Volume: 32 (1), June 2024 ISSN: 0970 - 1842

JAS Journal of Anatomical Sciences

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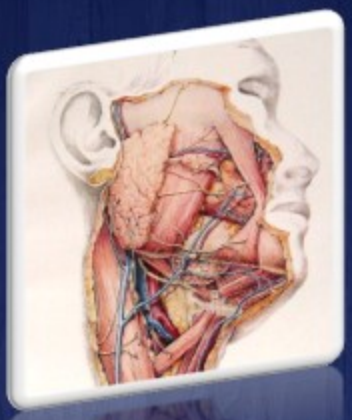
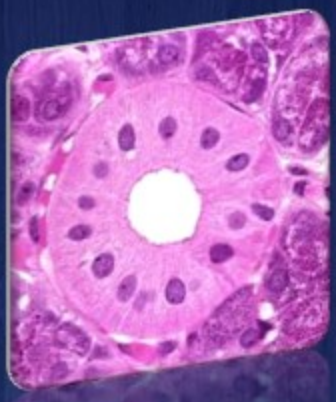
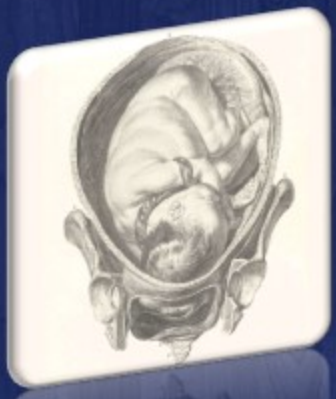


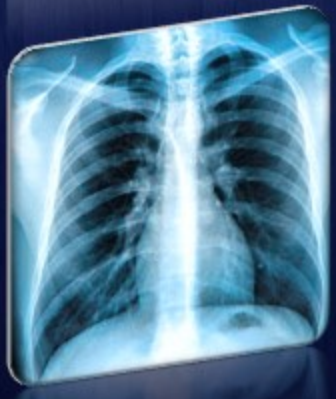

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https://doi.org/10.46351/jas.v32i1pp01-10

JAS Journal of Anatomical Sciences (U.P. Chapter of Anatomical Society of India)

Original Article

HISTOMORPHOMETRIC ANALYSIS OF SUN EXPOSED AND NON- SUN EXPOSED AREA OF HUMAN SKIN

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ABSTRACT

Introduction: Knowledge of basic elements gives a clear vision of the structure of any organ. Skin is continuously being exposed to various external environmental factors, one of them is sun induced UV radiation, major environmental factor that affects the structure and function of human skin. On excessive exposure, UV radiation can cause premature aging and even skin cancer. Histological analysis of the variations among sun exposed and non-sun exposed human skin is of relevance in dermatologic research and dermatopharmacokinetics.

Materials and Methods: This study was conducted on 10 male and 10 female human cadavers. The rectangle shaped skin specimen (1 cm × 1 cm) was taken from two sites sun exposed (forehead) and non sun exposed (lower abdomen) and stained with hematoxylin and eosin stain. A total of 40 slides were prepared. Readings were obtained with the help of cellSens /OLYMPUS Stream software, using UIS2 (Universal Infinity System) optical design camera fitted in the light microscope.

Results: There were statistically significant differences among sun exposed and non-sun exposed area was found in epidermis (p=0.008 & r=0.754), no. of rete pegs (p=0.05 & r=0.573), no. of hair follicles (p=0.04 & r=0.565) and depth of rete pegs (p=0.03 & r=0.102).

Conclusions: The mean value of epithelium of sun exposed site is marginally thicker than non-sun exposed sites. The number of rete pegs per field was higher in exposed site as compared to non-sun exposed site.

Keywords: **D**ermatopharmacokinetics, Skin, Histomorphometry

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Date of Receiving: 24 Nov 2023
Date of Acceptance: 12 Jan 2024

INTRODUCTION

Knowledge of basic elements gives a clear vision of the structure of any organ. Researches emphasized that the skin is irregular undulating structures, especially the epidermis. Its depth is an important determinant of percutaneous absorption of ultraviolet rays as stratum corneum acts as rate limiting barrier. Therefore, thickness of different layers of skin is helpful in evaluating, ultraviolet radiation induced carcinogenesis and aging [1-3].

Skin, is composed of the epidermis and the dermis, is the outermost tissue of the human body. The epidermis consists of four layers (from deep to superficial): basal layer, spinous layer, granular cell layer, and stratum corneum, whereas the dermis involves cells, connective tissue and ground substance and consists of blood and lymphatic vessels, nerves, glands, and hair follicles. The dermis is divided into two layers as the papillary dermis and the reticular dermis. There is a variable amount of subcutaneous fatty tissue beneath the skin [1,4].

Skin is continuously being exposed to various external environmental factors, one of them is sun induced UV radiation, major environmental factor that affects the structure and function of human skin. UV radiation has been known to cause skin cancer and premature aging on excessive exposure.

Solar UV radiation reaching the earth is a combination of UVB (290–320 nm) and UVA (320–400 nm) wavelengths [5]. It is now proved that UVA radiation plays a major role for the damaging effects of solar radiations. In fact, UVA radiation is the most prevalent component as it penetrates deeper than UVB radiation into the skin and induces profound alterations of the dermal connective tissue [1]. The consequences of UVA exposure on skin are particularly important in Asia because of the low latitude. It is also responsible for the early appearance of signs of photoaging, which include pigmentation, wrinkling, laxity, sagging, dryness, etc. One of the major detrimental effects of UVA radiation is the generation of oxidative stress which is a well-known factor in the photoaging pathogenesis [5-6].

Histological analysis of the variations among sun exposed and non-sun exposed human skin is of relevance in dermatologic research and dermatopharmacokinetics [4]. The aim of this study was to compare the microscopic anatomy of sun exposed (face) and non-sun exposed (lower abdomen) sites of human skin.

Objectives:

1. To measure the total skin thickness.
2. To measure the thickness of epidermis and its various layers

3. To measure the thickness of papillary and reticular layer of dermis.
4. To observe number and pattern of rete pegs at dermo-epidermal junction.
5. To estimate the distribution of hair follicles, sebaceous glands and sweat gland in dermis

MATERIALS AND METHODS

Study type: Observational study.

The present study was done in Department of anatomy, Government Doon Medical College, Dehradun (Uttarakhand) on 10 human male and 10 human female cadavers which were procured from donated body received in the department of anatomy within, 4 to 5 hours after death. The age of both the genders was ranged between 25- 70 years (mean age 47.5). The ethical clearance was obtained from the Ethics Committee, Government Doon Medical College, Dehradun.

Inclusion criteria: Samples were taken from sun exposed and non-sun exposed area of skin from the fresh corpses arrives at GDMC in anatomy department, within 48 hours of death. They were residents of Dehradun.

Exclusion criteria: Cadavers and deceased residing outside Dehradun and beyond 48 hours were not included in the study. The area of skin present with abrasion, infections, breech such as boils, crusting were excluded.

Tissue processing and staining: Full-thickness skin biopsy specimens were taken using scalpels measuring 1 cm × 1 cm. The biopsy specimens were taken from two sites, sun exposed (forehead) and non-sun exposed (right iliac fossa). The specimens were preserved in formalin, processed, sectioned and stained with haematoxylin and eosin stain and mounted on slides. Skin thickness measurements were performed under light microscopy using 10x and 4x magnification.

Parameters were individually determined per slide and were then averaged to a single data set to prevent errors. Each of the slide contained horizontal sections of tissue. Parameters such as epithelium thickness, depth, number, and number of rete pegs at the dermoepidermal junction,

Thickness of dermis were taken in 4x except thickness of stratum corneum (Tsc) and epidermal thickness which was taken at 10x. Readings of the above-mentioned parameters were analysed by cellSens/OLYMPUS Stream software, using UIS2 (Universal Infinity System) optical design camera fitted in the light microscope.

Statical analysis: All data were tabulated in Microsoft excel sheet and statically analyzed. Findings were expressed in mean and standard deviation.

RESULTS

The mean value of stratum corneum, epidermis, papillary dermis and total skin thickness were found to be more in sun exposed area whereas, thickness of reticular dermis and total dermis was more in non-sun exposed area. Number of rete pegs and depth of rete pegs were higher at the exposed site along with number of sweat glands and hair follicles.

Statistically significant differences among sun exposed and non-sun exposed area was found in epidermis (p=0.008 & r=0.754), no. of rete pegs (p=0.05 & r=0.573), no. of hair follicles (p=0.04 & r=0.565) and depth of rete pegs (p=0.03 & r=0.102).

S.NO.	PARAMETERS (µm)	SUN EXPOSED SITE (MEAN ± STD.DEV)	NON SUN EXPOSED SITE (MEAN ± STD.DEV)	t-TEST (p- value)	CO-RELATION
1	STRATUM CORNEUM	94.12 ± 51.67	6.63 ± 6.84	0.059	0.131
2	EPIDERMIS	107.65 ± 66.08	58.02 ± 39.39	0.008	0.754
3	PAPILLARY DERMIS	70.54 ± 34.13	49.80 ± 48.63	0.119	0.331
4	RETICULAR DERMIS	1180.45 ± 105.18	1355.69 ± 140.08	0.383	0.048
5	DERMIS	1251 ± 98.25	1405.50 ± 159.98	0.395	0.092

Table 1(a). Comparison of different parameters of sun exposed and non sun exposed area of human. skin

S.NO.	PARAMETERS	SUN EXPOSED SITE (MEAN ± STD.DEV)	SUN NON- EXPOSED SITE (MEAN ± STD.DEV)	t-TEST (p- value)	CO-RELATION
1	TOTAL SKIN THICKNES	1358.65 ± 97.64	1463.52 ± 147.11	0.427	0.109
2	NO. OF RETE PEGS	11.4 ± 5.85	6.5 ± 3.95	0.0541	0.573
3	NO. OF HAIR FOLLICLES	4.5 ± 3.32	2.4 ± 2.28	0.049	0.565
4	NO. OF SWEAT GLANDS	13.2 ± 12.01	8.5 ± 5.67	0.311	0.165
5	DEPTH OF RETE PEGS	144.7 ± 77.55	69.36 ± 19.73	0.0378	0.102

Table 1(b). Comparison of different parameters of sun exposed and non sun exposed area of human skin.

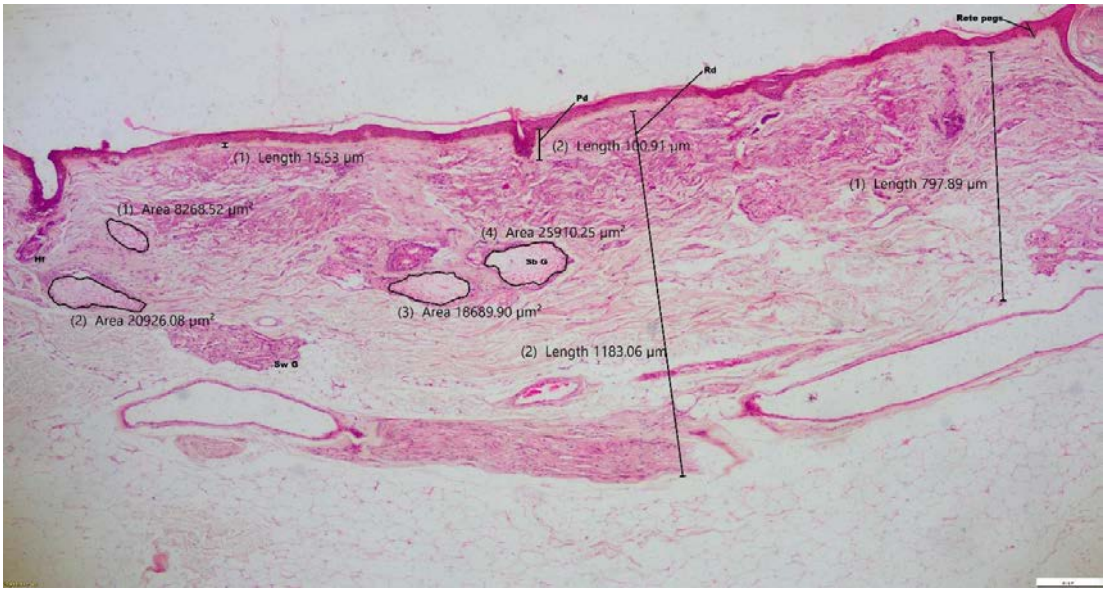

Fig. 1. Histological image showing showing papillary dermis, reticular dermis, rete pegs, sebaceous gland, sweat gland and hair follicle in non-sun exposed area at 4X

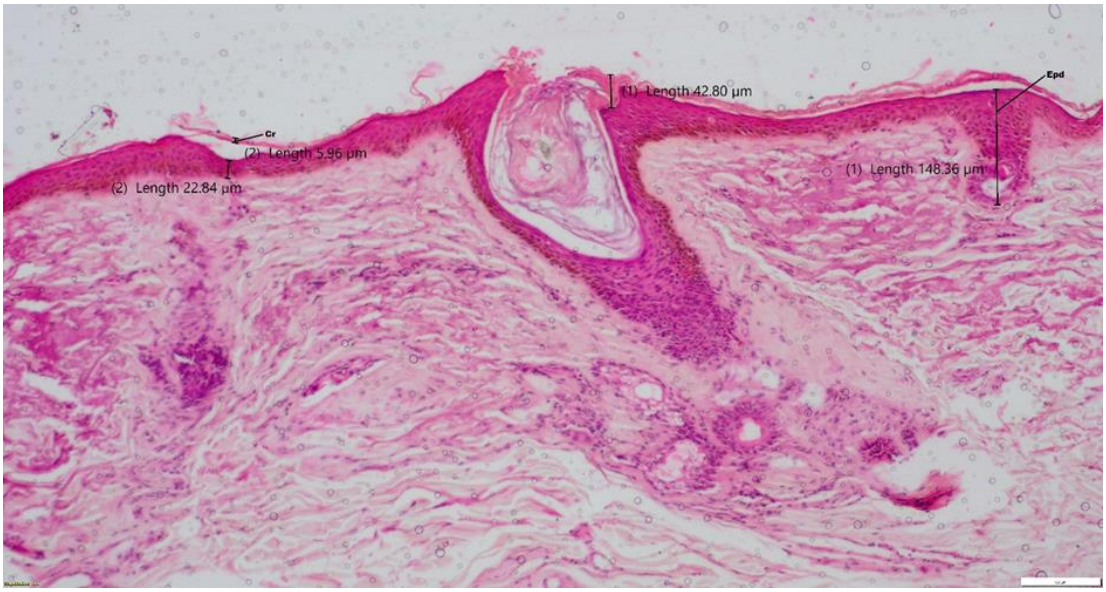

Fig. 2. Histological image showing stratum corneum and epidermis of non- sun exposed area at 10x

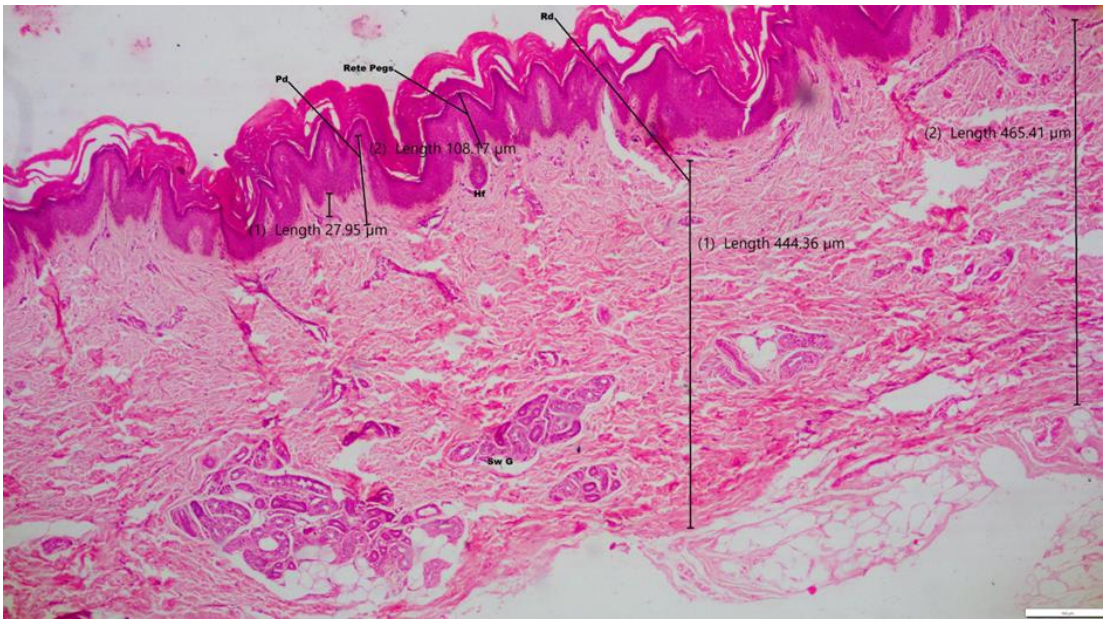

Fig. 3. Histological image showing papillary dermis, reticular dermis, rete pegs, sebaceous gland, sweat gland and hair follicle in sun exposed area at 4X

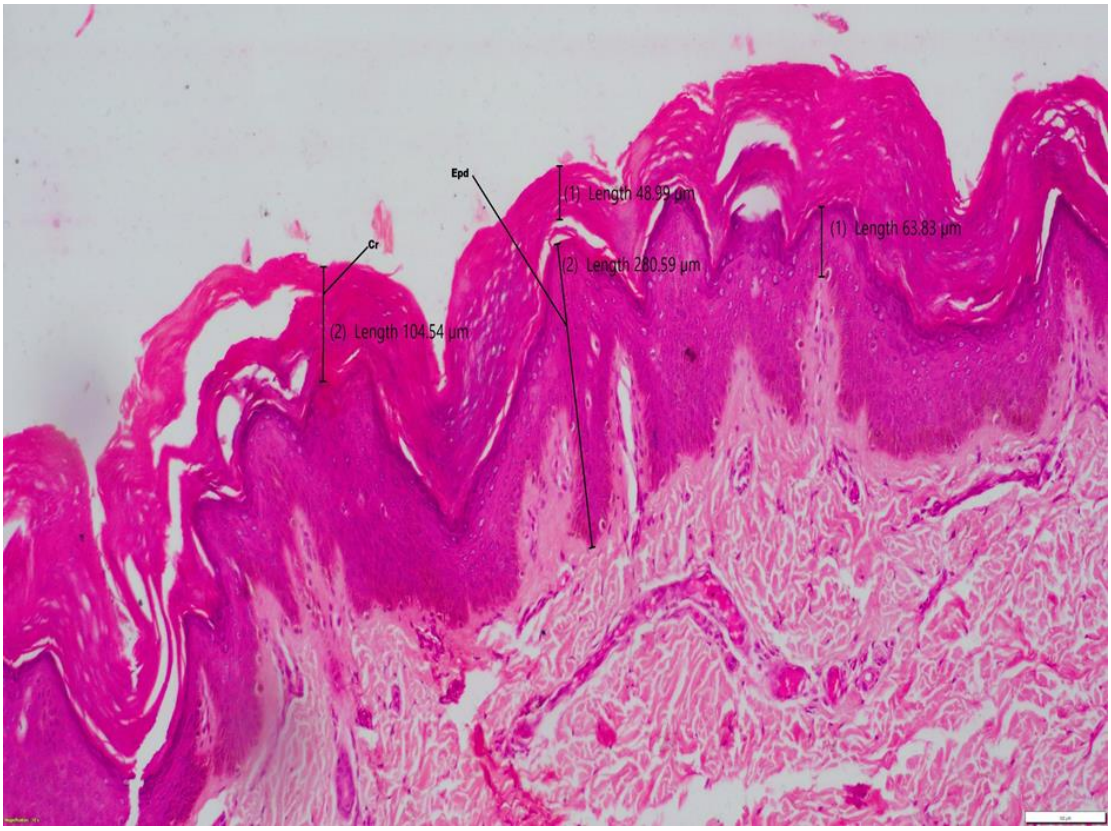

Fig. 2. Histological image showing stratum corneum and epidermis of non- sun exposed area at 10x

DISCUSSION

Histologic analysis of the normal skin is of relevance in dermatological research. Knowledge about the normal values of dermis, epidermis, or total ST is essential for various drug and vaccine research, skin related clinical investigations, and skin transfer plastic surgeries. Pembe Oltulu et al in 2022 observed that the thickness of epidermis, dermis and total skin thickness of dorsum of hand was found to be 244.8±92.9µm, 2538.5±13µm and 2284±14µm respectively in below 50 years age group whereas, thickness of epidermis, dermis and total skin thickness of abdominal skin was 163.3±44.5µm, 5497.7±17µm and 5661±18µm respectively. Data was found to be nearly similar with the finding of our study except the dermal and total skin thickness of abdomen which was found to be higher in our study.[14] whereas, dermis and total skin thickness was similar with the study of Chopra et al [12]. Number of hair follicles, rete pegs, sweat glands and depth of rete pegs were found to be variable with other studies.

S.NO.	AUTHOR'S NAME	YEAR	N	STRATUM CORNEUM		EPIDERMIS	
				EXP.	NON-EXP.	EXP.	NON-EXP.
1	Freemann et al.[7]	1962	28	16	28	67	95
2	Hoffmann et al.[8]	1994	40	2.23±0.23	1.80±0.32	_	_
3	Lavker et al. (mm) [5]	1995	23	15.0±0.7	8.1±0.7	81.5±2.5	76.0±0.3
4	Huzaira et al.[9]	2001	10	13.66±29	8.08±1.8	_	_
5	Sandby-Moller et al.[10]	2003	76	18.3±49	14.9±3.4	74.9±12.7	96.5±16.1
6	Robertson et al.[11]	2010	25	9.3	6.3	62.5	61.5
7	Chopra et al.[12]	2015	10	_	_	44.70±13.99	_
8	Khiao et al.[13]	2019	11	6.6±0.5	13.2±2.3	51.6±3.5	59.9±8.5
9	Saxena et al.[4]	2022	10	14.21±4.69	_	86.72±31.49	_
10	Oltulu et al.[14]	2022	180	224.8±92.9	163.3±44.5	_	_
11	Jeong et al. (mm) [15]	2023	99	_	_	0.334±0.157	_
12	Present study	2023	10	94.12± 51.67	6.63±6.84	107.65±66.08	58.02±39.39

Table (2a). Showing difference between stratum corneum and epidermis thickness of sun exposed and non sun exposed skin

S.NO.	AUTHOR'S NAME	YEAR	N	DERMIS		TOTAL SKIN THICKNESS	
				EXP.	NON-EXP.	EXP.	NON-EXP.
1	Chopra et al.[12]	2015	10	1200.93±297.23	_	1245.63	_
2	Khiao et al.[13]	2019	11	952.4±127.0	1831.5±29.6	_	_
3	Saxena et al.[4]	2022	10	578±296.76	_	664.72±293.11	_
4	Oltulu et al.[14]	2022	180	2538.5±1373.9	5497.7±1722.2	2284±1407	5661±1733.2
5	Jeong et al. (mm) [15]	2023	99	1.019±0.534	_	1.353±0.57	_
6	Present study	2023	10	1251±98.25	1405.50±159.58	1358.65±97.64	1463.52±147.11

Table (2b). Showing difference between dermis and total skin thickness of sun exposed and non sun exposed skin

S.NO.	AUTHOR'S NAME	YEAR	N	NO. OF HAIR FOLLICLE		NO. OF RETE PEGS		NO. OF SWEAT GLANDS		DEPTH OF RETE PEGS	
				EXP.	NON-EXP.	EXP.	NON-EXP.	EXP.	NON-EXP	EXP.	NON-EXP.
1	Huzaira et al.[9]	2001	10	_	_	_	_	_	_	130.25±10.55	110.58±8.87
2	Robertson et al.[11]	2010	25	_	_	_	_	_	_	39.6	50.8
3	Khiao et al.[13]	2019	11	30.7±4.3	7.0±3.3	_	_	30.8±8.1	15.7±1.1	1131.2±39.9	1419.5±46.7
4	Saxena et al.[4]	2022	10	_	_	7.10±0.80	_	_	_	225.60±126.32	_
5	Present study	2023	10	4.5±3.32	2.4±2.28	11.4±5.85	6.5±3.95	13.2±12.01	8.5±5.67	144.7±77.55	69.36± 19.73

Table (2c). Showing no. of hair follicles, no. of rete pegs, no. of sweat glands and depth of rete pegs in various studies

CONCLUSION

The present observational study was undertaken to assess the difference between sun exposed and non-sun exposed sites of human skin histologically. The mean value of epithelium of sun exposed site is marginally thicker than non-sun exposed sites. The number of rete pegs per field was higher in exposed site as compared to non-sun exposed site.

This study tried to create a baseline comparison to establish the presence of histological variations caused by UV radiations which is different from chronological changes. The measurement of skin thickness, stratum corneum, dermal thickness can also prove useful in plastic surgery.

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https://doi.org/10.46351/jas.v32i1pp11-17

JAS Journal of Anatomical Sciences (U.P. Chapter of Anatomical Society of India)

Original Article

MICROSCOPIC ANATOMY OF DEVELOPING SPLEEN: A CROSS-SECTIONAL STUDY FROM NORTH INDIA

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ABSTRACT

Introduction: Spleen is the largest lymphatic organ present in the upper part of the abdominal cavity. In fetal life it is a haemopoietic organ while it destroys blood in the postnatal life. It filters the blood from blood borne antigens and microorganisms. The present study was conducted to describe the detailed histological changes of human fetal spleen during its development.

Materials and Methods: The present study was a prospective, observational study conducted in the Department of Anatomy along with the Department of Obstetrics and Gynaecology at a tertiary care teaching hospital situated in Uttarakhand state from March 2021 to July 2023. Human fetuses between 13 to 40 weeks of gestational age and without any congenital malformations were collected after routine medical termination of pregnancies, still birth or intra uterine death for study.

Results: The microscopic anatomy of the spleen was observed at different gestational ages. During first trimester of pregnancy primary vascular system was seen. Formation of red pulp and white pulp was seen clear during second trimester of pregnancy. At the beginning of the third trimester, white pulp shows lymphatic nodule with eccentrically placed arteriole.

Conclusions: The detailed study of development of fetal spleen suggest the functional aspect of spleen in fetal life.

Keywords: Microscopic anatomy, Spleen, Histogenesis, Fetal autopsy, Embryology

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Date of Receiving: 21 Nov 2023
Date of Acceptance: 18 Jan 2024

INTRODUCTION

Appearing at about the sixth week of gestation, the spleen is the largest lymphoid organ [1]. The lobulated spleen of dual origin develops simultaneously in several adjoining areas which soon fuse together. The spleen is capsulated and is situated in the pathway of the blood stream (splenic artery and vein). The spleen is enclosed by a dense connective tissue capsule from which trabeculae extend into the parenchyma of the organ [2]. Myofibroblasts are present in the connective tissue of the capsule and trabeculae [3,4]. These contractile cells also produce extracellular connective tissue fibers.

The substance of spleen known as the splenic pulp, is made up of red pulp and white pulp [5]. The red pulp consists of a dense network of reticular fibers that contains numerous erythrocytes, lymphocytes, plasma cells, macrophages and other granulocytes. The main function of the red pulp is to filter the blood. It removes antigens, microorganisms, platelets, and aged or abnormal erythrocytes from the blood [6]. Mainly lymphatic tissue make up the white pulp and is the immune component of the spleen [7]. Lymphatic cells surrounding the central arteries of the white pulp are primarily T cells, while the lymphatic nodules contain mainly B cells. The spleen carries out many supporting roles in the body. It acts as filter for blood as part of the immune system, which helps fight infectious diseases. It also detects abnormal red blood cells.

The variations in the lymphoid tissue, including spleen are well documented in the adults but few studies have documented the variations in the structure of spleen at different stages of development in the prenatal period. The present study was conducted at a tertiary care center to study the macroscopic and histological development of the human spleen, by observing changes in the gross splenic morphology and histology in fetuses of different age groups during the prenatal period.

MATERIALS AND METHODS

The present study was a prospective, observational study conducted in the Department of Anatomy at a tertiary care teaching hospital situated in Uttarakhand state from March 2021 to July 2023.

Inclusion and exclusion criteria: All fetuses ranging from the gestational age of 13 to 38 weeks, obtained from the Department of Gynaecology and Obstetrics of the tertiary care teaching hospital as a result of medical termination of pregnancy (MTP), intra-uterine death or still birth were included in the study. Fetuses showing any sign of congenital malformation were excluded from the study.

Specimen collection and preservation: The specimen/ fetus were collected from the Department of Obstetrics and Gynaecology after obtaining due written, informed consent

from the parents. These fetus specimen were collected within a window of one to two hours of the delivery. The gestational age was determined by reviewing the medical records available in the hospital and confirmation was done by taking the following measurements: crown-rump length, crown-heel length, length of the foot and the bi-parietal diameter. The weight of the fetus specimen was measured followed by injection of 10% formalin in the body cavities. Each fetus was then transferred and kept in a container filled with 10% formalin solution for seven to ten days.

Specimen processing: The abdomen of the fetus was opened and the spleen, the location and appearance of the spleen was observed and recorded. Careful dissection of the spleen was carried out [2,8,9] and the spleen tissue was further processed as per standard histological techniques. Briefly, the specimen underwent grossing, fixation, dehydration, clearing and impregnation. The spleen tissue was then embedded in paraffin blocks and sectioning was done to obtain slices of around 10-12µm thickness. Finally, staining of the slides was done using Haematoxylin and Eosin stain and the slides were observed under light microscope using 10x (low power) and 40x (high power) objective lenses.

Ethical considerations: The study was conducted as per the ethical guidelines for biomedical research on human Informed consent was taken from all cases.

subjects as given by the Central Ethics Committee on Human Research (CECHR) of the Indian Council of Medical Research (ICMR) and the 'Declaration of Helsinki' revision of 2013 after obtaining due ethical clearance from the Institute ethics committee.

RESULTS

The study was conducted on 60 fetuses received in the department of anatomy. So, a total of 60 fetal spleen were included in the study. Thirty four spleen belonged to fetus between 13 to 20 weeks of gestation, 17 had a gestational age of 21 to 30 weeks while nine had a gestational age of 31 to 40 weeks. The following microscopic features at different gestational ages were observed in these fetuses.

Group 1: 13-20 weeks of gestation: At 13 weeks, Spleen was covered by thin capsule made up of connective tissue. Fibroblast were observed in the capsule. Splenic interstitial tissue was dominated by collagen fibers. More reticular fibers, sinusoidal spaces, and blood vessels appeared. Development of trabeculae begins within the capsule. Number of haemopoietic cells were increased. Numbers of lymphocytes arranged in groups are seen but they were scattered. At 18 weeks, lymphoid aggregation with centrally placed arteriole was seen. At the margins of these groups, sinusoids and large number of RBCs were observed. At 20 weeks, division of Red and white pulp appeared. Fig. 1 is a

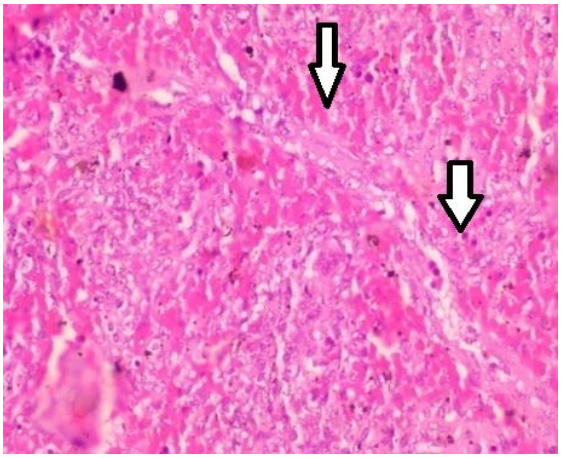

Fig. 1. Photomicrograph of spleen at 14 weeks showing lymphoblasts and reticular system

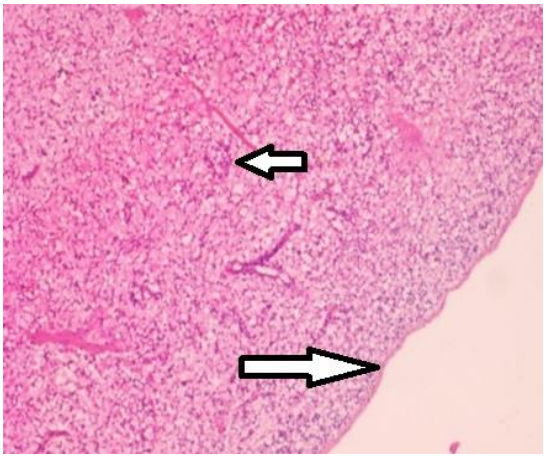

Fig. 2. Photomicrograph of spleen at 20 weeks showing well-developed capsule along with trabecular vessels

histological image of a spleen at 14 weeks showing lymphoblasts and reticular system.

Group 2: 21-30 weeks of gestation: Capsule and trabeculae were seen easily and they become thick. Red pulp and white pulp were seen clearly. Large number of blood vessels were noted. Red pulp containing RBCs and sinusoids were seen. At 30 weeks, white pulp showing lymphatic nodules with eccentrically placed arteriole were seen. Fig. 2 is a histological image of a spleen at 20 weeks showing well-developed capsule along with trabecular vessels.

Group 3: 31-40 weeks of gestation: At 31-35 weeks, numerous sinusoids were appeared in red pulp, denser lymphocytic aggregation in lymphoid follicles were seen. Well defined white pulp was seen. Primary lymphoid follicles with germinal centers were also present. At 37 weeks, heamopoietic activity is completely absent. At 38-40 weeks, fetal spleen resembled that of an adult spleen. Figure 3 is a histological image of a spleen at 38 weeks showing well-developed red and white pulp with eccentrically placed arterioles.

DISCUSSION

In a study by Mukhia et al [10] 10-15 gestational week the spleen was covered by thin capsule made up of connective tissue. Splenic tissue dominated by collagen fibers. Fibroblast cells observed inside the capsule. Blood cells were RBC'S only. At 14 weeks, capsule along with developing trabeculae were seen in interstitial tissue. Reticular cells forming network were present, but they were smaller in size, lymphocytes were present in scattered groups. At 16-20 weeks, spleen shows mixed population of cellular connective tissue components.

Blood vessels and splenic sinusoids were more in number lymphocytes aggregation become prominent and could be detected at

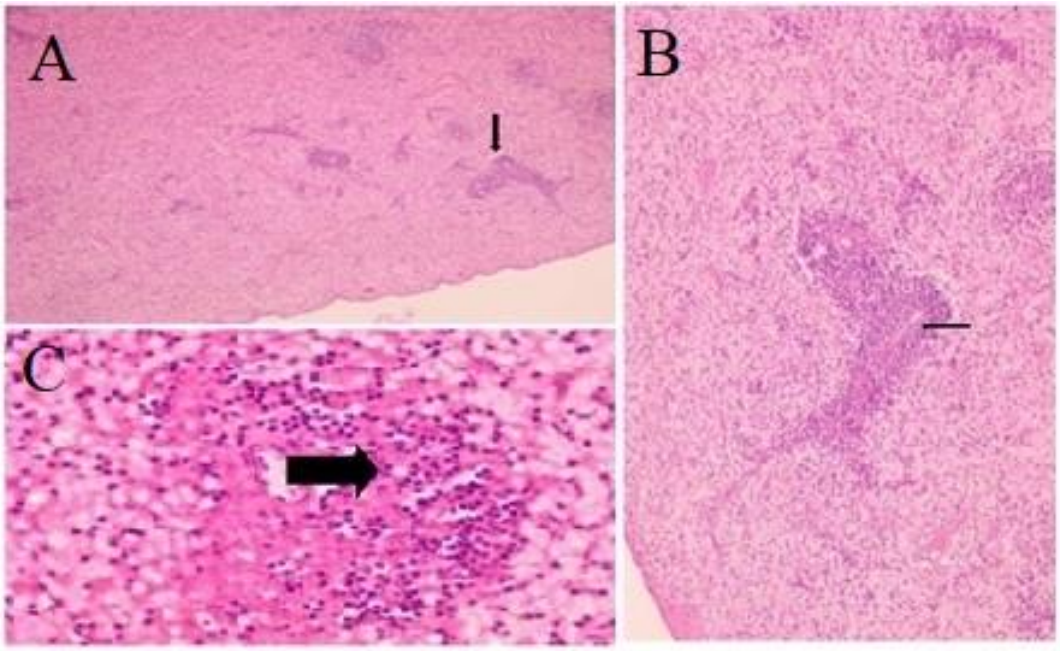

Fig. 3. Photomicrograph of spleen at 38 weeks showing well-developed red and white pulp with eccentrically placed arterioles under 4x objective (A), 10x objective (B) and 40x objective (C)

periphery of arteriole. At 20 weeks, the lymphocyte aggregations started differentiating around the central arteriole forming the peri-arteriolar lymphatic sheath. At 22 weeks, lymphoid aggregation with centrally placed arteriole was seen. At 31 gestational weeks, aggregation of lymphocytes in lymphoid follicle was denser and white pulp was defined.

In the present study, at 13 week, the spleen was covered by thin capsule consist of connective tissue, fibroblast and fibrocyte is present, development of trabeculae begins, heamopoietic cells increases. Thomas et al [11] used hematoxylin and eosin stain to describe microscopic structure of spleen in fetus at 15 weeks, and observed that the trabeculae arose from the capsule by this time. Arterioles present with no aggregation of lymphocytes. At 16 weeks, arteries were seen within trabeculae at 21 weeks lymphocytic differentiation starts around arteriole.

In the present study from 21 weeks onwards capsule within trabeculae seen prominently. Red and white pulp was distinct. Lymphoid aggregation were present around arterioles forming a peri-arteriolar lymphatic sheath. In a study by Holkunde et al [12], by the end of 13 weeks of gestation, a thin capsule was developed, reticular cells and lymphoblast were seen. By 20 weeks, red and white pulp were seen prominently and lymphocytes were compactly arranged surrounding arterioles. At 36 weeks, onwards pattern of trabeculization

was seen, division of red and white pulp were seen prominent. Lymphocytes were compactly arranged, and arterioles were eccentric in position. The above findings are consistent with the results of the present study.

Sandhya et al [13] studied the histogenesis of human fetal spleen at different gestational ages. According to their study the spleen is lined by capsule at 12 weeks. Central arteriole starts appearing at 17 weeks, and venous sinuses are present with scattered hematopoietic cells. Lymphocytes were seen around central arteriole. Around 18-24 weeks, capsule was thicker, trabeculae were seen, and central arteriole were surrounded by few lymphocytes. At 20 weeks, red and white pulp was seen at 24 weeks reticular fibers were seen around white pulp. At 24-30 weeks germinal center was seen at 28th weeks eccentrically placed central arteriole was seen. At 30 -36 weeks, at 31 weeks capsule was thick, white pulp was well defined with germinal center. 36-40 weeks, the fetal spleen resembled that of an adult spleen, the heamopoietic activity is completely stopped. A few studies reporting the histogenesis of spleen at various gestational age are summarized in table 1.

Author	n	Capsule	Lymphocyte aggregation	Lymphoid follicle	Central arteriole	Resemblance with adult spleen
Souza[14]	15	T1	T2	20-23 wk	30 wk	36 wk
Mukhia[10]	50	12-14 wk	-	18 wk	22 wk	38 wk
Thomas[11]	34	10-15 wk	20 wk	21-30 wk	31-40 wk	-
Holkunde[12]	30	13-14 wk	-	20 wk	22 wk	38 wk
Yatagiri[13]	100	12 wk	-	18-24 wk	24-30 wk	38-40 wk
Haldar[2]	9	12 wk	T2	-	-	36 wk

Table 1. Previous studies reporting histogenesis of spleen

CONCLUSION

The present study sheds light on the histological and developmental changes in the human spleen at different ages of gestation. Splenic histogenesis is a multistep process which depends upon the gestational age. Various structural and functional abnormalities later in life are thus dependent on any deviation from normal development.

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https://doi.org/10.46351/jas.v32i1pp18-26

JAS Journal of Anatomical Sciences (U.P. Chapter of Anatomical Society of India)

Original Article

CLINICAL SIGNIFICANCE OF MORPHOLOGICAL AND MORPHOMETRICAL ANALYSIS OF FORAMEN MAGNUM

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ABSTRACT

Introduction: The foramen magnum is a transitional zone between cranial cavity and spinal canal, and it is related with the very important neuro-vascular structures like vertebral arteries, spinal accessory nerves and spinal arteries and terminal part of medulla oblongata. Thus, cranio-cervical junction surgeries require a thorough knowledge about the variations in the morphometry and morphology of the foramen magnum.

Materials and Methods: This study analyzed 70 dried human skulls from the Departments of Anatomy at TS Misra Medical College & Hospital, Era's Lucknow Medical College & Hospital, and KGMU, Lucknow. The shape of the foramen magnum was classified, and its transverse and anteroposterior (AP) diameters were measured using a vernier caliper. The foramen magnum index (FMI) and the foramen magnum area (FMA) were also calculated.

Results: The foramen magnum showed six distinct shapes: oval (47%), round (30%), tetragonal (10%), triangular and irregular (10% each), pentagonal (2%), and hexagonal (1%). The average AP diameter was 34.3±2.90 mm, and the average transverse diameter was 28.9±2.80 mm. The average FMI was 77.80±27.80, while the average FMA was 845.90±87.50 mm².

Conclusions: The data from this study are valuable for neurosurgeons performing surgeries at the cranio-cervical junction and posterior cranial fossa. Understanding the morphometric and morphological characteristics of the foramen magnum is crucial for the prognosis and treatment of neurological conditions like Arnold Chiari syndrome, achondroplasia, and posterior cranial fossa lesions.

Keywords: Foramen magnum, Transcondylar approach, Foramen magnum index, Foramen magnum area, Transverse diameter (TD), Anteroposterior diameter, Trigonal

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Date of Receiving: 23 Jan 2024
Date of Acceptance: 05 Mar 2024

INTRODUCTION

The foramen magnum is an intraosseous foramen which is located at antero-median position in the occipital bone of skull.[1] It provides passageway to the lower end of the medulla oblongata with its meninges, vertebral arteries and veins, spinal accessory nerves, spinal arteries, apical ligament of the dens and the tectorial membrane [1]. The knowledge of anatomical variations of foramen magnum are important in terms of its morphology as well as morphometry because in cases of congenital abnormalities and pathologies at cranio-cervical junction, the morphometry and morphology of foramen magnum is greatly affected.

Therefore, the neurosurgeons should know about the anatomical variations of foramen magnum and its related structures, prior to surgery and the knowledge of anatomical variation of foramen magnum also help to the physical anthropologist and forensic experts for identification of mutilated bodies in the conditions of war fare, nuclear explosions or natural disasters. Very less work is done on basic morphometric and morphological variations of foramen magnum [2].

In addition to the best of our knowledge, till date there is only one research done by Philipp Guber et. al., where they tried to explore any change in biological characters of foramen magnum that occurs from generation to generation [2].

The aim of present study was to determine and analyze the morphometric and morphological variations of foramen magnum which will help the neurosurgeons, prior to surgeries done at cranio-cervical junction in the cases of cerebellar herniation or Achondroplasia.

MATERIALS AND METHODS

This observational study was carried out on 70 dried adult human skulls of unknown age and gender. The skulls were obtained from the Department of Anatomy, TS Misra Medical College, Era's Lucknow Medical College & Hospital and KGMU, Lucknow. The approval from Institutional Ethics Committee was obtained prior to the study. The fully cleaned, undamaged skulls were selected whereas deformed and damaged skulls were excluded. The shape of foramen magnum was observed. The anteroposterior and transverse diameters were measured with the help of digital vernier caliper. The precision of measurement of caliper was 0.01mm. The FMI (foramen magnum index) and FMA (Foramen magnum Area) were also calculated and registered in the tabulated form.

Antero-posterior diameter (AP) was measured from basion (midpoint of anterior margin of foramen magnum) to opisthion (midpoint of posterior margin of foramen magnum). Transverse diameter (TD) was measured between the maximum concavity of right and

left lateral margins of foramen magnum (figure-1). The following formulae were used to calculate the Foramen magnum Index (FMI) and Foramen magnum area (FMA)-

- FMI = Transverse diameter × 100/ Antero-posterior diameter [3]
- Radinsky formula- FMA= ¼ × π × TD × AP^3

Where "π" was accepted as 3.14 in both formulas.

Statistical Analysis: All the data was expressed as mean ± SD and all the statistical analysis was done by using the SPSS software version16.0.

Fig. 1. Landmarks and dimensions of foramen magnum

RESULTS

In the current study, the morphometric and morphological parameters were studied in 70 dried adult human skulls of unknown age and gender of North Indian population.

The most common shape was oval shaped foramen magnum found in maximum skulls (in 33 skulls) and its percentage was 47.1%. The second most common shape was round shaped foramen magnum which was 22.8% (in 16 skulls). The tetragonal shaped foramen magnum was found in 14.2 % (in 10 skulls). The irregular shaped foramen magnum was 7.1 % (in 5 skulls), and hexagonal shaped foramen magnum was only 1.7 % (in single skull). The new variant "trigonal" shaped foramen magnum was 7.1 % (in 5 skulls). The data is presented in table 1 and figure 2 which shows the different shapes of foramen magnum observed in the current study.

Table 2 shows all the morphometric and morphological parameters of foramen magnum according to the different shapes of foramen magnum which were found in this study.

The mean AP and TD diameter of oval shaped foramen magnum was 35.0±3.1 mm and 28.7±2.2 mm respectively and the mean FMA and FMI was 826.7±84.0 mm^2 and 78.8±28.0 respectively.

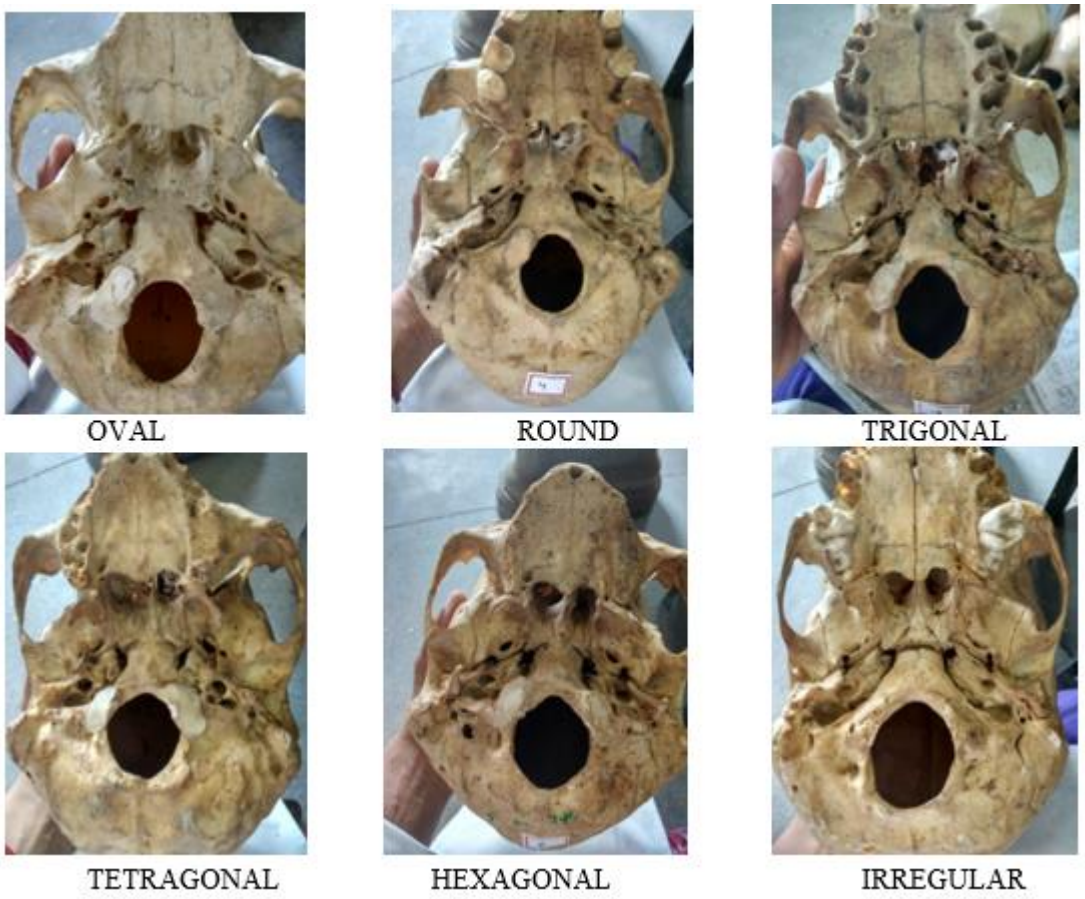

Fig. 2. Different shapes of foramen magnum

S. No.	Shapes of FM	Number of FM	Percentage %
1	Oval	33	47.1%
2	Round	16	22.8%
3	Trigonal	5	7.1%
4	Tetragonal	10	14.2%
5	Hexagonal	1	1.7%
6	Irregular	5	7.1%

Table 1. Number of different shapes of foramen magnum and their percentage

The mean AP and TD of round shaped foramen magnum was 33.5±2.9 mm and 30.9±3.1 mm (transverse diameter) and mean of FMA and FMI was 951.6±39.0 mm^2 (FMA) and 81.2±28.4 (FMI) respectively.

The mean AP, TD, FMA, and FMI of trigonal shaped foramen magnum was 34.6±1.6 mm (AP diameter), 27.6±1.9 mm (transverse diameter), 764.7±25.0 mm^2 (FMA) and 74.9±27.3 (FMI).

S. No.	Shapes of FM	AP diameter (mm) Mean ± SD	Transverse diameter (mm) Mean ± SD	FMI (mm) Mean± SD	FMA (mm^2) Mean± SD
2	Oval	35.0±3.1	28.7±2.2	78.8±28.0	826.7±84.0
2	Round	33.5±2.9	30.9±3.1	81.2±28.4	951.6±39.0
3	Trigonal	34.6±1.6	27.6±1.9	74.9±27.3	764.7±25.0
4	Tetragonal	32.4±2.5	29.0±3.2	73.8±27.1	868.2±77.0
5	Hexagonal	35.0±0.0	24.0±0.0	65.9±25.6	685.7±0.0
6	Irregular	34.6±1.8	26.0±1.0	70.6±26.5	778.7±43.0

Table 2. Dimensions of foramen magnum according to the different shapes

The mean AP, TD, FMA, and FMI of tetragonal shaped foramen magnum were 32.4±2.5 mm (AP diameter), 29.0±3.2 mm (transverse diameter), 868.2±77.0 mm^2 (FMA) and 73.8±27.1 (FMI).

The hexagonal shaped foramen magnum was observed only in single skull (7.1%). The anteroposterior diameter was 35.0±0.0 mm and transverse diameter was 26.0±1.0 mm. The foramen magnum index of hexagonal shaped foramen magnum was 70.6±26.5 and foramen magnum area was 778.7±43.0 mm^2.

The mean AP, TD, FMA, and FMI of irregular shaped foramen magnum were 34.6±1.8 mm (AP diameter), 26.0±1.0 mm (transverse diameter), 70.6±26.5 (FMI) and 778.7±43.0 mm^2 (FMA).

Table 3 shows the details of morphometric parameters of total studied skulls (70 skulls). The mean AP and TD dimensions of foramen magnum of overall studied 70 skulls were 34.3±2.90 mm, and 28.9±2.80 mm and mean FMI and FMA were 77.80±27.80 and 845.90±87.50 mm^2. The minimum mean values of AP and TD of foramen magnum all the skulls were 32.44 mm and 24.00 mm. while the minimum FMI and FMA of foramen magnum were 73.80 and 611.72 mm^2. The maximum mean value of AP and TD of foramen magnum of all studied skulls were 35.09 mm and 30.90 mm. The maximum mean value of FMI and FMA of all skulls were 88.05 and 851.93 mm^2.

DISCUSSION

The knowledge of various morphometric parameters of the foramen magnum helps to determine some congenital malformations such as Achondroplasia and the Arnold-Chiari malformation in which the shape and size of foramen magnum is variable in humans [4]. The patients with achondroplasia have extremely small foramen magnum, whereas in cases of Arnold-Chiari malformation, there is unusually large foramen magnum [4].

Total number (N) – 70	Antero-posterior (AP) diameter (mm)	Transverse Diameter (mm)	Foramen magnum Index (FMI)	Foramen magnum Area (FMA) (mm^2)
Mean ± SD	34.3±2.90	28.9±2.80	77.80±27.80	845.90±87.50
Minimum value	32.44	24.00	73.98	611.72
Maximum value	35.09	30.90	88.05	851.93

Table 3. Dimensions of foramen magnum of total sample (n = 70)

The “oval shaped” foramen magnum was most common shape found in current study. This shape of foramen magnum was also the dominant shape observed in the studies done by Kulesh et.al (2017) [5], Bharati et.al (2021) [6], Bharath et.al (2022) [7] and Gupta AK et.al (2022).[8] However, Faazila et al. (2015) [9] found that the most dominant shape of the foramen magnum in their study was egg-shaped (36%). Rohini devi et.al, (2016) [10] and Sarthak et.al (2017) [11] found round shaped of foramen magnum as most common shape.

In the present study, the second most common shape of the foramen magnum was round, observed in 22.8% of the skulls. These findings were similar to the findings of Bharati et.al (2021) [6], Gupta AK et.al (2022) [8], and Kulesh et.al (2017). [5] The result of the current study was different from the findings of Faazila Fathima et.al (201) [9] and Bharath et.al (2022) [7] where the most common shape of foramen magnum was “egg shape’ while in our study it was round shape.

In the current study, a new uncommon shape “trigonal” shaped foramen magnum, was also observed in 5 skulls. Similarly, the uncommon shape of foramen magnum was also reported by Archana et.al, (2019) [12] and Giridhar et.al (2020). [13] Archana et.al, (2019) [12] found “pear shaped” foramen magnum in 8 skulls and Giridhar et.al (2020) [13] found “leaf shaped” foramen magnum in 6% skull.

In the current study, the mean antero-posterior diameter was 34.3±2.90 mm and mean transverse diameter was 28.9±2.80 mm. These findings were consistent with the findings of Archana et al (2019), [12] Giridhar et.al, (2020), [13] Bharat. J. Sarvaiya et.al, (2018) [14] and M. Rohinidevi et.al, (2016) [10] (Table 5). Gruber P et al. (2009) and Shikha Sharma et al. (2015) reported higher anteroposterior and transverse diameters compared to those found in our study (Table 5).

In the current study, the FMI was 77.80±27.80 which is lower as compared to the findings of Bharat. J. Sarvaiya et.al (2018) [11] and M. Rohini Devi et.al (2016). [12] The present study recorded significantly higher values of FMI (77.80±27.80) as compared to Giridhar et.al. (2020), [13] (1.21±0.12).

Sr. No.	Shapes of FM	Faazila Fathima et. al, 2015[9]	Kulesh S Chandekar et. al, 2017[5]	Archana et.al, (2019)[12]	Giridhar et.al (2020)[13]	Bharati et al 2021[6]	Gupta AK et. al, 2022[8]	Bharath et al. 2022[7]	Present study (2023)
1	Oval	26.42%	38.75%	33.3%	30%	35%	46.9%	36%	47.1%
2	Round	13%	32.5%	13.3%	12%	32.5%	18.8%	18%	22.8%
4	Trigonal	0	0	0	0	0	0	0	7.1%
5	Tetragonal	0	0	16.6%	0	25%	15.6%	8%	14.2%
6	Hexagonal	20.75%	0	16.6%	3%	7.5%	12.5%	6%	1.7%
7	Irregular	0	28.75%	0	27%	0	6.3%	0	7.1%
10	Egg	35.85%	0	0	17%	0	0	24%	0
11	Pentagonal	3.77%	0	13.3%	5%	0	0	8%	0
12	Leaf shaped	0	0	0	6%	0	0	0	0
13	Pear shaped	0	0	6.6%	0	0	0	0	0
Total		53	80			40	32	50	70

Table 4. Comparison of shape of foramen magnum with the result of other studies

S. No.	Authors	No.	Mean Antero-Posterior diameter (mm)	Mean transverse diameter (mm)	Foramen magnum index	Foramen magnum area (mm^2)
1	Gruber P et al 2009[2]	110 skulls	36.6±2.8	31.1±2.7	-	-
2	Shikha Sharma et al 2015[3]	50 skulls	38.76	33.44	87.68	970.57
3	M. Rohinidevi et al 2016[10]	35 skulls	34.80	28.5	82.54	820.53
4	Bharat.J.Sarvaiya et al 2018[14]	326 skulls	34.18±2.74	28.49±2.13	83.60±6.21	766.86±104.76
5	Archana et al 2019[12]	120 skulls	33.79±2.60	28.25±1.83	83.91±6.43	-
6	Giridhar et al 2020[13]	64 skulls	34.10±2.63	28.07±1.87	1.21±0.12	752.07±111.97
7	Bharati et al 2021[6]	40 skulls	Male- 30±2.35 Female- 29.43±2.69	Male- 26.1±2.13 Female- 25.03±1.84	Male- 87.33±8.20 Female- 85.54±7.88	Male- 616.39±82.20 Female- 580.48±80.23
8	Present study	70 skulls	34.3±2.90	28.9±2.80	77.80±27.80	845.90±87.50

Table 4. Comparison of shape of foramen magnum with the result of other studies

The mean foramen magnum area calculated in the present study was 845.90±87.50 mm2. This value was similar to the values obtained by M. Rohinidevi et.al. (2016), [10] whereas this value was high in comparison to the values by Giridhar et.al. (2020), [13] Bharati et.al. (2021) [6] and Bharat. J. Sarvaiya et.al. (2018). [14] Our recorded mean FMA was lower as compared to Shikha Sharma et al (2015) [3].

Limitations: The sample size of the present study was small and study done on dry human skulls of unknown age and gender.

CONCLUSION

Bony abnormalities of cranio-vertebral junction are of interest not only to an anatomist and physical anthropologist but also to the surgeons as they produce clinical symptoms which affect human health drastically. Abnormalities of foramen magnum can be classified as congenital, developmental, acquired, traumatic and pathological. These abnormalities can occur either individually or in combination. The data analysis and values of current study may help the anatomist, radiologist and neuro-surgeons for transcondylar surgical approaches which are in increasing trend in recent time for brain stem lesion and surgeries at cranio-cervical junction. The thorough knowledge of anatomical variation of foramen magnum helps radiologists to differentiate deformities such as Arnold Chiari malformation in which the transverse diameter of foramen magnum is increased. These findings can also be useful to neurosurgeons for better approach to treat foramen magnum meningiomas and other posterior cranial fossa lesions. The morphology and morphometry of foramen magnum also has some evolutionary importance. More studies are required, as there may be variations in the shapes and dimensions of the foramen magnum across different regions in India.

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https://doi.org/10.46351/jas.v32i1pp27-37

JAS Journal of Anatomical Sciences (U.P. Chapter of Anatomical Society of India)

Original Article

CHALLENGES AND COPING MECHANISMS AMONG FIRST-YEAR MBBS STUDENTS IN INDIA

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ABSTRACT

Introduction: First-year MBBS students encounter a wide array of academic, social, and personal challenges during their transition into medical school. These challenges can cause a significant impact on their well-being and academic performance. This study aimed to identify the key issues faced by first-year MBBS students and explore the coping mechanisms they employ to manage stress during their initial year of medical education.

Materials and Methods: An online cross-sectional survey was conducted among 256 first-year MBBS students using Google Forms. The survey included questions about demographic information, the primary challenges students faced, their motivations for pursuing medicine, and the coping mechanisms they used. Data were analyzed descriptively to calculate the prevalence of different challenges and coping strategies. The study population consisted of 166 females, 89 males, and 1 other student from various medical colleges in India.

Results: The most commonly reported challenge was balancing studies with personal life (22.27%), followed closely by academic pressure and workload (21.88%). Other significant challenges included time management (11.72%), adapting to a new environment (11.72%), and difficulty in understanding course material (7.03%). Students commonly relied on social support (16.20%), exercise (12.50%), and taking breaks (14.81%) as coping mechanisms.

Conclusions: First-year MBBS students face significant academic and personal challenges. The results suggest a need for enhanced institutional support, personalized interventions, and structured programs to help students navigate this critical period in their medical education more effectively.

Keywords: First-year MBBS students, Challenges, Coping mechanism, Stress

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Date of Receiving: 11 May 2024
Date of Acceptance: 18 Jun 2024

INTRODUCTION

First-year MBBS students in India encounter a complex array of challenges that span academic, social, and personal domains, reflecting the demanding nature of medical education. The transition from pre-university life to the rigors of medical school is often marked by significant psychological and emotional strain. Studies have shown that adjustment disorder is prevalent among first-year medical students, with approximately 67% of respondents in one study exhibiting signs of this condition within six months of enrollment. This condition is largely attributed to various stressors, including the intense time and work pressure, financial burdens, and the substantial changes in living situations that accompany the start of medical training [1].

Academically, students often find themselves overwhelmed by the sheer volume of content and the rapid pace at which it is delivered, particularly during the Foundation Course (FC). The FC, designed to ease students into the medical curriculum, is intended to provide essential knowledge and skills. However, the course has been criticized by some students for its overwhelming nature, particularly due to the heavy use of technical jargon and the logistical challenges associated with training sessions. Despite these criticisms, other students have expressed satisfaction with the FC, appreciating the structured orientation and the valuable knowledge it imparts. This dichotomy highlights the varied experiences of students, where some benefit from the organization and content of the program, while others struggle to cope with the academic demands placed upon them [2, 3].

In addition to the challenges posed by the FC, there is a notable gap in students' pre-medical exposure to certain disciplines, such as community medicine. This lack of awareness and understanding prior to formal education underscores the need for better preparatory programs that can provide a more comprehensive introduction to the various fields of medicine. This gap in exposure may contribute to the initial difficulties students face when adapting to the medical curriculum [4].

Another critical factor influencing student performance is their study habits. Research has demonstrated a strong correlation between effective study strategies and academic success, emphasizing the need for students to develop efficient learning techniques early in their medical education. Poor study habits can exacerbate the already considerable pressures faced by first-year students, leading to suboptimal academic outcomes [5].

Beyond academics, personal well-being is a significant concern among first-year MBBS students. Poor sleep quality is a prevalent issue, with studies indicating a notable gender

disparity, where female students report more sleep-related problems than their male counterparts [6]. These sleep issues, coupled with the academic and social pressures of medical school, can severely impact students' mental and physical health.

Orientation programs have been identified as a positive influence in this challenging environment. These programs help to alleviate anxiety, build confidence, and provide students with the tools they need to navigate the complexities of medical education. While some students benefit greatly from these structured introductions to the medical field, others continue to struggle with the demands of the curriculum and issues related to personal well-being, such as sleep quality [7].

In summary, first-year MBBS students in India face a myriad of challenges, including adjustment difficulties, academic overload, and insufficient pre-medical exposure to certain disciplines. While structured orientation and foundation courses provide valuable support for some students, others continue to grapple with the demands of the curriculum and personal well-being issues.

These findings underscore the importance of developing tailored support systems to address the diverse needs of medical students [1-7].

MATERIALS AND METHODS

Study Design & Participants: This study was a cross-sectional survey at understanding the challenges that-year MBBS students encounter during their education journey. A total of 256 students participated, representing three medical colleges in North India. To maintain anonymity, participants could choose to remain unidentified when responding to the online survey created via Google Forms. The data were collected over a span of two months, specifically from March to April 2024.

Questionnaire Development: The survey Questionnaire was carefully crafted after a thorough review of existing literature related to the challenges experienced by medical students. Questions were tailored to cover a broad spectrum of issues—these include academic, personal, social, & psychological challenges. The questionnaire featured both closed-ended questions and open-ended ones, which enabled students to share their experiences in greater detail. The questions included in the survey are presented in Table 1.

Data Collection & Analysis: Responses to the survey were automatically gathered and organized by Google Forms. Data analysis was done via quantitative and qualitative methods. Closed-ended questions received analysis through descriptive statistics. On the

Table 1. Questions included in the survey questionnaire

Question	Type
Name (Leave blank if you wish to remain anonymous)	Open ended
Gender	Open ended
Name of your medical college (Optional)	Open ended
Why did you choose to become a doctor?	Open ended
What is the biggest challenge you have faced during your first year of MBBS?	Open ended
Anything else that has been the biggest challenge for you during the first year of MBBS.	Open ended
What are the other challenges you have faced during your first year of MBBS?	Multiple choice
Any other challenges/problems/issues that you faced during your first year in MBBS.	Open ended
What helped you cope with stress during your first year in MBBS?	Open ended
What helped you cope with stress during your first year in MBBS? (Anything else not mentioned above)	Multiple choice
How often did you seek help from your professors or teaching staff?	Multiple choice
How well do you think your medical college supports student well-being?	Multiple choice
What motivates you to continue your studies despite the challenges?	Multiple choice
Any suggestion(s) that you feel would make life easier for a medical student, especially in the first year of MBBS.	Open ended
Any other information that you would like to add personally.	Open ended

other hand, answers to open-ended questions went through thematic analysis, allowing researchers to identify recurring themes and patterns among the various challenges reported by students. These findings provide valuable insights into the diverse challenges encountered by first-year MBBS students and lay the groundwork for recommendations aimed at enhancing student support systems within medical colleges.

RESULTS

The survey conducted among first-year MBBS students yielded several important insights into the challenges, motivations, and coping mechanisms of these students. A total of 256 students participated in the survey, including 166 females, 89 males, and 1 student who identified as "Other."

1. Challenges Faced During the First Year

One of the key questions posed to students

Table 2. Challenges Faced During the First Year

Challenge	Female	Male	Other	Total (%)
Balancing Studies with Personal Life	32 (19.28%)	25 (28.09%)	0	57 (22.27%)
Academic Pressure and Workload	33 (19.88%)	22 (24.72%)	1	56 (21.88%)
Adapting to a New Environment	24 (14.46%)	6 (6.74%)	0	30 (11.72%)
Time Management	22 (13.25%)	8 (8.99%)	0	30 (11.72%)
Difficulty in Understanding Course Material	12 (7.23%)	6 (6.74%)	0	18 (7.03%)
Financial Issues	5 (3.01%)	4 (4.49%)	0	9 (3.52%)
Difficulty in Socializing and Making Friends	6 (3.61%)	3 (3.37%)	0	9 (3.52%)
Homesickness	6 (3.61%)	3 (3.37%)	0	9 (3.52%)
Health Problems	6 (3.61%)	2 (2.25%)	0	8 (3.13%)
Hostility from Seniors	3 (1.81%)	4 (4.49%)	0	7 (2.73%)
Lack of Support from Faculty	3 (1.81%)	3 (3.37%)	0	6 (2.34%)

was, "What is the biggest challenge you have faced during your first year of MBBS?" The data shows a wide array of responses, with academic and personal life challenges being the most significant concerns. Below is a breakdown of the responses (Table 2).

The most prevalent issue was "Balancing Studies with Personal Life," reported by 22.27% of students. The second most significant issue was "Academic Pressure and Workload" (21.88%). This highlights the dual burden faced by students as they try to excel academically while also managing their personal lives.

2. Motivations for Choosing Medicine

When asked, "Why did you choose to become a doctor?" the responses reflected a blend of personal ambition, family influence, and career aspirations. Table 3 summarizes the responses.

Table 3. Motivations for Choosing Medicine

Motivation	Female	Male	Other	Total (%)
Childhood Dream or Ambition	51 (30.72%)	20 (22.47%)	0	71 (27.73%)
Inspired by a Doctor or Medical Professional	29 (17.47%)	21 (23.60%)	0	50 (19.53%)
Interest in Science and Human Biology	36 (21.69%)	10 (11.24%)	0	46 (17.97%)
Influence of Family and Friends	15 (9.04%)	19 (21.35%)	0	34 (13.28%)
Prestige and Respect in Society	13 (7.83%)	5 (5.62%)	0	18 (7.03%)

Table 4. Coping Mechanisms

Coping Mechanism	Female (%)	Male (%)	Total (%)
Talking to Friends and Family	20 (15.50%)	15 (17.24%)	35 (16.20%)
Exercise and Physical Activity	15 (11.63%)	12 (13.79%)	27 (12.50%)
Hobbies and Recreational Activities	18 (13.95%)	10 (11.49%)	28 (12.96%)
Taking Breaks and Rest	18 (13.95%)	14 (16.09%)	32 (14.81%)
Meditation and Mindfulness	12 (9.30%)	7 (8.05%)	19 (8.80%)

The largest motivation for students to pursue medicine was a "Childhood Dream or Ambition" (27.73%), followed by being "Inspired by a Doctor or Medical Professional" (19.53%) and "Interest in Science and Human Biology" (17.97%).

3. Coping Mechanisms

Coping mechanisms varied among students, with a preference for talking to friends and family and engaging in physical activities. Table 4 shows the most frequently reported coping mechanisms.

The most common coping strategies were "Talking to Friends and Family" (16.20%) and "Taking Breaks and Rest" (14.81%). A notable minority of students turned to more structured approaches such as meditation and mindfulness, as well as physical activity.

4. Seeking Help from Professors

The frequency of students seeking help from their professors varied significantly. The results of the survey are shown in Table 5. The data reveals that while some students sought help occasionally, a significant proportion either rarely or never sought assistance from professors (32.81%).

5. Institutional Support

Finally, students were asked to rate the support they received from their medical college in terms of well-being. The distribution of responses is summarized in Table 6. A large portion of students (31.25%) expressed a neutral opinion regarding their institution's support for their well-being, while 21.48% rated the support as poor, and 16.80% as very poor. Only 8.59% of students felt very well supported.

Table 5. Seeking Help from Professors

Frequency of Seeking Help	Female (%)	Male (%)	Total (%)
Very Often	8 (4.82%)	6 (6.74%)	14 (5.47%)
Often	25 (15.06%)	15 (16.85%)	40 (15.63%)
Occasionally	47 (28.31%)	37 (41.57%)	84 (32.81%)
Rarely	60 (36.14%)	24 (26.97%)	84 (32.81%)
Never	26 (15.66%)	7 (7.87%)	34 (13.28%)

Table 6. Institutional Support

Perceived Support	Female (%)	Male (%)	Total (%)
Very Well	11 (6.63%)	11 (12.36%)	22 (8.59%)
Well	37 (22.29%)	19 (21.35%)	56 (21.88%)
Neutral	52 (31.33%)	28 (31.46%)	80 (31.25%)
Poorly	36 (21.69%)	19 (21.35%)	55 (21.48%)
Very Poorly	30 (18.07%)	12 (13.48%)	43 (16.80%)

The results of this survey indicate that first-year MBBS students face a variety of academic, personal, and social challenges, with balancing studies and personal life being the most prominent issue. While many students find support through family and friends, the data suggests that institutional support, particularly in terms of well-being, may need improvement.

DISCUSSION

The survey results provided a detailed understanding of the multifaceted challenges faced by first-year MBBS students, reinforcing and expanding upon themes highlighted in existing literature. The complexities of balancing academic pressures, personal life, and adapting to a new environment reveal significant stressors that these students face. In this discussion, we will critically examine these challenges, their interrelationships, and the coping mechanisms students utilize, drawing connections to the research outlined in the introduction.

Academic Pressure and Work-Life Balance

The survey found that 22.27% of students reported "Balancing Studies with Personal Life" as their biggest challenge, closely followed by "Academic Pressure and Workload" (21.88%). These results are consistent with findings from Agarwal and India (2024), who identified adjustment disorder as a prevalent issue among first-year students due to stressors like intense time and work pressure [1]. The academic overload experienced by first-year students is further exacerbated by the demanding nature of the Foundation Course (FC), which is intended to ease students into the medical curriculum but often ends up overwhelming them with technical jargon and logistical complexities [2].

Interestingly, while many students find it difficult to maintain a balance between academic responsibilities and personal life, the introduction of structured programs like the FC and orientation sessions has shown potential in alleviating some of these pressures. Studies suggest that these programs help build confidence and provide essential skills to navigate the medical curriculum [3]. However, as reflected in the survey, these benefits are not uniformly experienced by all students. For

some, the FC adds to the overwhelming nature of their first year, while for others, it provides much-needed structure and guidance.

This disparity in experiences suggests that a one-size-fits-all approach to the FC may not be the most effective strategy for addressing the varied needs of students. Tailoring the program to individual needs, perhaps through more personalized support systems or flexibility in pacing, could help mitigate the overwhelming nature of academic work during the first year.

Adapting to a New Environment and Time Management

Adaptation to the medical school environment emerged as a significant challenge for many students. The transition from pre-university life to medical education involves adapting to a new academic environment, social setting, and often a new living situation. This adjustment difficulty was highlighted by 11.72% of respondents. Similar findings were noted in the literature, where the initial months of medical education are marked by substantial psychological strain due to these environmental and social transitions [4].

Time management, reported by 11.72% of students as their biggest challenge, plays a critical role in how well students adapt to the academic rigors of medical school. Poor time management has been linked to exacerbating feelings of being overwhelmed, leading to suboptimal academic outcomes. The need for efficient study habits is well-documented, with research suggesting that early development of effective learning techniques can significantly alleviate academic pressures [5].

The survey results also indicated that students who were able to develop effective time management strategies often cited them as coping mechanisms for stress, suggesting that interventions aimed at improving time management skills could play a crucial role in helping students adjust to medical school. These could include workshops on study habits, structured schedules, or mentoring programs where senior students share their experiences and strategies for managing time effectively.

Social and Psychological Challenges

Another aspect of the survey results relates to the social and psychological challenges faced by students. Difficulty in socializing and making friends, homesickness, and health problems were reported by a significant portion of the cohort. Social isolation, in particular, is known to exacerbate feelings of stress and anxiety, making it difficult for students to cope with the demands of medical education.

A notable 3.52% of respondents indicated that they struggled with homesickness, while 3.52% reported difficulty in making friends and 3.13% cited health problems. These issues, though reported by a smaller percentage of students, can compound the academic stress experienced during the first year. Literature highlights that poor social integration can negatively impact a student's mental health, making it more difficult to manage academic pressures and personal responsibilities [6].

The impact of these social and psychological challenges on academic performance cannot be understated. While academic difficulties are often the most visible signs of distress, underlying social and psychological issues frequently contribute to these struggles. It is imperative that medical colleges recognize the importance of fostering a supportive and inclusive social environment to help students adjust more effectively. Programs that encourage socialization, peer support groups, and counseling services can provide critical support to students facing these challenges.

Gender Disparities in Stress and Coping Mechanisms

The survey also revealed gender disparities in the challenges faced and the coping mechanisms used by students. Female students were more likely to report issues with balancing personal life and academic demands, while male students reported a higher incidence of academic pressure and workload challenges. These findings align with previous studies that have shown gender differences in how students perceive and manage stress [7].

In terms of coping mechanisms, female students were more likely to engage in activities like talking to friends and family, while male students were more likely to engage in physical activity or exercise. These gender-specific coping strategies are consistent with existing literature, which suggests that women tend to rely more on social support networks, whereas men may turn to physical outlets for stress relief [1,7].

This gender disparity in coping strategies suggests that support systems need to be gender-sensitive, providing both social and physical outlets for stress relief. For female students, peer counseling and social support groups may be more effective, while male students may benefit from programs that encourage physical activity as a means of managing stress.

Institutional Support and Well-being

The survey results also brought to light concerns about institutional support for student well-being. While 31.25% of students reported a neutral perception of their institution’s support for well-being, a significant 21.48% rated it as poor, and 16.80% rated it as very poor. This indicates that a substantial portion of students feel that their institutions are not adequately

addressing their well-being needs.

This finding is particularly concerning, as literature has shown that institutional support plays a crucial role in alleviating stress and promoting student well-being. Programs that focus on student well-being, such as mental health services, academic tutoring, and social support systems, have been shown to improve students' overall experience and reduce the risk of burnout [7]. However, the survey results suggest that these programs may not be reaching all students effectively, or that there are gaps in how these services are delivered.

One possible explanation for this gap is the variability in how different students perceive and access institutional support. While some students may actively seek out support services, others may be reluctant to do so due to stigma or lack of awareness. This underscores the importance of making support services more visible and accessible to all students, perhaps through mandatory orientation sessions, regular check-ins, or integrating mental health and well-being into the curriculum itself.

Implications for Future Interventions

The results of this study highlight the need for medical institutions to adopt a more holistic approach to supporting first-year students. Academic challenges, while significant, are only one aspect of the difficulties students face. Personal, social, and psychological factors also play critical roles in shaping the student experience, and addressing these issues requires comprehensive support systems that go beyond academic tutoring.

Institutions must consider developing tailored interventions that address the diverse needs of students. For instance, time management workshops, peer mentoring programs, and increased access to counseling services could help alleviate some of the pressures faced by first-year students. Additionally, creating a more inclusive and supportive social environment could help mitigate feelings of isolation and homesickness, which are common during the first year of medical school.

Furthermore, the gender differences observed in both challenges and coping mechanisms suggest that interventions should be gender-sensitive, offering a range of support options that cater to the different ways in which male and female students cope with stress.

CONCLUSION

In conclusion, the survey results provide valuable insights into the challenges faced by first-year MBBS students. Academic pressures, personal life balance, and social integration are key areas of concern, and the coping mechanisms employed by students reflect a range of strategies for managing these challenges. However, the variability in how students experience and cope with stress highlights the need for more

personalized and comprehensive support systems. By addressing the academic, personal, and social needs of students in a more targeted and gender-sensitive manner, medical institutions can help improve the overall well-being and academic success of their students.

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https://doi.org/10.46351/jas.v32i1pp38-44

JAS Journal of Anatomical Sciences (U.P. Chapter of Anatomical Society of India)

Case Series

VERTEBRAL SYNOSTOSIS AND ITS CLINICAL IMPORTANCE – A CASE SERIES

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ABSTRACT

Synostosis/ block vertebrae/ fusion of vertebrae occurs due to congenital fusion or due to spinal diseases like tuberculosis, juvenile rheumatoid arthritis, traumatic conditions. The synostosis may be either complete or incomplete or may be either acquired or congenital. The fused vertebrae function as one vertebra, and are usually asymptomatic until adulthood, where degenerative changes occur, and nerve root compression symptoms are noticed. This study aimed to find incidence of vertebral synostosis in population of Garhwal region of Uttarakhand. In the present study a total of 575 vertebrae were examined for presence of block vertebrae/ synostosis/ fusion and found a total of 08 cases (Incidence = 1.39%) out of which we found mostly in cervical region – 04 out of 08 cases (Incidence = 0.69%), followed by thoracic region – 03 out of 08 cases (Incidence = 0.52%) and cervicothoracic region – 01 out of 08 cases (Incidence =0.17) This is the first study for vertebral synostosis in Garhwal region of Uttarakhand, to the best of our knowledge.

Keywords: Block, Ossification, Synostosis, Vertebrae

INTRODUCTION

Synostosis of vertebrae occurs due to congenital fusion or may be due to spinal diseases like tuberculosis, juvenile rheumatoid arthritis, and traumatic condition. A synostosis or block vertebra means fusion of vertebrae.

Anatomical defects have been reported which include sacralization, lumbarization, occipitalization, lack of posterior vertebral arch and spinal synostosis. Fusion of successive vertebral segments may lead to block spines, block vertebrae, vertebral synostosis or spinal fusion, which may lead to limited or restricted movements, degenerative

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Date of Receiving: 24 Nov 2023
Date of Acceptance: 06 Jan 2024

disc changes and associated neurological deficits which are visible clinically. The synostosis may be complete or incomplete, acquired or congenital [1].

The vertebral column is flexible because it contains many small bones – vertebra, in between vertebrae resilient intervertebral disc is present. The vertebra articulate with each other at synovial zygapophysial joint which provide flexibility to vertebral column [2].

A typical vertebra consists of a vertebral arch, vertebral foramen, body, transverse process and a spinous process. Vertebral body is massive and provides strength to vertebral column. The vertebral arch is present posterior to the body and is formed by two right and left pedicles and laminae. The walls of vertebral foramina are form by vertebral arch and posterior surface of vertebral body. The vertebral notches are present superior and inferior to each pedicle between the superior and inferior articular processes posteriorly and the corresponding projections of the body anteriorly [2].

Congenital vertebral synostosis (CVS) is a rare developmental condition which occurs due to segmentation or metamerism process failure. Block vertebrae or vertebral synostosis result from incomplete vertebral fusion. CVS can be isolated or may be due to syndromic manifestations like Klippel-Feil syndrome. Acquired vertebral synostosis (AVS) is due to some pathology like fibrodysplasia or progressive juvenile rheumatoid arthritis or following infection such as tuberculosis or is post-surgical or post-traumatic [3].

There are usually two congenital fused cervical vertebrae (CFCV) and more than two are present rarely. They constitute a single unit functioning as one vertebra. Until adulthood, these are usually asymptomatic, where degenerative changes such as arthritis, disc hernias occur adjacent to CFCV level and nerve root compression symptoms are noticed [4].

The upper part of cervical spine has highest frequency of synostosis, which decreases gradually downwards [5]. Formation of osteophytes on the adjacent levels is one of the secondary effects of CFCV [6]. The aim of present study is to report incidence of cases of vertebral synostosis in population of Garhwal region of Uttarakhand.

CASE SERIES

Eight cases of vertebral synostosis were observed in the vertebrae present in the museum of Department of Anatomy, GDMC, Dehradun, Uttarakhand. The present study was done after obtaining ethical clearance from institutional ethical committee (IEC/GDMC/2020/91). Gender and age could not be specified. Vertebrae having synostosis were observed and photographs were taken.

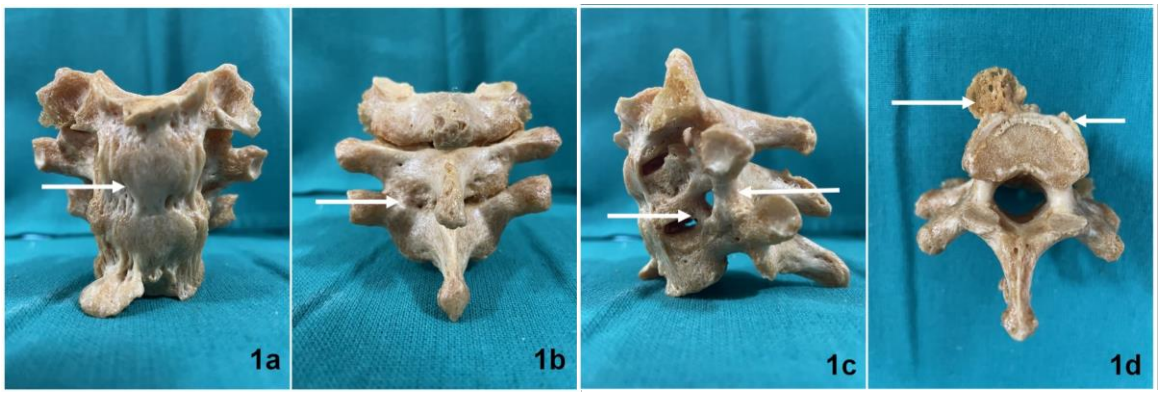

Fig. 1. a) Showing anterior view of fused vertebrae C7-T1-T2 with ossification at anterior longitudinal ligament; b) Showing posterior view with ossification between articular facets of left T1-T2 vertebrae; c) Showing left lateral view with fusion of lamina between left T1-T2 vertebrae and posterior longitudinal ligament; d) Showing superior view with osteophytes on superior margin of C7 and body of T2 vertebrae.

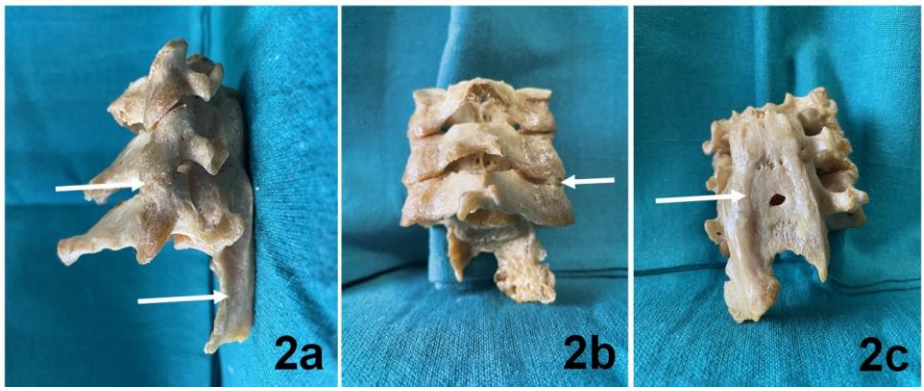

Fig. 2. a) Showing left lateral view of fused vertebrae C4-C6 with fusion of articular facets of right C5-C6 vertebrae and extended ossified anterior longitudinal ligament; b) Showing posterior view of fusion of right articular facets of C5-C6 vertebrae; c) Showing anterior view with ossified anterior longitudinal ligament.

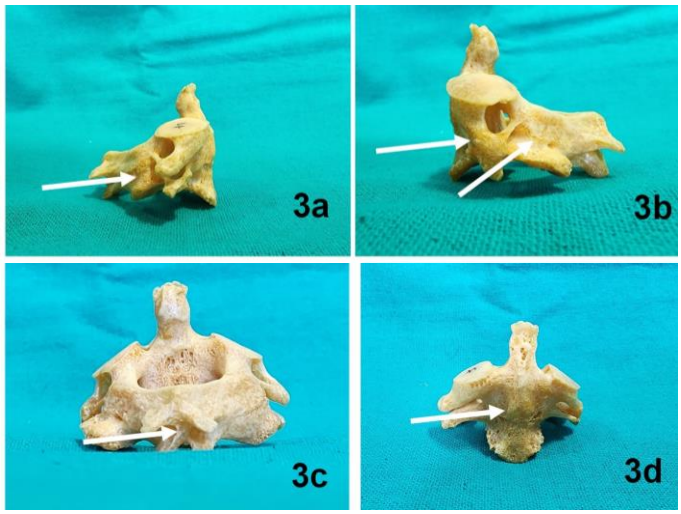

Fig. 3. Showing right lateral view of fused vertebrae C2-C3 with fusion of right lamina and articular facets; b) Showing left lateral view with fusion of left lamina and articular facets; c) Showing anterior view with ossification of anterior longitudinal ligament.

The present case series shows incidence of synostosis as 1.39%. The incidence of synostosis was found to be 0.69% in cervical, 0.52% in thoracic and 0.17% in cervicothoracic region in the present study.

Case 1: Cervico-thoracic synostosis was observed between C7-T1-T2 vertebrae. (Fig. 1) In these vertebrae, ossification/fusion of anterior longitudinal ligament and posterior longitudinal ligament (full length) was observed. Osteophytes were observed on the superior margin of C7 and body of T2. Fusion of articular facets – between left T1-T2 and right C7-T1 vertebrae was observed. Ossification of ligaments was observed in between the laminae of left T1-T2 and body of T1-T2.

Case 2: Cervical synostosis was observed between C4-C5-C6 vertebrae. (Fig. 2) In this case, ossification/fusion of anterior longitudinal ligament (full length), body of C4-C5, C5-C6, and of articular facet (between right C5-C6) were seen.

Case 3: Cervical synostosis was observed between C2-C3 vertebrae. (Fig. 3) and ossification was seen at anterior longitudinal ligament (full length), posterior longitudinal ligament (full length), in between laminar ligaments (bilaterally), and at spinous process (interspinale ligaments). Fusion of left transverse process, at articular facets – bilaterally was also present.

Case 4: Thoracic synostosis was observed between five typical thoracic vertebrae (exact levels could not be identified). (Fig. 4) Ossification was seen at anterior longitudinal ligament (full length), anterior and right lateral aspect. Fusion of articular facet (between right 2nd and 3rd vertebrae) was also observed.

Case 5: Thoracic synostosis was observed between two typical thoracic vertebrae (exact levels could not be identified). (Fig. 5) Ossification of anterior longitudinal ligament was also observed.

Case 6: Cervical synostosis was observed between two typical cervical vertebrae (exact level could not be identified) (Fig. 6). The ossification of anterior longitudinal ligament (full length), was seen. The fusion of right articular facet and body was also observed.

Case 7: Thoracic synostosis was observed between two typical thoracic vertebrae (exact levels could not be identified) (Fig. 7). The ossification was seen only between articular facets (bilaterally).

Case 8: Cervical synostosis was observed between C2-C3 vertebrae. (Fig. 8). The ossification of anterior longitudinal ligament (full length) and interlaminar ligament (bilaterally) was observed. Fusion occurs at spinous process, left transverse process and articular facets (bilaterally).

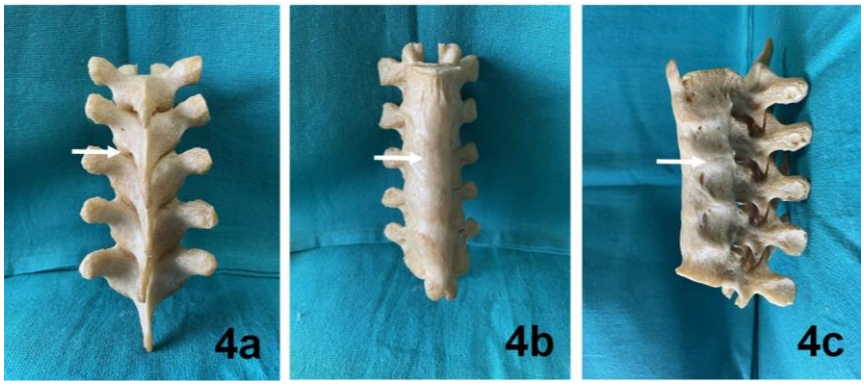

Fig. 4. a) Showing posterior view of fused vertebrae - five typical thoracic vertebrae with fusion of articular facets between 2nd and 3rd; b) Showing anterior view with ossification of anterior longitudinal ligament; c) Showing right lateral view with fusion of bodies of all vertebrae.

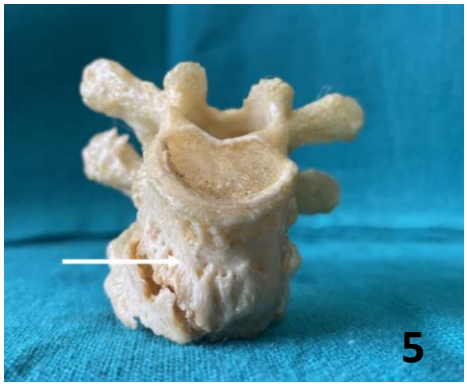

Fig. 5. Showing anterior view of fused vertebrae – two typical thoracic vertebrae with ossification of anterior longitudinal ligament.

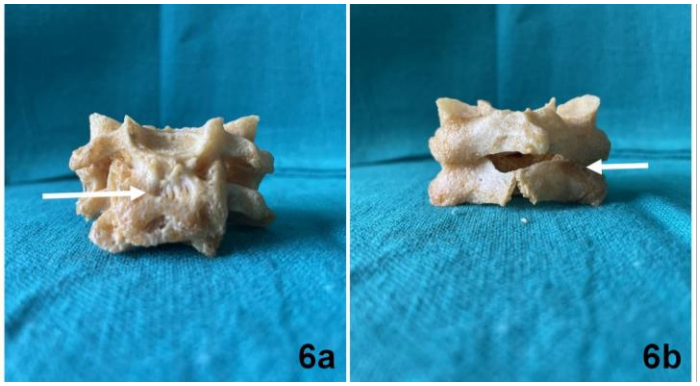

Fig. 6. a) Showing anterior view of fused typical cervical vertebrae with ossification of anterior longitudinal ligament; b) Showing posterior view with fusion of right articular facets.

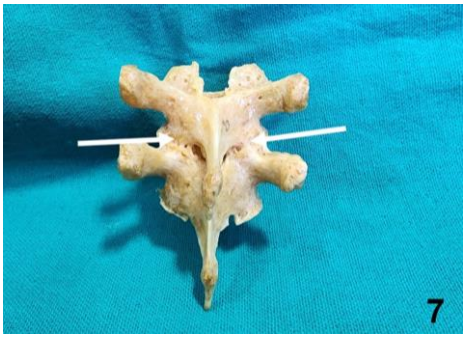

Fig. 7. Showing posterior view of fused vertebrae – two typical thoracic vertebrae with fusion of bilateral articular facets.

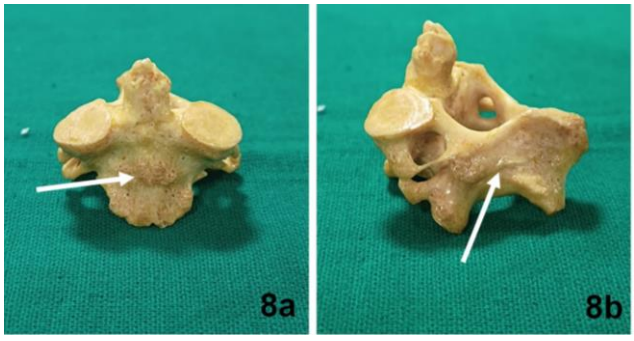

Fig. 8. a) Showing anterior view of fused vertebrae C2-C3 with ossification of anterior longitudinal ligament; b) Showing left lateral view with fusion of left lamina, articular facets and spine.

DISCUSSION

Vertebral column is the part of axial skeleton which develops from paraxial mesoderm, lateral plate mesoderm and neural crest cells. On each side of neural tube, paraxial mesoderm forms segmented series of tissue blocks known as somitomeres in the head region and somites in occipital region caudally [7].

Sclerotome is ventromedial portion of somites and forms vertebrae, during 4th week migration of sclerotome cells occurs around spinal cord and notochord and merging of cells occurs with cells from opposing somite on the other side of neural tube, followed by resegmentation, where caudal half of each sclerotome grows and fuses with cephalic half of each subjacent sclerotome [7].

If two adjacent somites or their associated mesenchyme fail to separate properly, they result into segmentation defect. A block vertebra is created when there is involvement of entire vertebral segment [8].

Vertebral fusion, in referred condition results in more biomechanical pressure in related segments leading to premature deteriorating changes at related motion segments, while during blastemal stage, environmental and genetic factors are involved in pathogenesis. Causes of CFVC may include malformations of notochord, retinoids, and decrease in local blood supply of spine in embryonic life and Klippel-Feil syndrome [6].

Sacrum is an example of normal block or fused vertebrae. The disruption of PAX-1 gene expression may result in vertebral fusion abnormalities. Acquired causes include trauma, tuberculosis, juvenile rheumatoid arthritis [1].

Vertebral anomalies are of importance to anatomists, neurosurgeons, neurologists, orthopaedicians and general surgeons. Vertebral fusion have clinical and embryological importance since the clinical symptoms vary according to degree and exact location of the fusion leading to limitation of movements, early degenerative changes and related neurological symptoms [1].

In a study by Nazeer et al, they found incidence of 0.25%, which is less than incidence of our study [9].

In a study by Masnicova et al, they found incidence of 2.6% in cervical, 1.6% in thoracic and 0.5% in lumbar vertebrae in Lithuanian population [10], whereas our study reported 0.69% in cervical, 0.52% in thoracic and 0.17% in cervicothoracic region.

In a study by Sharma et al, they found incidence of 6.25% in cervical, 4.16% in thoracic and 2.08% in lumbar region [11],

while, in the present study the incidence of synostosis is 0.69% in cervical, 0.52% in thoracic and 0.17% in cervicothoracic region.

CONCLUSION

In the present study a total of 575 vertebrae were examined for presence of block vertebrae/ synostosis/ fusion and found a total of 08 cases (Incidence = 1.39%) out of which we found mostly in cervical region – 04 out of 08 cases (Incidence = 0.69%), followed by thoracic region – 03 out of 08 cases (Incidence = 0.52%) and cervicothoracic region – 01 out of 08 cases (Incidence =0.17) This is the first study for vertebral synostosis in Garhwal region of Uttarakhand, to the best of our knowledge.

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https://doi.org/10.46351/jas.v32i1pp45-52

JAS Journal of Anatomical Sciences (U.P. Chapter of Anatomical Society of India)

Review Article

THERAPEUTIC EFFECT OF OMEGA-3 FATTY ACID IN POLYCYSTIC OVARIAN DISEASE

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ABSTRACT

Polycystic ovarian disease is the most common endocrine condition in reproductive-aged women. Its common characteristics are reproductive, metabolic, endocrine, and psychological changes in women. We review here the therapeutic effect of omega-3 polyunsaturated fatty acids on polycystic ovarian disease (PCOD). Therefore, the aim of conducting a review was to study the possible effects and their mechanism. A comprehensive systematic search was conducted in MEDLINE/PubMed, Google Scholar, and SCOPUS, to find studies investigating omega-3 fatty acids as a preventative or therapeutic agent for the attenuation of PCOD complications. Subsequently, the impact of omega-3 on PCOD, inflammation, insulin resistance, obesity, and hormonal imbalance were discussed. Although most of the studies in patients with PCOD reported an improvement in many complications after administration of omega-3 supplements, there is a distinct shortage of studies investigating the dietary intake of these types of fatty acids. A balanced amount of omega-3 fatty acid is important for prevention and reducing complications of PCOD.

Keywords: Omega-3, Fatty acids, PCOD, PUFA

INTRODUCTION

Polycystic ovarian disease (PCOD) is the most common female reproductive disorder in women aged 15 to 48 years. It is an endocrine and metabolic disorder in women, reflecting major hormonal imbalance and long-term complications [1].

PCOD is a disease affecting approximately 6 to 10% of women in their reproductive age [2]. PCOD was first discovered by the American gynecologist F Stein and M Leventhal in 1935 as an accumulation of many fluid-filled sacs in follicles of ovary [3]. There are several characteristics of PCOD like irregular menstrual cycles, amenorrhea and

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Date of Receiving: 27 May 2024
Date of Acceptance: 22 Jun 2024

oligomenorrhea, acne or hirsutism, enlarged ovary, insulin resistance, obesity, and infertility.

Polycystic Ovary Syndrome (PCOS), also known as Polycystic Ovary Disease, is the most common disorder affecting women of childbearing age. PCOD is a heterogeneous disease with a variety of signs and symptoms and severe disturbance of endocrine and metabolic functions [2]. Recently, European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine (ESHRE/ASRM) stated a refined definition of PCOD: particularly the presence of 2 out of the subsequent 3 criteria: (i) oligo- and/or anovulation; (ii) hyperandrogenism (clinical and/or biochemical); (iii) polycystic ovaries, with the exclusion of different etiologies [4].

Clinically, PCOD women diagnosed with associated inflated sterility risks like dysfunctional hemorrhage, endometrial and ovarian cancer, form a pair of polygenic disorder [5]. Additionally, several endocrine abnormalities in PCOD result from metabolic alteration like dyslipidemia, obesity, metabolic syndrome, insulin resistance, and hyperinsulinemia [6]. PCOD phenotype is a prominent clinical issue from the symptomatic and therapeutic point of view [7]. The specific causes are not known for PCOD till now, but some of the factors that can affect are environmental factors, genetic factors, sedentary lifestyle, etc.

The cure for PCOD are firstly, lifestyle changes, dietary modification, behavioral therapy, physical activity, and exercise. The nutritional intervention & therapeutic approach represent a favorable strategy for the treatment of PCOD [8]. Omega-3 fatty acids, mainly polyunsaturated fatty acids, play a very effective role to prevent anovulation. Omega-3 fatty acids have been found to have very health benefits like anti-inflammatory properties, anti-insulin resistance, and anti-obesity properties [9]. Evidence suggests that role of omega-3 fatty acid supplementation increase insulin sensitivity, and decrease plasma triglyceride, reduce oxidative stress, and plasma adiponectin level, and reduce hyperinsulinemia in adults [10].

A good source of omega-3 fatty acid is Alpha-linolenic acid which is found in plant-based diets such as flax seed oil and walnut, Animal-based diet like fish oil is rich in docosahexaenoic acid which is also a source of omega-3 fatty acid. These fatty acids are essential for our body's functions and activities. The essential fatty acids are not synthesized in our body and are only fulfilled through the diet [11].

In PCOD, there is an imbalance of sex hormones, that causes ovarian cysts and irregular menstrual cycle or amenorrhea. These complications have been mainly attributed to the suppression of the follicle-stimulating hormone (FSH) secretion by an

excess androgen produced from the theca cells of the ovary [12].

Pathophysiology of PCOD (Fig.1)

Hyperandrogenism is the key feature of PCOS. This causes a direct increase in the production of androgen probably by an increased level of insulin in the ovaries and a decrease in sex hormone-binding globulin (SHBG). This protein keeps testosterone in its bound forms & thus reduces the free testosterone level in the body [14].

In addition to this, patients with PCOS have high levels of luteinizing hormone, in which level of androgen is elevated and secondarily

It leads to the disturbance of the menstrual cycle, infertility, hirsutism, acne, alopecia. Elevated LH levels play a vital role in the development of reproductive and metabolic disorders, based on the evidence. Firstly, LH stimulates androgen production in ovarian theca cells, resulting in hyperandrogenemia and halted follicle development [15]. Secondly, an increased frequency of LH pulses disrupts the synthesis of estrogen and FSH, thereby inhibiting follicle growth and ovulation. Thirdly, LH enhances the ovarian secretion of IGF-1, which further promotes LH binding and androgen production in theca cells, contributing to the development of polycystic ovaries in patients with PCOS [16].

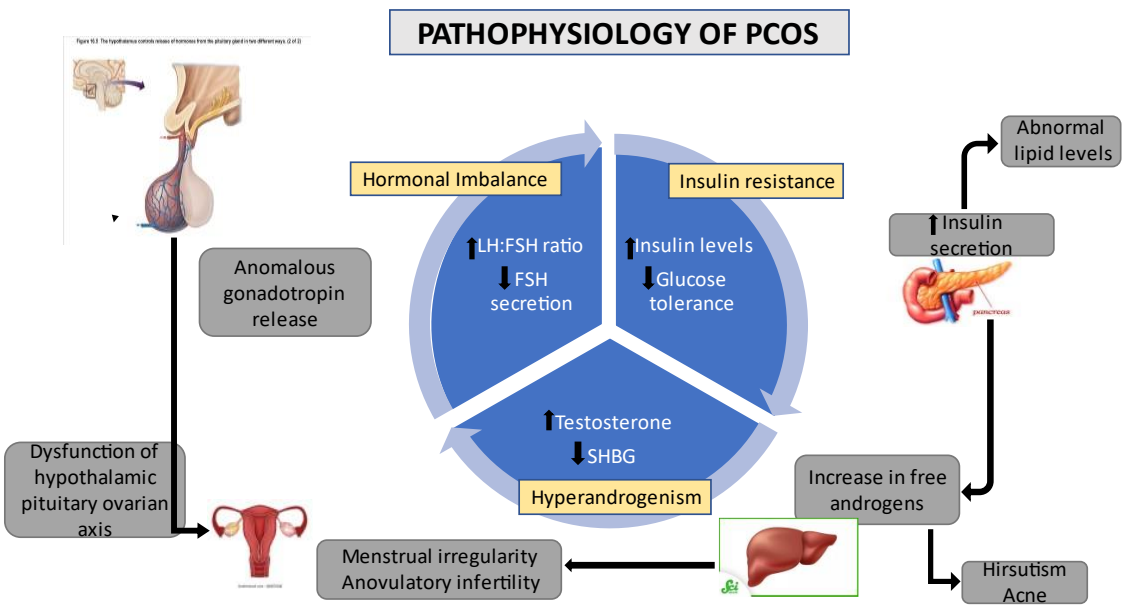

Fig. 1. Pathophysiology of Poly Cystic Ovarian Syndrome

Physiological mechanism of omega-3 polyunsaturated fatty acid

Polyunsaturated fatty acids (PUFAs) are categorized into omega-3 (n-3) and omega-6 (n-6) fractions. Omega-3 PUFAs are primarily synthesized from α-linolenic acid, while omega-6 PUFAs are synthesized from linoleic acid (LA) [17]. Linoleic acid can be metabolized to n-6 via desaturase, resulting via biosynthesis of gamma-linolenic acid (GLA), dihomo—gamma-linolenic acid (DGLA), and finally AA. The largest amount of arachidonic acid (AA), however, is found in phospholipids membranes, competing with n-3 acids for metabolism and with their products for receptors [18].

Under the action of cyclooxygenase (COX) enzymes, arachidonic acid (AA) is converted into prostaglandins (PG), thromboxanes, and leukotrienes. Eicosanoids, mainly epoxyeicosatrienoic acids (EETs) and 20 hydroxyeicosatetraenoic acid (20-HETE), are produced throughout cytochrome P450 (CYP) enzyme activity [19]. However, as a result of AA metabolism mediated by lipoxygenase (LOX) enzymes, including 5-, 8-, 12-, and 15-LOX, from which, in turn, HPETE acids are adequately produced, followed by HETE and oxo-ETE (Fig. 2) [20]. 5-oxo ETE and 12-HETE are potent chemo-attractants for basophils, eosinophils, monocytes, and neutrophils. Moreover, 15 HETE stimulates

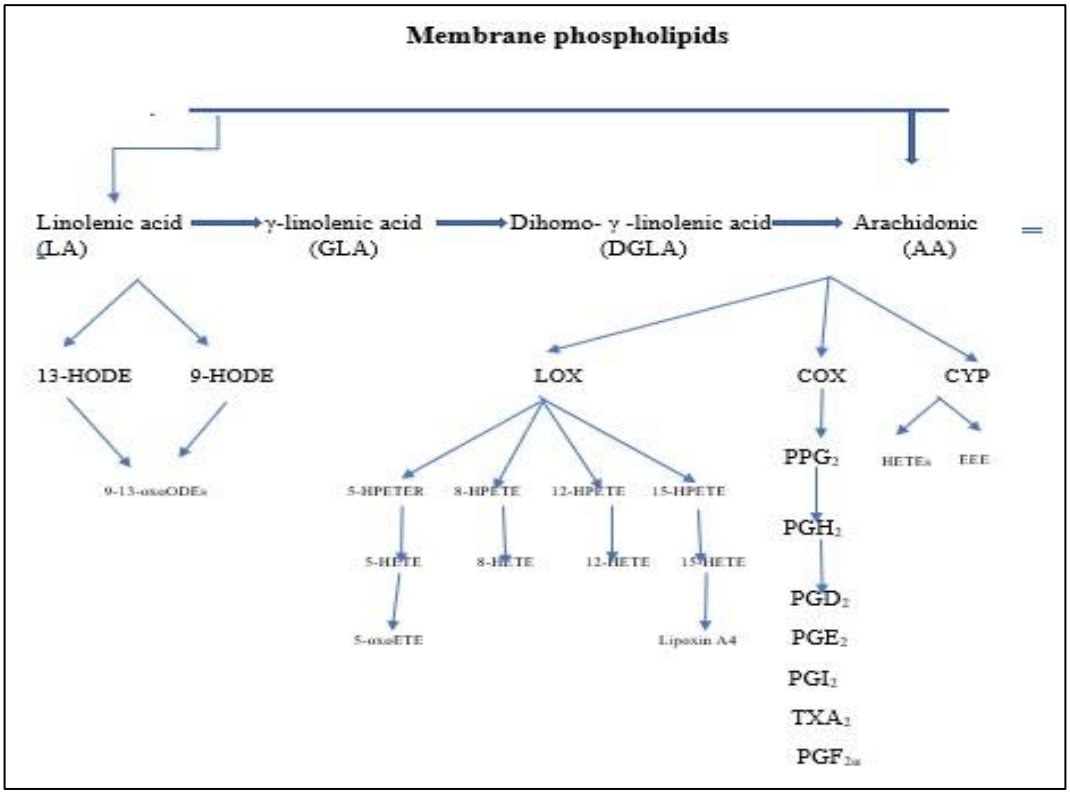

Fig. 2. Synthesis of inflammatory mediators from linoleic acid (LA) and metabolic acid (AA). LOX-lipoxygenase, HETE- hydroperoxyl eicosatetraenoic acid, HPETE-Hydroperoxyeicosatetraenoic acid, HODE-hydroxyoctadecadiene acids, COX-cyclooxygenase, CYP-cytochrome P450, HETEs- hydroxyeicosatetraenoic acids, EETs-epoxyeicosatrienoic acids, PG- prostaglandins, TX-thromboxane.

mitogenesis of endothelial cells, increasing the activity of granulocytes and lymphocytes [21].

Omega 3 fatty acid and insulin resistance

Insulin resistance is a condition where the peripheral tissues have a diminished response to insulin. Insulin resistance is commonly encountered in spread to muscles and liver causing a negative impact of glucose metabolism which is attributed to defective regulation of glucose transporter [4]. Among the complications related to insulin resistance are the suppression of gluconeogenesis, glycogenolysis in the liver, and reduction of glucose output.

Omega-3 fatty acid protest glucose tolerance and avoid the accumulation of lipid mediators by up-regulating the mRNA expression of insulin-stimulated glucose transporter 4 (GLUT4) insulin receptors substrate-1 (IRS-1) and glycogen synthase-1 (GYS). Additionally, by reducing endoplasmic reticulum stress, increasing β-oxidation of mitochondrial fatty acid and mitochondrial uncoupling as well as limiting lipid deposits and reactive oxygen species, generation omega-3 PUFA could further improve insulin sensitivity.

Omega-3 fatty acid and obesity

Overweight and obesity are observed in 40-50% of PCOS patients and are considered a major risk factor for PCOS [22]. Excess weight accumulation can cause dysfunction in adipose tissue, which is mechanistically linked to the development of metabolic syndrome and associated complications, including insulin resistance in the liver and skeletal muscle.

Natural bioactive compounds, such as n-3 PUFA, have minimal side effects and may be a safer alternative compared to other treatment options. There are a variety of putative mechanisms by which n-3 PUFA, particularly EPA, and DHA could work in improving body composition, modulating energy metabolism, and reducing body weight [23].

It has been shown that DHA, in dosages of >50 μM, could facilitate the differentiation of adipocytes by up-regulation of mRNA levels of adipocyte protein [24]. N-3 PUFA of marine origin may have the potential to control the number and size of adipocytes by influencing their differentiation and apoptosis [25].

Omega-3 fatty acid and inflammation

Omega-3 PUFA also has also have anti-inflammatory properties. Omega-6 PUFA arachidonic acid (AA) is stored in cell membranes and is released upon cell stimulation. It is then metabolized by proinflammatory lipid mediators, such as prostaglandins and leukotrienes in the AA cascade, which exacerbates existing inflammation. Omega-3 PUFA are also stored in cell membranes, where they replace AA,

thereby reducing its storage. Although omega-3 PUFA are also metabolized by proinflammatory lipid mediators in the AA cascade, their active metabolites are considered to be less potent than those of AA, shifting the balance toward reduced inflammation [26]. DHA-rich fish oil extends survival in a mouse model of systemic lupus erythematosus, a common autoimmune disease [27].

The key factors involved are resolvins and neuroprotectins derived from omega-3 fatty acids, especially DHA, which are produced at the conclusion of an inflammatory response. [28] RvE1 plays an active role in halting leukocyte movement to the inflamed area, enhancing the removal of inflammatory cells and debris, and inhibiting cytokine production, thus facilitating the resolution of acute inflammation. [29]

CONCLUSION

In this review, we find out that Omega-3 supplementation in PCOD, promotes indirect benefits by changing the metabolic profile associated with the disease. For the hormonal profile and biomarkers of the inflammatory process, positive results were observed for the reduction of CRP levels. However, the great heterogeneity in the studies to standardize the dosages and the timing of administration.

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https://doi.org/10.46351/jas.v32i1pp53-58

JAS Journal of Anatomical Sciences (U.P. Chapter of Anatomical Society of India)

Case Report

UNILATERAL COLPOCEPHALY WITH BILATERAL PARTIAL AGENESIS OF CORPUS CALLOSUM IN ADULT MALE –A CASE REPORT

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ABSTRACT

This case report presents a rare instance of unilateral colpocephaly with bilateral partial agenesis of the corpus callosum in a 63-year-old asymptomatic male cadaver. Colpocephaly, typically identified in infancy due to associated intellectual disabilities and neurological symptoms, is characterized by disproportionate enlargement of the posterior horns of the lateral ventricles. During routine dissection, a striking case of colpocephaly with reduced white matter in the parietal and occipital lobes of the left cerebral hemisphere was observed. The right cerebral hemisphere appeared normal, except for the partial agenesis of the corpus callosum. Morphometric analysis revealed an anteroposterior length of 13.2 cm and a supero-inferior length of 6.5 cm for the left lateral ventricle, with a posterior-to-anterior horn ratio of 3.1. These findings suggest colpocephaly rather than normal pressure hydrocephalus. This case underscores the importance of morphometric analysis in differentiating colpocephaly from other forms of ventriculomegaly, aiding in accurate diagnosis and preventing unnecessary interventions. To the best of our knowledge, this is the first documented cadaveric case of colpocephaly in an asymptomatic adult.

Keywords: Colpocephaly, Corpus callosum agenesis, Ventriculomegaly, Morphometry,

INTRODUCTION

Colpocephaly is a rare congenital abnormality in the ventricular system of the brain. It is characterized by disproportionate enlargement of posterior horn of lateral ventricle as compared to anterior horn.

Other neurological malformations particularly agenesis of corpus callosum and microgyria is associated with this condition. It can be differentiated from hydrocephalus where there is proportionate ventriculomegaly of the horns of lateral ventricles [1].

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Date of Receiving: 24 Feb 2024
Date of Acceptance: 02 Mar 2024

The radiological diagnosis is usually made in the prenatal period and later manifests as intellectual disability [2].

CASE REPORT

In routine dissection for undergraduates at Government Doon Medical College, Dehradun Uttarakhand, King George Medical College, Lucknow and CDSIMER, Harohalli, Ramnagara district from the period of 2020 to 2023, a total of 20 sagittal sections of brains were dissected.

While removing the brain after removing the calvaria, a striking case of massive colpocephaly with small cerebral white matter in parietal and occipital lobes of left cerebral hemisphere along with bilateral partial agenesis of corpus callosum was incidentally reported in a 63 yrs old male cadaver who had a natural death at CDSIMER, Harohalli, Ramnagara district in 2021. Rest all 19 brains were found to be with normal anatomy of lateral ventricles. To the best of our knowledge, this is the first reported cadaveric case of colpocephaly in an asymptomatic adult and the first described in previous literatures.

Morphometric analysis of colpocephalic sagittal sections of brain was done by an inch tape under the parameters viz. anteroposterior length of anterior and posterior horn and body of lateral ventricle and height (supero-inferior length) of body of left ventricle.

The measurements were made in the sagittal and transverse sections of the brain. The posterior to anterior (P/A) ratio was also calculated by taking the maximal width of posterior horn and dividing by the maximal width of anterior horn of lateral ventricle in transverse section of left cerebral hemisphere.

RESULTS

The right cerebral hemisphere of this cadaveric male seemed to have a normal anatomy except partial agenesis in the center of body of lateral ventricle. However, in the left cerebral hemisphere, massive disproportionate enlargement of lateral ventricle was seen with anterior posterior length of 13.2cm and supero-inferior length (heigth) of 6.5cm with P/A Ratio 3.1(>3) (maximal width of posterior and anterior horn was found 4.96cm and 1.6cm respectively) which highly suggests a case of colpocephaly rather than normal pressure hydrocephalus [3]. (Fig. 1-4)

DISCUSSION

Colpocephaly is typically discovered in infancy due to associated intellectual disability, seizures, motor abnormalities, or visual abnormalities [4]. Discovery in adulthood is remarkably uncommon. Colpocephaly can be detected radiographically by measuring the maximal width of the anterior and occipital horns of the lateral ventricles. A ratio of the occipital horn

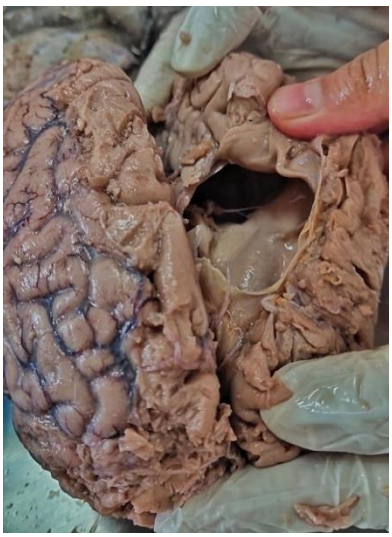

Fig. 1. Colpocephalic brain (intact right and left cerebral hemisphere)

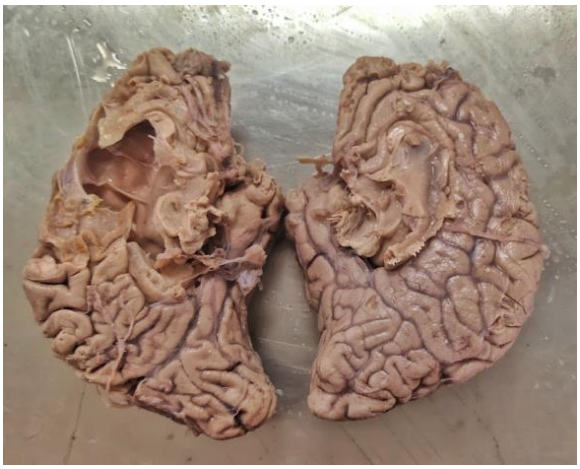

Fig. 2. Left and right cerebral hemisphere showing Massive colpocephaly on left side and bilateral partial agenesis of corpus callosum on right side

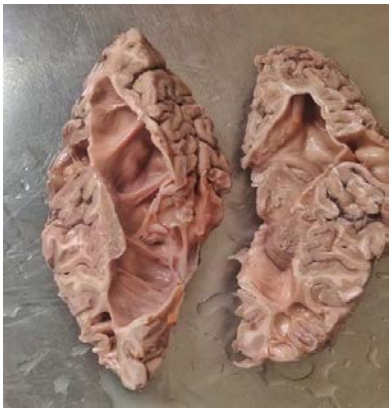

Fig. 3. T.S. of left cerebral hemisphere showing massive colpocephaly

Fig. 4. Length of posterior horn of left cerebral hemisphere

to the anterior horn greater than 3 is highly specific for colpocephaly, though it has relatively low sensitivity [5].

According to Benda et al, intermediate zone fibers originating from the thalamus and corpus callosum in vesiculocephaly fail to develop at the end of fifth embryonic month and its architectonic appearance suggests of a colpocephaly [6]. Yakovlev et al. stated that colpocephaly results from a disturbance in the hydrostatic balance between intra and extra-ventricular pressures, caused by the failure of cerebral wall development, resulting in outpocketing of the ventricular wall. His study also stated that other anomalies seen

in association with colpocephaly suggested an insult not later than the second embryonic month [7].

Noorani et al in their CT study of 14 cases of colpocephaly in a series of 3,411 consecutive CT scans in 1988 in California found the P/A ratio as 2.90±1.44 which almost approximate our findings. This study also stated that periventricular leukomalacia which results due to destruction of the optic radiations and subsequent degeneration in the white matter of the occipital lobe could be the possible explanation for the development of disproportionately enlargement of the occipital horns of the lateral ventricles [8].

Honnegowda et al reported mean antero-posterior length of body and frontal horn of lateral ventricle in non colpocephalic brain as 7.6cm and 3.0cm respectively in their CT study of brain which is similar to our findings thereby proving that in the present study, a defect was present only in posterior horn suggesting more of colpocephaly [1].

Gyldensted et al found the width of left anterior horn as 1.9 cm in the CT study of non colpocephalic brain which approximate our finding there by proving, that no abnormality is present in anterior horn. Therefore, it proves that in our hypothesis the present case was of colpocephaly which does not involve anterior horns [9].

Duffner et al in their MRI study for non colpocephalic brains, found mean total length (antero-posterior) of lateral ventricle, posterior horn and height of lateral ventricle as 9.1cm, 2.8cm and 1.7cm respectively which are not found to be in unison with our findings (13.2 ,4.2cm and 6.5cm respectively) suggesting that in our present specimen of brain, dimensions found were abnormal, proving the hypothesis of colpocephalic brain [10].

Previous reported cases of colpocephaly were diagnosed incidentally in adulthood during CT examination post onset of mild neural symptoms by Wunderlich et al in 1996 [11], Cheong et al in 2012 [12], Esenwa et al in 2013 [13], Brescian et al [14], Nasrat et al in 2014 [15], Bartolome et al.in 2016 [16].

CONCLUSION

Colpocephaly discovered in asymptomatic adults is exceedingly rare. It may be misdiagnosed as normal pressure hydrocephalus. Knowing the respective morphometry of lateral ventricle can aid clinicians in differentiating this disproportionate ventriculomegaly affecting posterior horn and body of left lateral ventricle in colpocephalic brain with that of common form of adult ventriculomegaly (idiopathic normal pressure hydrocephalus) and thereby preventing unnecessary interventions.

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