increased from 30-39 years to 50-59 years, then decreased in 60-69 years followed by an increase in 70-79 years. In all the age group SL gradually increased from L1-L2 to L4-L5 level in cephalo-caudal gradient then decreased in L5-S1 level except in the 30-39 years group where SL gradually increased and in 70-79 years group it decreased after L3-L4 level. In all the age group IL gradually increased from L1-L2 to L4-L5 level then decreased in L5-S1 level in all the age groups. The ADH increased cephalocaudally from L1-L2 to L5-S1 except in 40-49 years it decreased from L4-L5 to L5-S1 level. At the level of L1-L2 the ADH increased from 30-39 years to 40-49 years, then decreased in 50-59 years and again increased up to 79 years. At the level of L2-L3 the ADH increased from 30-39 years to 40-49 years, then decreased up to 69 years and again increased in 70-79 years group. At L3-L4 and L5-S1 level the ADH decreased from 30-39 years to 40-49 years and also from 60-69 years to 70-79 years. At L4-L5 level ADH showed alternative decrease and increase pattern from 3<sup>rd</sup> to 7<sup>th</sup> decade. In all the age groups the MDH increased cephalocaudally from L1-L2 to L5-S1 except in 40-49 years it decreased from L4-L5 to L5-S1 level, in 60-69 years it decreased from L3-L4 to L4-L5 level, in 70-79 years it decreased from L2-L3 to L3-L4 level. MDH decreased from 30-39 years group to 40-49 years in all level. In the L1-L2 level MDH was increased after 59 years, in the L3-L4 and L5-S1 level MDH was increased after 49 years and again decreased in 70-79 years group. At L2-L3 level MDH increased after 4<sup>th</sup> decade to 7<sup>th</sup> decade. At L4-L5 level MDH decreased after 4<sup>th</sup> decade to 6<sup>th</sup> decade then increased up to 7<sup>th</sup> decade. The PDH increased cephalocaudally from L1-L2 to L4-L5 level in all age groups except in 70-79 years it decreased from L1-L2 to L2-L3 level. PDH decreased from

L4-L5 to L5-S1 level in all age groups. PDH increased from 30-39 years to 40-49 years in the level of L1-L2, L2-L3 and L4-L5 then decreased in 50-59 years group. In the level of L1-L2, L3-L4 and L5-S1 the PDH decreased from 60-69 years to 70-79 years. In L2-L3 level PDH decreased from 50-59 years to 70-79 years and in L4-L5 level PDH increased from 5<sup>th</sup> decades to 7<sup>th</sup> decades. In L5-S1 level PDH decreased from 30-39 years to 50-59 years (Table -I).

**Table I** Mean values and standard deviations of SL, IL, ADH, MDH and PDH of lumbar intervertebral disc at different lumbar vertebral levels in different age groups

Vertebral level	Length of IVD	Age groups				
		30-39 (n=46)	40-49 (n=21)	50-59 (n=18)	60-69 (n=8)	70-79 (n=7)
L1-L2	SL	28.40 $\pm$ 3.10	29.06 $\pm$ 2.84	30.37 $\pm$ 2.65	29.53 $\pm$ 1.23	33.21 $\pm$ 4.89
	IL	28.73 $\pm$ 3.24	29.36 $\pm$ 2.87	29.97 $\pm$ 2.49	29.43 $\pm$ 1.46	33.84 $\pm$ 5.77
	adh	8.28 $\pm$ 1.05	8.34 $\pm$ 1.41	7.84 $\pm$ 1.17	8.26 $\pm$ 1.03	8.41 $\pm$ 1.95
	MDH	7.44 $\pm$ 1.10	7.39 $\pm$ 1.27	7.19 $\pm$ 0.83	7.28 $\pm$ 0.98	7.44 $\pm$ 1.40
	PDH	7.69 $\pm$ 1.12	7.88 $\pm$ 1.61	7.56 $\pm$ 1.22	7.70 $\pm$ 0.61	7.51 $\pm$ 0.89
L2-L3	SL	29.22 $\pm$ 2.90	29.60 $\pm$ 2.09	31.26 $\pm$ 2.08	30.79 $\pm$ 1.61	35.30 $\pm$ 5.39
	IL	29.55 $\pm$ 2.94	30.26 $\pm$ 2.18	31.58 $\pm$ 2.01	31.46 $\pm$ 1.47	35.99 $\pm$ 5.01
	ADH	9.04 $\pm$ 1.08	9.05 $\pm$ 1.41	8.79 $\pm$ 0.95	8.74 $\pm$ 0.89	9.39 $\pm$ 0.78
	MDH	8.19 $\pm$ 1.05	7.80 $\pm$ 1.05	8.09 $\pm$ 0.88	8.38 $\pm$ 0.88	8.63 $\pm$ 0.84
	PDH	8.07 $\pm$ 1.21	8.07 $\pm$ 0.90	8.03 $\pm$ 0.89	8.00 $\pm$ 0.60	7.23 $\pm$ 0.66
L3-L4	SL	30.16 $\pm$ 2.37	30.74 $\pm$ 2.05	32.62 $\pm$ 1.86	32.69 $\pm$ 1.57	36.91 $\pm$ 4.71
	IL	30.36 $\pm$ 2.47	31.48 $\pm$ 2.02	32.76 $\pm$ 1.96	32.30 $\pm$ 1.43	37.41 $\pm$ 4.52
	ADH	10.16 $\pm$ 1.35	10.00 $\pm$ 1.43	9.77 $\pm$ 1.33	10.39 $\pm$ 0.94	9.77 $\pm$ 0.84
	MDH	9.14 $\pm$ 1.14	8.68 $\pm$ 1.29	8.93 $\pm$ 1.09	8.95 $\pm$ 0.88	8.46 $\pm$ 0.82
	PDH	8.55 $\pm$ 0.98	8.76 $\pm$ 1.14	8.74 $\pm$ 1.16	8.81 $\pm$ 1.08	8.80 $\pm$ 1.30
L4-L5	SL	30.94 $\pm$ 2.70	31.65 $\pm$ 2.41	33.84 $\pm$ 1.39	33.30 $\pm$ 1.77	36.56 $\pm$ 2.60
	IL	31.27 $\pm$ 2.90	32.64 $\pm$ 2.91	33.84 $\pm$ 1.44	33.60 $\pm$ 1.92	37.90 $\pm$ 3.20
	ADH	11.48 $\pm$ 1.95	11.82 $\pm$ 1.98	10.71 $\pm$ 1.39	11.49 $\pm$ 1.25	10.54 $\pm$ 1.33
	MDH	10.14 $\pm$ 1.31	9.83 $\pm$ 1.51	9.18 $\pm$ 1.22	8.86 $\pm$ 1.10	9.06 $\pm$ 1.87
	PDH	9.26 $\pm$ 1.23	9.31 $\pm$ 1.40	8.90 $\pm$ 1.17	9.21 $\pm$ 1.71	9.27 $\pm$ 1.71
L5-S1	SL	31.07 $\pm$ 2.79	31.35 $\pm$ 2.28	33.54 $\pm$ 1.59	32.26 $\pm$ 2.52	35.39 $\pm$ 3.42
	IL	30.95 $\pm$ 3.07	31.31 $\pm$ 2.68	33.26 $\pm$ 1.93	32.16 $\pm$ 2.87	34.53 $\pm$ 3.10
	ADH	12.23 $\pm$ 2.06	11.73 $\pm$ 2.51	12.08 $\pm$ 2.46	14.35 $\pm$ 2.12	12.33 $\pm$ 3.35
	MDH	10.20 $\pm$ 1.55	9.52 $\pm$ 1.98	9.87 $\pm$ 2.09	11.49 $\pm$ 2.32	9.29 $\pm$ 2.81
	PDH	9.00 $\pm$ 1.20	8.62 $\pm$ 1.28	8.61 $\pm$ 1.37	9.19 $\pm$ 1.11	8.56 $\pm$ 2.00

ANOVA test showed that the mean of Superior Length (SL) and Inferior Length (IL) of the disc was statistically highly significant in relation to different age group. According to post hoc (Bonferroni) the mean of SL in all the level of lumbar vertebra was significantly higher in 70-79 years age group than that of 30-39 years and 40-49 years groups. The mean of IL in all the level of lumbar vertebra was significantly higher in 70-79 years age group than that of 30-39 years. The

mean of IL in all the level of lumbar vertebra except L5-S1 level was significantly higher in 70-79 years age group than that of 40-49 years [Table II and III].

**Table II** Comparison of SL of IVD among different age groups

Vertebral level	Parameters are measured in mm	ANOVA		Post hoc (Bonferroni)	
		F	p value	Significant	p value
L1-L2	SL	4.557	p<0.05	(70-79) vs (30-39)	0.002
				(70-79) vs (40-49)	0.022
L2-L3	SL	8.338	p<0.05	(70-79) vs (30-39)	0.000
				(70-79) vs (40-49)	0.000
				(70-79) vs (50-59)	0.015
				(70-79) vs (60-69)	0.022
L3-L4	SL	14.488	p<0.05	(50-59) vs (30-39)	0.004
				(70-79) vs (30-39)	0.000
				(70-79) vs (40-49)	0.000
				(70-79) vs (50-59)	0.001
				(70-79) vs (60-69)	0.010
L4-L5	SL	11.916	p<0.05	(50-59) vs (30-39)	0.000
				(70-79) vs (30-39)	0.000
				(70-79) vs (40-49)	0.000
L5-S1	SL	6.666	p<0.05	(50-59) vs (30-39)	0.007
				(70-79) vs (30-39)	0.001
				(70-79) vs (40-49)	0.004

**Table III** Comparison of IL of IVD among different age groups

Vertebral level	Parameters are measured in mm	ANOVA		Post hoc (Bonferroni)	
		F	p value	Significant	p value
L1-L2	IL	4.055	p<0.05	(70-79) vs (30-39)	0.001
				(70-79) vs (40-49)	0.017
L2-L3	IL	9.196	p<0.05	(70-79) vs (30-39)	0.000
				(70-79) vs (40-49)	0.000
				(70-79) vs (50-59)	0.005
				(70-79) vs (60-69)	0.020
L3-L4	IL	14.208	p<0.05	(50-59) vs (30-39)	0.006
				(70-79) vs (30-39)	0.000
				(70-79) vs (40-49)	0.000
				(70-79) vs (50-59)	0.000
				(70-79) vs (60-69)	0.001
L4-L5	IL	11.058	p<0.05	(50-59) vs (30-39)	0.008
				(70-79) vs (30-39)	0.000
				(70-79) vs (40-49)	0.000
				(70-79) vs (50-59)	0.009
				(70-79) vs (60-69)	0.024
L5-S1	IL	4.135	p<0.05	(50-59) vs (30-39)	0.038
				(70-79) vs (30-39)	0.022

ANOVA test showed that ADH, MDH and PDH was not statistically significant in relation to different age group (Table IV).

**Table IV** Comparison of the of ADH, MDH and PDH of lumbar intervertebral disc at different lumbar vertebral levels in different age group

Vertebral level	Height of IVD	ANOVA	
		F	p value
L1-L2	ADH	0.551	0.698
	MDH	0.189	0.944
	PDH	0.211	0.932
L2-L3	ADH	0.504	0.733
	MDH	1.162	0.333
	PDH	1.060	0.381
L3-L4	ADH	0.501	0.735
	MDH	0.961	0.433
	PDH	0.121	0.975
L4-L5	ADH	1.360	0.254
	MDH	1.008	0.222
	PDH	0.317	0.866
L5-S1	ADH	1.900	0.117
	MDH	1.929	0.112
	PDH	0.688	0.602

## Discussion

In the current study at the level of L3-L4 SL increased with advancing age. In the other levels SL increased from third to fifth decade then decreased in sixth followed by an increase in seventh decade. Cephalocaudally in all the age group SL gradually increased from L1-L2 to L4-L5 level then decreased in L5-S1 level except in the third decade SL gradually increased and in seventh decade it decreased after L3-L4 level. One way ANOVA test showed that the mean of superior length of the discs was statistically highly significant in relation to different age group ( $p < 0.01$ ). According to post hoc (Bonferroni) the mean of SL in all the level of lumbar vertebra was significantly higher in 70-79 years age group than that of 30-39 years and 40-49 years groups. All the corresponding values of the study carried out by Bepat et al are higher than present study.<sup>12</sup> In the present study at all the level IL increased from third to fifth decade; then decreased in sixth decade followed by an increase in seventh decade. In all the age group cephalocaudally IL gradually increased from L1-L2 to L4-L5 level then decreased in L5-S1 level. One way ANOVA test showed that the mean of inferior length of the disc was statistically highly significant in relation to different age group ( $p < 0.01$ ) According to post hoc (Bonferroni) the mean of IL in all the level of lumbar vertebra was significantly higher in 70-79

years age group than that of 30-39 years. The mean of IL in all the level of lumbar vertebra except L5-S1 level was significantly higher in 70-79 years age group than that of 40-49 years.

In this current study in all the age groups the ADH increased cephalo-caudally from L1-L2 to L5-S1 except in fourth decade. The study by Mansur et al presented that in all the age groups the ADH increased craniocaudally from L1-L2 to L5-S1 which is nearly similar with this study.<sup>13</sup> At different vertebral level ADH showed increased and decreased pattern with advancing age. This pattern with advancing age was nearly similar in all the vertebral level with the study of Mansur et al and Aydinlioglu et al but dissimilar with Fetouh that showed that at the upper 4 discs, the male discs showed alternating increase/decrease pattern through the age decades from 3<sup>rd</sup> to 6<sup>th</sup>, while in females there was steady increase in the height to reach the maximum at 6<sup>th</sup> decade which is partially similar with present study.<sup>13-15</sup> ANOVA test showed that the mean of ADH was not statistically significantly different for the various age groups. Gocmen et al revealed there was no statistically significant between male and female with regard to age ( $p > 0.05$ ). This is similar with current study.<sup>16</sup> Onishi et al found that the anterior disc height showed progressive decrease with aging ( $p < 0.05$ ) for L4-L5. The L5-S1 anterior disc height has not change with aging ( $p > 0.05$ ).<sup>17</sup> In the study performed by Fetouh it is shown that for ADH of discs at levels of L1-L2, L4-L5 & L5-S1 showed significant changes with age progress. This is dissimilar with present study.<sup>15</sup> This difference may be due to racial difference and sample size.

This study presented that in all the age groups the MDH increased cephalo-caudally from L1-L2 to L5-S1 except in fourth decade where it decreased from L4-L5 to L5-S1 level. In all lumbar level MDH showed increase and decrease pattern with advancing age. Mansur et al showed the increase and decrease pattern with advancing age was not very similar in all the vertebral level which is similar with present study.<sup>13</sup>

Cephalocaudal gradient of increase in central disc heights was observed in the study of Fetouh from L1-L2, L4-L5 discs in all age group then, at L5-S1 disc, they decreased in 3<sup>rd</sup> and 4<sup>th</sup> decades and increased in 5<sup>th</sup> and 6<sup>th</sup> decades which are also dissimilar with current study.<sup>15</sup> This difference may be due to racial cause.

ANOVA test showed that the mean of MDH was not statistically significantly different for the various age groups. In the study of Maher et al. it is found that at the following lower levels L4-L5 and L5-S1, the midpoint disc height displayed age-dependent, though still sex-independent changes. The L4-L5 disc heights remained relatively unchanged or showed minimal insignificant change, while disc heights at L5-S1 tended to decrease in younger age groups namely, 3<sup>rd</sup> to 5<sup>th</sup> decades.<sup>18</sup> Which is nearly similar with current study but Fetouh revealed all discs showed significant changes in their central heights with age ( $p < 0.05$ ).<sup>15</sup>

The present study depicted that the PDH increased cephalocaudally from L1-L2 to L4-L5 level in all age groups except in seventh decade, where it decreased from L1-L2 to L2-L3 level. PDH decreased from L4-L5 to L5-S1 level in all age groups. PDH increased from third decade to fourth decade in the level of L1-L2 and L4-L5 then decreased in fifth decade. In all the level except L4-L5 the PDH decreased from sixth to seventh decade. Mansur et al showed the almost similar increase and decrease pattern with advancing age in all the vertebral level.<sup>13</sup> Here ANOVA showed that the mean of PDH was not statistically significantly different for the various age groups. The result of Konrad et al. was for men L3-L4, L5-L4 and L5-S1 did not demonstrate any significant correlation for any disc height measurements to age. This is nearly similar with current study.<sup>19</sup> But Fetouh and Malkoc et al showed significant changes of discs with age progress which were not similar with current study.<sup>15, 20</sup>

A study quoted that there is a continuous development and remodeling of vertebrae which may be due to the changing demands of the body.<sup>21</sup> In fact, in the intervertebral disc receiving continuous stress for a long period, a process of the decomposition and regeneration should be available to sustain its function.<sup>20</sup> It is well known that the general population has a propensity to grow taller for reasons that are currently being investigated. Anthropometric analysis shows that humans get taller as they reach adult years and consequently the intervertebral discs height are also raised.<sup>17</sup> These may be the cause that in our study there was increase and decrease pattern in all vertebral level with advancing age.

**Limitation**

The study was conducted in a selected area within short time frame. Sample size is relatively small. So the present study may not be truly representative of Bangladeshi population.

**Conclusion**

The study reported a highly significant difference between superior and inferior length of the disc in relation to different age group in normal population of Chattogram, Bangladesh. In case of anterior disc height, midpoint disc height and posterior disc height, there was no significant difference found in different age group. Results of the present study provided some baseline information about morphology of lumbar intervertebral disc of normal Bangladeshi population. This would help to develop a standard for such data on various populations as a whole which will encourage further research in this field.

**Recommendation**

Based on the understanding of the research problems and considering the experience gained from the present study, the following suggestions can be made regarding further studies:

- Studies with larger sample size are required to confirm the finding of such study.
- Multicenter based study can be performed.
- In this study tribal population were excluded.

So, further studies can be undertaken to observe any significant difference of lumbar intervertebral disc between tribal and normal Bengali population.

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**Contribution of authors**

RR- Conception, design, acquisition of data, drafting and final approval.

MA- Interpretation of data, critical revision and final approval.

TZ- Data analysis, critical revision and final approval.

SF- Data analysis, critical revision and final approval.

BB- Data collection, manuscript writing and final approval.

KC- Design, data collection, manuscript writing and final approval.

**Disclosure**

All the authors declared no competing interests.

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