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EDITORIAL

ESIC Healthcare Institutions: Steering the Well-being of Workers through Health and Occupational Research in the Modern Work Environment

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The Employees' State Insurance Corporation (ESIC) was established under ESI Act, 1948 with an objective to provide Social Security Benefits to organised workers in industries and establishments. Presently, the act is applicable to the Industries and Establishments employing ten or more persons and the persons drawing monthly wages of up to ₹ 21000/- working in such units. ESI scheme is a continuously evolving multi-faceted Social Security scheme that provides beneficiaries with comprehensive Healthcare services and cash benefits to compensate the loss earning due to Sickness, Maternity and Employment Injury. The scheme relieves the burden of the employers to take care of their employees when the aforesaid contingencies arose and enables to them to have a Healthy Workforce all the time. It is a tripartite scheme in which the Government, Employers and Employees are collectively involved in running of the scheme.

ESIC believes that “Health of the workers is the wealth of the Nation," and has been working for the past 72 years to create and sustain a healthy workforce for the Nation. Shift in the structure of the economy and the changing dynamics, large-scale urbanisation, as well as changes in workers' lifestyles has made sustaining the country's workforce healthy a big challenge.

It is common wisdom that prevention is preferable to cure. Disease prevention saves people from suffering severe physical, mental, and financial hardships, increasing their productivity and enhance their quality of life. Preventive care provides the nation with dual benefits of increased output, significant savings on future Healthcare costs and a Happy and Healthy Society.

Section 59 B of the ESI Act, 1948 enabled ESI Corporation to establish Health Care institutions to improve the quality of services provided under the Employees' State Insurance Scheme. Occupational Health is the domain of Health care that promotes and enhances the level of physical, mental, and social well-being of workers in all occupations. Occupation Health has a direct impact on the overall efficiency, effectiveness and productivity in both Goods and Services Sectors. Achieving holistic health for the workforce needs a well-planned and strategized specific approach of Healthcare delivery because of the unique challenges associated with it. These challenges range from symptomatic health issues, intrinsic psychosocial and mental health conditions, lack of care seeking behaviour in case of adverse asymptomatic health conditions, financial incapacity and Poor Health Literacy. At the same time, health status of workers are vulnerable due to various factors such as exposure to carcinogens, accidents prone machineries, hazardous industrial settings, work related stress. Lifestyle related disorders, and communicable infections. It is crucial to ensure the safety of employees, especially against hazards specific to the workplace.

Due to the peculiar characteristics of the determinants of health status and the specific challenges involved necessitates the approach towards Occupational Health of ESI covered workers to be well thought-out, more comprehensive and implementation oriented. Such approach calls for a thorough study of the Workers’ Health Status along with the Workplace dynamics, consolidating the knowledge of Health Care developed so far, developing a strategy and delivering such planned care at each worker level. The care delivery would bring maximum benefit when the same is customised

for each individual. It can be said that such a specialised and comprehensive Healthcare is not possible by standalone Hospitals. But, such Quality care can be extended to each stakeholder, if strategy/policy is formulated by Healthcare institutions and delivered through Hospitals and Dispensaries.

ESIC health care institutions are to steer the task of grooming the wellbeing of the Workers covered under ESI Act through Industry and Occupation specific Health Care Research endeavours. The institutions are endowed with the following capabilities to spearhead this mission.

- **Aspiring Young Doctors and Researchers:** These Institutions have a pool of young doctors with high degree of aspirations to excel in their career. They have knowledge seeking mindset and quest for innovation. These young talents can be easily channelized towards the pursuits of occupational health research.

- **Capacity building using institutional experiences:** ESIC has been delivering health care and social security services for the past 72 years. By virtue of its structure, all the stakeholders of Occupational Health have been aligned under one umbrella i.e ESI Scheme. The only task ahead is to prepare a blueprint and assign roles for them to work towards universal healthcare for ESI Insured persons.

- **EASE of conducting Research:** Since, the two main stakeholders for occupational Health Research i.e Employers and Insured Persons are part of the ESI Health system, conducting research is a very easy task. Effective cooperation of the stakeholders could be achieved with minimum sensitisation efforts.

- **Research pluralism:** The Insured Population of ESIC consist of persons representing almost all the types of occupations present in formal Sectors. There is also diversity of Age, Gender. Location etc. Hence, the Research can be very easily conducted across different factors like Industry specific, age specific, with the industry gender specific, gender neutral, across the occupations for a particular gender etc. It is a unique advantage available to ESIC only. Such Research outcome are very crucial input for devising Healthcare Strategies.

- **Building knowledge Bridges through Collaboration:** Department of Integrative Medical Research, as recommended by the National Medical Commission, 2023 Guidelines, would function as holistic research initiative integrating all branches of Medicine, Dental sciences and AYUSH. Such integrative approach helps all the benefits of each stream is available for the users.

Research is the gateway to Innovation; Pathway to Progress and Professionalism. Amount spent towards research is not expenditure but a prudent investment. It is all the more true in the case of Occupational Health Research. **Health is a state of complete physical, mental and social well-being, not just the absence of disease or infirmity.** Research outcomes play a key role in enabling ESIC to move towards realising such a complete well being for its insured population.

Providing healthy workforce to the Nation would make, ESIC a meaningful contributor towards achieving the mission 'Viksit Bharat'. ESIC Healthcare institutions are committed to steer this historic journey with the effective support of all the Stakeholders.

Shramev Jayate !

ORIGINAL ARTICLE

Trichoscopic Evaluation of Hair Disorders: A Cross-Sectional Study from a Tertiary Care Centre in North India

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ABSTRACT :

Background: Trichoscopy is defined as the dermoscopic examination of the hair and scalp. It is an invaluable, indispensable, and non-invasive technique. We intend to evaluate the dermoscopic findings in various disorders involving hair and scalp.

Material & Methods: A total of 209 patients participated in the study. Dermoscopy was done using a handheld dermoscope. (DermliteTM DL4, Gen, USA). The dermoscopic findings are documented in the various lesions.

Results: In different scalp and hair disorders, the typical scalp features become distorted. Knowing these findings is important since many of them are characteristic of different diseases while others are encountered occasionally. The most common dermoscopic findings in Androgenetic alopecia (AGA) were anisotrichosis and pilosebaceous single hair units. Alopecia areata showed yellow dots, black dots, and coudability hairs. In tinea capitis comma hairs and zig zag hairs were seen. In Telogen effluvium single follicular hair unit dominance was observed. In Seborrheic dermatitis (SD) perifollicular scales were seen. Red dots, globules and silvery white scales were seen in scalp psoriasis. In Lichen Plano Pilaris (LPP) pigment incontinence and perifollicular scaling was seen. In Trichotillomania broken hairs and peripilar hemorrhages were seen.

Conclusion: In this study we have briefly presented the dermoscopic findings in various disorders involving hair and scalp.

Keywords: *Trichoscopy, Hair, Scalp.*

Introduction

The term "Trichoscopy" was coined by Lidia Rudnicka and Malgorzata Olszewska in 2006.[1] It is defined as the dermoscopic examination of the hair and scalp. It is an invaluable, non-invasive and low-cost technique for rapidly differentiating common hair disorders.

Trichoscopy allows for high magnification, visualization and evaluation of the scalp and hair. It helps select the appropriate biopsy site to confirm the diagnosis, provides clues to disease progression and helps assess response to treatment.

The main aim of this study was to evaluate the dermoscopic findings in various disorders involving hair and scalp.

Material and methods

Over the course of nine months, 209 patients participated in this study. The study comprised all patients who presented to Outpatient Dermatology Department with scalp and hair disorders. Institutional ethical clearance was obtained. All patients provided their written informed consent.

Patients who suffered hair loss owing to any type of external damage, prior chemotherapy, drug intake or any type of treatment history during the previous six months were excluded. Following a thorough history and clinical examination, the diagnosis was made. Additional investigations like 10% KOH mount and biopsy were done in clinically ambiguous cases.

The findings were recorded using a handheld dermoscope (DermliteTM DL4, Gen, USA) of magnification 10X, attached with iPhone 10 and digital photographs were obtained. Dermoscopy was done using two different methods. Initially dry method was used followed by wet method. Multiple

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fields were examined as all trichoscopic findings were not visible in one frame. The average number of fields examined / photographed was five to six.

Data was spread over Microsoft Excel sheet and analyzed at the end of the study. Data is being presented in the form of frequency and percentage.

Results

Of the 209 patients who participated in our study, 69 had Androgenetic alopecia (AGA), 34 had Alopecia areata (AA), 32 had Tinea capitis, 31 had Telogen effluvium (TE), 15 had seborrheic dermatitis (SD), 10 had scalp psoriasis, 9 had Lichen planopilaris (LPP), 5 had Trichotillomania (TTM), 2 had pediculosis capitis, 1 had frontal fibrosing alopecia (FFA) and 1 patient presented with Pili Torti. The demographic profile of patients including age group, sex and duration of disease, is summarized in Table 1

Table 1. Demographic profile of patients

Demographic profile	Categories	Number of patients	Percentage (%)
Age group	<10 years	41	19.6
	11-20 years	31	14.8
	21-30 years	120	57.4
	>30 years	17	8.1
Sex	Males	95	45.5
	Females	114	54.5
Duration of disease	<6 months	40	19.1
	7-12 months	119	56.9
	12-24 months	34	16.3
	>24 months	16	7.7

Table 2. Dermoscopic Findings in Androgenetic Alopecia

Findings	Number of patients (69)	Percentage (%)
Hair Diameter Variability > 20%	69	100.0
Thin Hair	69	100.0
Single-Hair Pilosebaceous Units	67	97.1
Vellus Hairs	65	94.2
White Dots	63	91.3
Focal Atrichia	51	73.9
Empty Follicles	50	72.4
Peripilar Sign	42	60.8

Table 3. Dermoscopic Findings in Alopecia Areata

Findings	Number of patients (34)	Percentage (%)
Yellow Dots	28	82.3
Black Dots	25	73.5
Coudability Hairs	24	70.5
Broken Hairs	20	58.8

Exclamation Mark Hairs	18	52.9
Hair Shafts of variable Thickness	15	44.1
White Dots	12	35.2
Clustered Short Vellus Hairs	12	35.2
Honey Comb Pigmentation	10	29.4
Pohl pinkus hair	7	20.5
Upright Regrown Hair	7	20.5
Tulip Hair	6	17.6
Pig Tail Hair / Circular Hair	5	14.7
Zig Zag Hair	3	8.8

Table 4. Dermoscopic Findings in Tinea capitis

Findings	Number of patients (32)	Percentage (%)
Comma hair	24	75.0
Zig zag hairs	21	65.6
Broken hair	18	56.2
Black dots	18	56.2
Fractured hair shafts	17	53.1
i-hair	16	50.0
Interrupted/ morse code hairs	15	46.8
Corkscrew hairs / spiral hairs	10	31.2

Table 5. Dermoscopic Findings in Telogen Effluvium

Findings	Number of patients (31)	Percentage (%)
Single follicular hair unit dominance	26	83.8
Numerous short regrowing hairs of normal thickness	24	77.4
Empty follicles	21	67.7
Focal atrichia	16	51.6
Short vellus hairs	13	41.9

Table 6. Dermoscopic Findings in Seborrheic Dermatitis

Findings	Number of patients (15)	Percentage (%)
Perifollicular white scales	15	100

Table 7. Dermoscopic Findings in Scalp Psoriasis

Findings	Number of patients (10)	Percentage (%)
Red dots and globules	10	100
Silvery white scales	10	100

Table 8. Dermoscopic Findings in Lichen planopilaris

Findings	Number of patients (9)	Percentage (%)
Pigment incontinence	9	100
Perifollicular scaling	9	100
Blue-gray dots arranged in a target pattern	9	100
Perifollicular white macules	8	88.8
Absent follicular opening	8	88.8
Perifollicular erythema	7	77.7
Fibrosis	7	77.7
Peripilar brown halo	6	66.6
Interfollicular scale	6	66.6
Follicular keratotic plugging	5	55.5
Telangiectasia	5	55.5
Broken hair	5	55.5
White dots	4	44.4
Black dots	4	44.4
Yellow dots	3	33.3

Table 9. Dermoscopic Findings in Trichotillomania

Findings	Number of patients (5)	Percentage (%)
Broken hairs of different length	5	100
Short hairs with trichoptilosis (split ends)	5	100
Irregular coiled hairs	5	100
“V” sign	5	100
Presence of scalp hemorrhages (peripilar hemorrhage)	5	100
Black dots	4	80
Question mark hairs	4	80
Flame hairs	4	80
Tulip hairs	4	80
Hair powder (hair dust)	4	80
Pig tail hair	4	80
Perifollicular scaling	3	60
Upright regrowing hairs	3	60

Table 10. Dermoscopic Findings in Pediculosis capitis

Findings	Number of patients (2)	Percentage (%)
Nits	2	100
Parasite	2	100

Discussion

Trichoscopy is a rapid, simple, unique, and effective diagnostic procedure that can save time and money. Despite its numerous benefits, it remains underutilized.

Based on data from literature and their own experience, Miteva and Tosti provided a complete and exhaustive description of the use of this technique.[2]

Trichoscopy of a typical scalp reveals follicular units comprising of 2-4 terminal hairs and 1 or 2 vellus hairs, simple fine red loops that indicate capillary loops in the dermal papilla, and a perifollicular pigmented network (honeycomb pattern) that is strongly appreciated in people with dark skin.[3]

In different scalp and hair disorders, these typical results become distorted or altered. Knowing these findings is important, since many of them are characteristic of different diseases while others are encountered occasionally. These findings are as under:

In AGA, Hair diameter diversity (HDD) or "Anisotrichosis" is characterised by progressive and unsynchronized miniaturization of hair follicles. AGA is defined as having hair diameter diversity of greater than 20%. This observation was found in all of our patients. Hu et al.[4], Inui et al.[5] and Lacharriere et al. 6 found similar results.

Vellus hairs, a sign of severe miniaturization, was seen in 94.2% of patients.

White dots which represent hypertrophied sebaceous gland openings were detected in 91.3% of patients. This could be because the majority of the patients in our study had long duration of disease. More than 70% of the patients in our study had focal atrichia and empty follicles as a result of follicular atrophy. This finding was comparatively higher in our study than in Inui et al.[5] indicating that more individuals with AGA had advanced disease activity. **(Fig. 1)**

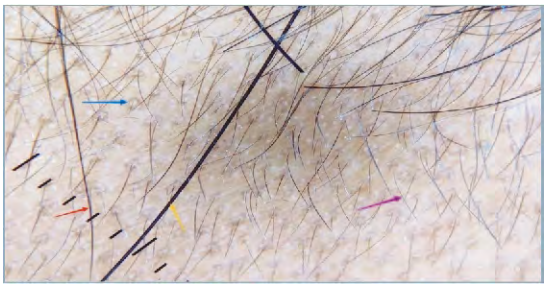

Fig. 1: Dermoscopic image of Androgenetic alopecia (AGA) showing -hair diameter heterogeneity >20%, miniaturized hair (pink arrow), brown peripilar sign (blue arrow), terminal hairs (yellow arrow), and thin terminal hair (red arrow).

A brown halo with a diameter of roughly 1mm surrounds the emerging hair shaft, identified as the Peripilar sign was seen in 60.8%. It is frequently seen in early AGA patients. Inui et al. reported peripilar sign in 66% of AGA patients.[5] **(Fig. 2)**

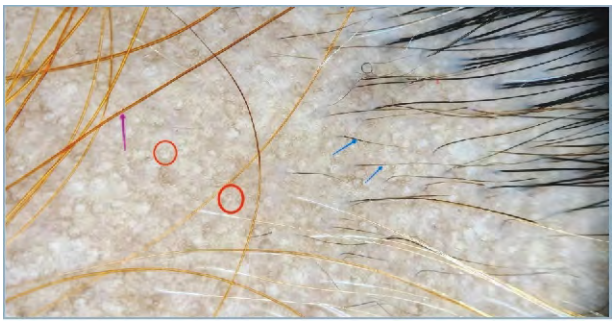

Fig. 2. Dermoscopic image of Androgenetic alopecia (AGA) showing -terminal hair (pink arrow), miniaturized hair (blue arrow) and ecrine white dots (red circle).

Alopecia areata is a type of autoimmune disease distinguished by an abrupt halt in the hair cycle and formation of fractured cadaverized hairs, miniaturized nanogen hairs, short re-growing vellus hairs, dystrophic and telogen (tapered) hairs.

Yellow dots (YDs), first proposed by Ross et al., are thought to be the most sensitive dermoscopic feature of AA.[7] YDs are seen as yellow-to-yellow pink, round or polycyclic dots that vary in size and are of uniform color. These are signs of follicular infundibulum distension caused by keratinous material and sebum. YDs were found in 82.3% of patients in our study while Ross et al.[7] (94.8%), Mane et al.[8] (81.8%) and Bapu et al.[9] found YD's in 89.6% of patients.

Black dots formerly known as "cadaverized hair", signify pigmented hair that has been damaged or destroyed at the scalp level, are characteristic of individuals with dark hair. These are important indicators of AA disease activity and severity. In our study, black dots were found in 73.5% of the cases. Similar results were obtained in study conducted by Hegde et al.[10] (84%) and Mane et al.[8] (67.7%). (Figure 3) Coudability hairs are long hairs with proximal hair-shaft tapering that can grow as a result of less severe injury to the hair follicle and persist into the anagen phase. In our study, it was seen in 70.5% of the patients.

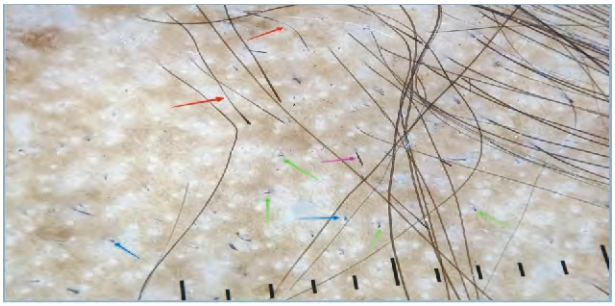

Fig. 3. Dermoscopic image of Alopecia areata showing – black dots (blue arrow), Tapered hair (pink arrow), pohl pinkus hairs (red arrow), broken hairs (green arrow) and numerous interspreaded yellow dots.

Broken hairs (BH) are dystrophic hairs formed by the less severely damaged AA follicles, was found in 58.8% of the cases in our study. Exclamation mark hairs have a larger diameter in distal hair shaft and a smaller diameter in proximal hair shaft which was found in 52.9% of patients. Short, upright vellus hairs and thin, twisted vellus hair (known as pigtail hair), the two types of hair suggestive of hair regrowth in AA, were seen in 20.5% and 14.7% patients respectively.

Tinea capitis is the most prevalent dermatophytic infection in children and it is diagnosed clinically. Culture, despite being regarded as the gold standard, has a lengthy waiting period. Patchy hair loss with scales and erythema are the typical presentation. KOH scraping for scales validated the diagnosis.

Comma hair is characteristic of tinea capitis. These are broken single hair shafts that coil into a comma-like structure because of a hair shaft bending and are visible as stubs of hair near to the skin surface. These were observed in 75% of the participants in our study. **(Fig. 4)** Hairs bent at several places, known as Zig zag hairs, were the second most common feature seen in 65.6% patients. **(Fig. 5)**

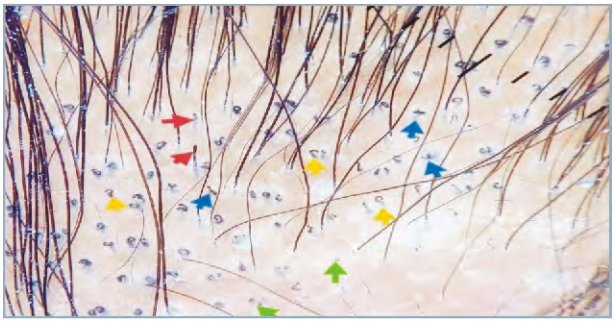

Fig. 4: Dermoscopic image of Tinea capitis showing – comma hairs (yellow arrow), Broken Hairs (red arrow), corkscrew hairs (blue arrow), and black dots (green arrow)

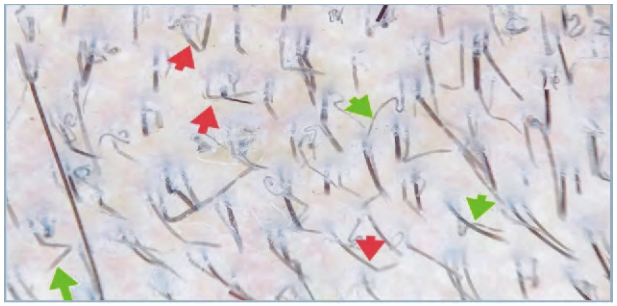

Fig. 5. Dermoscopic image of Tinea capitis showing – zig-zag hairs (green arrow), bent hairs (red arrow).

The non-inflammatory variant of tinea is distinguished by many broken hair shafts that appear as black dots over the scalp. These are shafts that have broken owing to destruction by fungal elements. This was observed in 56.2% of our patients. Morse code hairs are hair shafts that are transversely interrupted by vertical white bands, regularly distributed along the hair shaft was seen in 50% of patients. Corkscrew hairs and dystrophic hairs were seen in 31.2% patients. Our results are in accordance with the study conducted by Refu et al.[11] **(Fig. 6)**

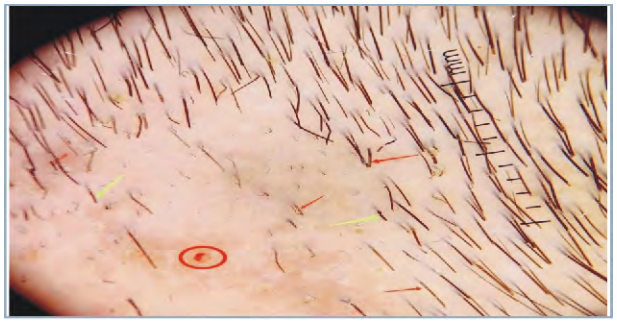

Fig. 6. Dermoscopic image of Tinea capitis showing - morse code hair(red arrow), broken hairs (yellow arrow), and perifollicular haemorrhage (red circle).

Telogen effluvium is characterized as telogen hair loss that occurs 2–4 months after a severe systemic stressful event. Unlike AGA, it affects the entire scalp. In our study, the most prevalent finding was single follicular unit hair dominance in 83.8% of the patients.

Seborrheic dermatitis (SD) on the scalp is characterized by dry greasy and yellowish scales, on erythematous plaque with diffuse border. The plaque's size varies from small to large and can be solitary or multiple. Subjective complaints are mostly pruritus. In our study the most common finding on trichoscopy seen was perifollicular white scales (100%). Arborizing thin vessels which are considered to be distinguishing feature of SD, were

seen in 50% of our patients. These findings have been previously reported in the studies done by Kibar et al.[14] and Widaty et al.[15]

Scalp psoriasis presents as sharply demarcated erythematous plaques with silvery-white scaling. Red dots and globules and silvery white scales are considered as characteristic features of scalp psoriasis on dermoscopy. These were seen in all patients in our study. These findings have been previously reported in study done by Kim et al.[16] **(Figure 7,8)**

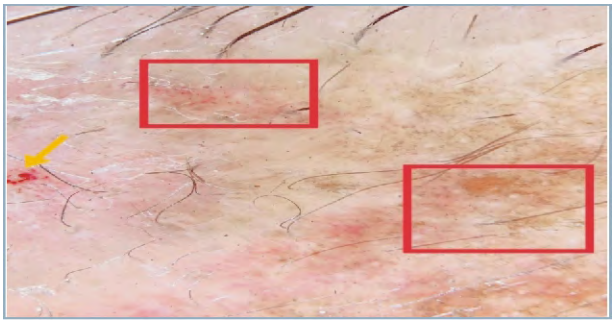

Figure 7: Dermoscopic image of Scalp psoriasis showing – extravasated blood (yellow arrow), Red dots and globules (red square).

Fig. 8. Dermoscopic image of Scalp psoriasis showing – extravasated blood (yellow circle), large sheets of white silvery scales.

In Cicatricial alopecia like Lichen planopilaris (LPP) White perifollicular tubular scale (also known as peripilar casts) at the base of hair shaft is the most characteristic trichoscopic feature of classic LPP. It is mostly visible at the periphery of the patch. It is accompanied by pigment incontinence, blue grey dots (target pattern), and perifollicular white macules. **(Fig. 9,10)**

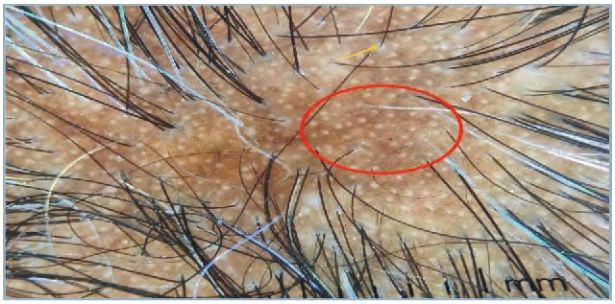

Fig. 9. Dermoscopic image of Lichen plano pilaris (LPP) showing – white dots amidst honeycomb pigment giving starry sky pattern.

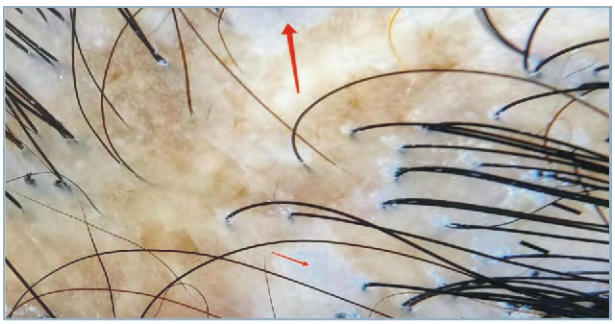

Fig. 10. Dermoscopic image of Lichen plano pilaris (LPP) showing – white areas (red arrows)

Frontal fibrosing alopecia (FFA) is a type of cicatricial alopecia seen mostly in postmenopausal women. The only dermoscopic finding seen in our study was a lonely hair sign. It describes the presence of one or few isolated terminal hairs in the middle of the forehead. This sign is helpful to clinically distinguish FFA from other similar conditions. **(Fig. 11)**

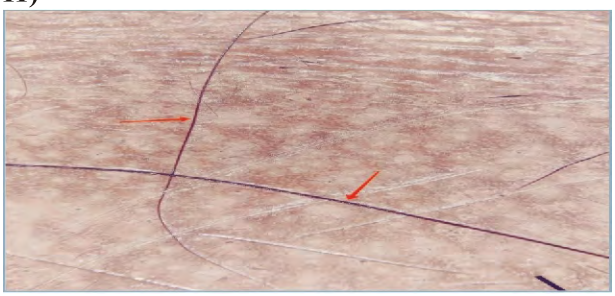

Fig.. 11. Dermoscopic image of Frontal fibrosing alopecia (FFA) showing – lonely hair (red arrow)

Trichotillomania is characterized by Pulling out one's own hair on a regular basis, resulting in hair loss. It manifests as alopecia patches with irregular and bizarre borders. Trichoscopy reveals varying length of broken hair shafts with longitudinal splitting and fraying. Irregular coiled hairs are fractured hairs that get coiled because of excessive traction. The term V-sign refers to 2 or more hairs that emerge from the same follicular unit and are broken at the same length. These findings were seen in all our patients. Other findings included peripilar hemorrhage (red dot corresponding follicular ostia that is swollen with the blood clot due to traumatic forceful hair plucking), flame hairs (semi-transparent, wavy and cone-shaped hair residues, resembling a fire flame), tulip hairs (short hairs with a tulip leaf-like hyperpigmentation at the distal end), and hair dust (only a sprinkled 'hair powder',

resulting from hair damage), were seen in 80% of our patients. Some less common findings seen were pig tail hairs and upright regrowing hairs. Our findings are in accordance with the study conducted by Najam et al.[12] and Elmas et al.[13] **(Fig. 12)**

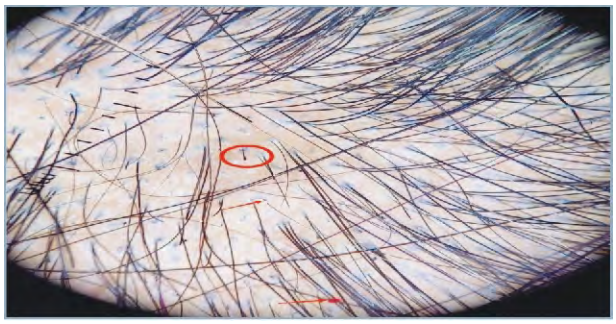

Fig. 12. Dermoscopic image of trichotillomania showing – mace sign (red circle), perifollicular haemorrhages (red arrow).

Head lice infestation, or pediculosis capitis, caused by Pediculus humanus capitis, is a common health concern. It presents as scalp pruritus[2]. Diagnosis sometimes becomes difficult if lice is not visible to the naked eye. Dermoscopy aids in such situations which enables visualization of lice, nits etc.

In our study nits were seen in all the cases, as brown to white, oval, transparent to translucent structures firmly attached to one side of hair shaft. Live parasites were also seen. **(Fig. 13 a,b)**

Pili torti is flattening of hair shaft that irregularly twists (3-5) over its own axis giving "Twisted look" Hairs are brittle especially in the occipital and temporal regions. Affected hairs are unable to resist stretching forces and break at the twists. **(Fig. 14)**

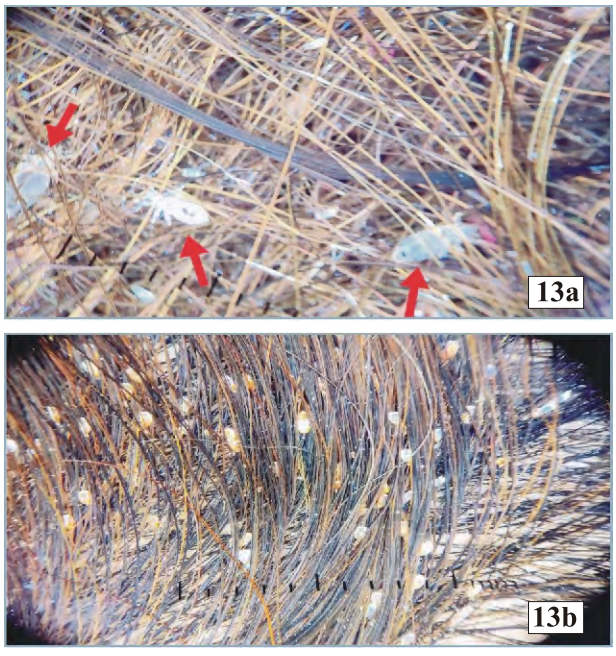

Fig. 13: Dermoscopic image of Pediculosis capitis showing – lice and nits (red arrow)

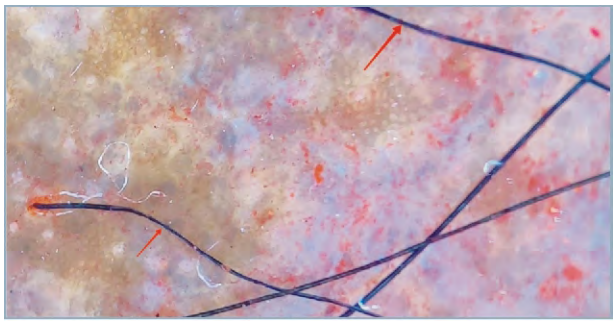

Fig. 14. Dermoscopic image of Pili Torti showing twisting of hair shaft (red arrow)

Conclusion

In this study we have briefly presented the dermoscopic findings in various hair and scalp disorders . It is a simple, reliable and handy tool and is well accepted by patients. It can aid in diagnosing and differentiating different types of hair and scalp disorders. The limitation of our study was the small number of patients in each group. Hence, further studies with larger sample size are needed which could represent each disease group holistically.

Acknowledgements

I feel privileged to express my deep sense of veneration for my co-authors for their constant support and guidance in this study throughout my research period. I extend my heartfelt gratitude towards my patients who participated in the study without whom this study would not have been possible.

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ORIGINAL ARTICLE

A Study on Impact of Burden, Perceived Stress and Coping Styles in Primary Caregiver of patients with Bipolar Disorder in Rural Population

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ABSTRACT :

Background : Bipolar Affective Disorder is a severe mental illness which is stressful not only for the patient but also for the family members. The families of persons with Bipolar Affective Disorder have been the subject of research interest for several decades. Researchers began to examine the impact of the illness and its consequences for the family.

Aims and Objectives: To assess the burden, the perceived stress and the coping styles adapted by caregiver of patients with bipolar affective disorder.

Materials and Methods: After getting institutional ethical clearance, the study was conducted in Department of Psychiatry, Burdwan Medical College and Hospital, Burdwan, West Bengal .The present study was carried out to assess the stress, burden and coping styles of caregivers of BPAD patients. 60 subjects were assessed using perceived stress scale, burden assessment schedule and ways of coping questionnaire.

Results: The perceived stress showed positive co-relation with total burden score($r=0.638$, $p<0.001$) which was statistically significant. Seeking social support (mean=0.2201±0.03) was the most commonly used coping mechanism in the primary caregivers followed by escape avoidance (mean=0.1841±0.04).

Conclusion: This study found negative correlation between burden and distancing, self control, seeking social support and positive re-appraisal and positive correlation between burden and confrontive, accepting responsibility, escape avoidance and planned problem solving coping styles in caregivers of BPAD patients.

Keywords: *Bipolar Aggressive Disorder, Primary Caregiver, Impact of Burden*

Introduction :

Stress can be defined as a circumstance that disturbs or is likely to disturb the normal physiological or psychological functioning of a person.[1] Family caregivers of person with severe mental illness suffer from significant stress, experience moderately high levels of burden and often receive inadequate assistance from mental health professionals.[2] A process-oriented approach to coping is directed toward what an individual actually thinks and does within the context of a specific encounter and how these thoughts and actions change as the encounter unfolds. This approach differs from traditional trait or disposition approaches, which attempt to identify what the person usually does or is most likely to do. Care giver burden refers to the negative feelings and subsequent strain experienced as a result of caring for chronically sick person.[1] Indications are found that caregivers who live with the person with a bipolar disorder experience a heavy burden (Gonzalez et al. 2007; Goossens et al. 2008, Post 2005).[3,4] Perlick et al. (2007) found that the majority of caregivers experience a moderate level of burden, not only during manic or depressive episodes, but continuously.[5] This burden is associated with symptomatic behaviour, decreased performance of tasks by the person being cared for, and negative consequences for family and household.

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The conviction that people with a bipolar disorder are actually able to control their mental illness has been found to be associated with higher levels of not only burden, but also dissatisfaction with the relationship (Lam et al. 2005).[6]

Aims and Objectives :

1) To assess the burden in caregiver of patients with bipolar affective disorder
2) To assess the perceived stress in caregiver of patients with bipolar disorder
3) To assess the coping styles adapted by primary care giver in patients of bipolar disorder

Materials anad Methods :

The study was conducted over one year (February 2012 to March 2013) after getting institutional ethical clearance. Study population was 60 Primary Care giver of patients of bipolar disorder attending psychiatry O.P.D in whom the duration of illness is at least 2 years. Exclusion criteria was Primary Caregiver of male and female patients aged below 18 years or above 60 years. Caregivers were assessed for level of stress using Perceived Stress Scale. The caregivers were then evaluated for burden by Burden Assessment Schedule. Ways of coping questionnaire was given to caregivers to assess the coping methods adapted by them.

Result and Analysis :

Severe burden was seen in domain of wellbeing, relationship with others and in the domain of perceived severity of disease. In other domains moderate levels of burden was found.

Table 1. Perceived severity of disease factor of burden & its socio-demographic correlates Perceived severity of disease factor of burden & its socio-demographic correlates

Characteristics	(Mean±SD)	Number of caregivers (n)
Total Score	9.3±1.61	60
AGE		
18-30	9.06±1.61	16
31-40	9.28±1.38	21
41-50	9.70±1.72	17
51-60	8.83±0.40	6
p-value	0.530	
SEX		
Male	8.8±1.55	25
Female	9.6±1.34	35
p-value	0.02	
EDUCATION		
Illiterate	9.63±0.92	11
Mid school	9.45±1.50	20
High school	8.92±1.64	26
Graduation	10.33±1.15	3
p-value	0.279	
S/E STATUS		
Lower	9.21±1.65	23
Lower middle	9.25±1.43	32
Upper middle	10±1.00	5
p-value	0.532	
DURATION OF ILLNESS		
<10yrs	9.33±1.45	39
≥10yrs	9.23±1.57	21
p-value	0.815	

The mean scores in the perceived severity of disease factor of burden was found to be 9.30±1.61. This factor of burden was highest in the age group 51-60 years (mean=9.75±1.83); in graduate caregivers (mean=10.33±1.15); and in caregivers belonging to upper middle socio-economic class

(mean=10.00±1.00). However these difference amongst various socio-demographic factors was not statistically significant. Female caregivers experienced greater burden in this factor (mean=9.3±1.61) and this difference was statistically significant (p=0.02).

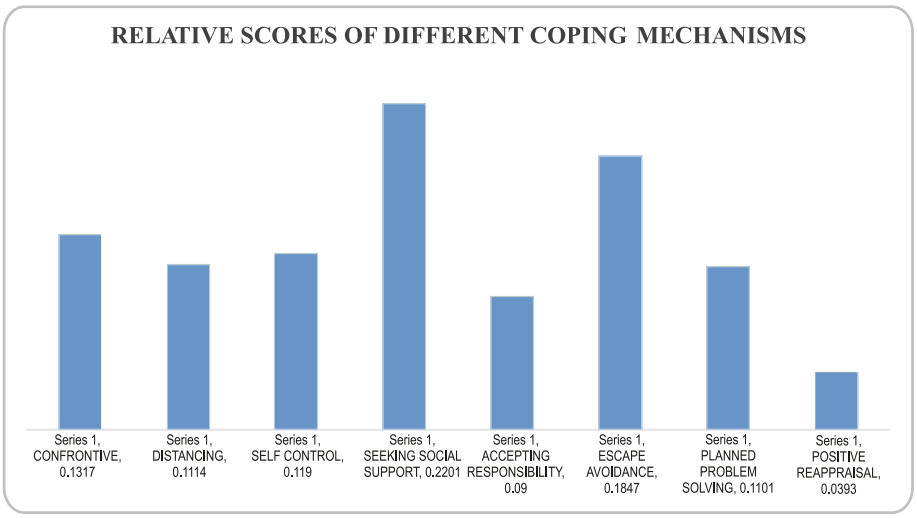

Fig. 1. Bar diagram showing mean values in various coping styles of the care givers

The mean scores show that seeking social support (mean=0.2201±0.03) was the most commonly used coping mechanism in the primary caregivers followed by escape avoidance (mean=0.1841±0.04).

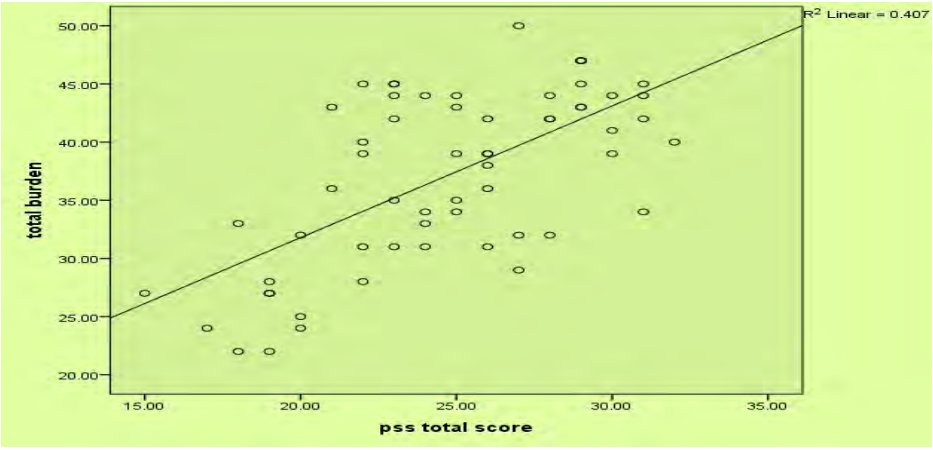

Fig. 2. Scatter diagram showing correlation between burden & stress of the care givers

The perceived stress showed positive correlation with total burden score(r=0.638, p<0.001) which was statistically significant.

Table 2. Assessment of Coping Styles

	Mean	S/D
Confrontive	0.132	0.105
Distancing	0.131	0.052
Self Control	0.12	0.049
Seeking Social Support	0.2036	0.053
Accepting Responsibilities	0.1134	0.043
Escape Avoidance	0.196	0.045
Planproblem Solving	0.098	0.033
Positive Re-appraisal	0.031	0.019

Discussion :

Caregivers of the BPAD patients experienced moderate levels of burden and distress. Higher means scores are recorded for perceived severity of disease and impact on wellbeing. Caregivers experienced severe burden in these factors of burden. Moderate levels of burden was experienced in factors of marital relationship, appreciation of caring and relationship with others aspects of burden. Other studies have found that caregivers who live with the person with a bipolar disorder experience a heavy burden (Gonzalez et al. 2007; Goossens et al. 2008, post 2005) [3,4]. The mean burden scores are higher in spouse than in non-spouse caregivers. Female spouse experienced more burden than male spouse and the difference was statistically significant. Burden in females is higher in all these areas. The result is corroborated by the findings of Morse 1992, Mishra, 2005 who reported that if the mentally ill patient is male, family stress level is likely to be significantly higher [7,8]

The group as a whole reported greater use of emotion focused coping strategies such as escape avoidance and seeking social support (Table 2). Caring for the mentally ill produces significant stress in the caregivers. Emotion focused coping styles help to reduce the stress and are thus the most common used coping styles in these situations. These findings are corroborated by the findings of Nehra et al who found that emotion focused coping was used predominantly in both schizophrenic and BPAD caregivers.[9] However the findings of Chakraborti et al differed from the findings of this study. [10] Chakraborti et al found that caregivers of BPAD patients used problem focused coping styles and caregivers of schizophrenic patients used more of emotion focused coping styles.

The overall sample of the caregivers of BPAD patients had a mean age of 37.9 ± 9.8. Female caregivers were 58.3% (n=35) of the caregivers were female. and male caregivers were 41.7% (n=25) of the caregivers were male. This finding is similar to majority of the studies on caregivers, where females as primary caregivers are largely represented. This is evident in both Indian settings[11] as well as the western literature.[12,13] Highest level of perceived stress was found in the age group of 41-50 years. However the difference in PSS scores among different age group was not statistically significant.

No significant difference was found between educational status, socio-economic status and duration of illness with respect to PSS scores. Most of the studies showed high levels of stress and burden in caregivers of bipolar disorder. [14]

Conclusion :

This study found negative correlation between burden and confrontive, self–control, seeking social support and planned problem solving coping styles , and positive correlation between distancing, accepting responsibility, escape avoidance and positive reappraisal. This study found negative correlation between burden and distancing, self control, seeking social support and positive re-appraisal and positive correlation between burden and confrontive, accepting responsibility, escape avoidance and planned problem solving coping styles in caregivers of BPAD patients.

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ORIGINAL ARTICLE

Cytomorphological Study of Abdomino-Pelvic Masses Using Image Guided Fine Needle Aspiration Cytology as A Diagnostic Tool

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ABSTRACT :

Background: Image guided fine needle aspiration cytology (FNAC) is a fast, easy, safe, accurate, and efficient technique that can be used to confirm suspected malignant masses in various intra-abdominal and pelvic locations as well as to make a cyto-histological diagnosis in space occupying lesions of the abdomen .Evaluation of image-guided fine needle aspiration cytology (FNAC) as a minimally invasive diagnostic procedure for intra-abdominal mass lesions and analysis of the diagnostic efficacy of cytohistologically correlated image-guided FNAC in the diagnosis of malignant intra-abdominal mass lesions were the objectives of the study.

Materials and Methods: This was a retrospective and prospective study done in the Department of Pathology, ESIC Medical college and PGIMSR, Rajajinagar, Bangalore for a period of 4years (January 2018 to December 2021).A total of 97 patients who were clinically and radiologically diagnosed with intra abdominal and pelvic lesions were included in the study.The coagulation profile was assessed in every patient. USG or CT scan guided aspiration were carried out by a pathologist in the department of radiology.

Results: The male to female ratio was 1.6:1, and the mean age was 58.2 years. In image-guided FNAC, the diagnostic yield was 82.6%. Out of 97 cases, 10 were unsatisfactory, 24 were non-neoplastic/inflammatory, 14 were benign, and 49 were malignant lesions. The most prevalent organs were lymph node masses, kidney, and retroperitoneal masses. Among malignant lesions, hepatocellular carcinoma was the most frequent.

Conclusions: FNAC is a quick, easy, affordable, non-invasive, and very successful therapy. With a satisfactory aspiration rate, FNAC performed by a pathologist under image guidance in a radiologist's presence improved diagnostic accuracy. When diagnosing and differentiating between neoplastic and non-neoplastic intra-abdominal lesions, image guided FNAC is significant.

Keywords: *Intra abdominal FNAC, Image guided FNAC, abdomino-pelvic mass.*

Introduction

Image guided fine needle aspiration is a widely used, rapidly growing and significant diagnostic technique that can be used to confirm suspected malignant masses in various intra-abdominal and pelvic locations as well as to render a cytohistologic diagnosis in lesions of the abdomen that occupy space. It is also safe, easy to use, quick, and efficient.[1]

The main benefits of image guided FNAC are that it guides the needle into lesions as tiny as 1 cm and in important anatomical locations, and it permits real-time visualisation of the needle tip as it traverses over tissue planes. The success percentage of the surgery is increased when the lesion is precisely targeted.[2,3]

Documentary evidence of the pathology's existence is crucial for both the prognosis and the beginning of therapy.[4] Since FNAC provides a quick diagnosis, the best course of treatment including medication and surgery can start right away. Imaging techniques may not always be able to distinguish between benign and malignant lesions when the majority of abdomino-pelvic masses presenting as non-palpable lesions are benign, malignant, or inflammatory in nature. It's critical to distinguish between benign and malignant tumours, particularly in cases of advanced

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cancer that are incurable and to prevent unnecessary exploratory laparotomies.

Taking all this into consideration, the present study was performed in order to evaluate the utility of image-guided fine needle aspiration cytology (FNAC) as a minimally invasive diagnostic procedure in intra-abdominal mass lesions, and its histopathological correlation was done wherever possible.

Material And Methods

The Department of Pathology at ESIC Medical College and PGIMSR, Rajajinagar, Bangalore, conducted the current retrospective and prospective study. For a total of four years, from January 2017 to December 2020, 97 abdomino-pelvic lesions that were found both clinically and radiologically were the subject of the study.

The investigation covered masses and lesions in the inguinal area, pancreatic, splenic, renal, retroperitoneal, lymph node, omental, pelvic, left iliac fossa, and hepatobiliary (liver and gall bladder) organs. All of the patients with intra-abdominal masses had coagulation profiles performed on a regular basis. For the investigation, only participants with normal coagulation profiles were chosen.

Prior to doing any CT or USG guided FNAC, the patient's consent was acquired. For superficial masses, a 10-milliliter syringe fitted with a 20–22 gauge needle attachment is utilised; for deep-seated lesions, 20–22 gauge spinal needles are employed. The aspirate smears were treated with 97% alcohol for the Leishman and H&E stains, respectively, after being let to air dry. These smears were classified as benign, malignant, and non-neoplastic/inflammatory lesions based on cytological features. When feasible, cyto-histopathological correlation was used to assess how accurate radiologically guided FNAC was in terms of diagnosis.

Results

There were 97 cases of intra-abdominal and pelvic lesions in our investigation. Of them, 12 were from CT guided FNAC and 85 were from USG guided FNAC. In contrast to CT guided FNAC, which had no unsatisfactory instances, USG guided FNAC had a diagnostic yield of 87.9% (10 cases).

Radiological guided FNAC had an overall diagnostic yield of 89.49%. Regarding the distribution of gender, there were 37 cases (36.84%) of women and 60 cases (63.15%) of men. The male to female ratio was 1.6:1, with 29 cases (29.8%) being under 50 years old and 68 cases (70.1%) being over 50.

Of the 97 cases, 44 cases (45.3%) were of the liver, followed by the renal system (12 cases; 12.3%); the retroperitoneum (10.3%); the abdomino-pelvic lymph nodes (9.2%); the omentum and pelvic masses (6 cases; 6.1% each); the left iliac fossa and the pancreatic masses (3 cases; 3.1%); the spleen and inguinal region (2 cases; 2.06%) (Table 1).

Table 1. Organ wise distribution of cases

SL NO.	SITE	TOTAL NO. OF CASES	PERCENTAGE
1.	HEPATOBILLIARY	44	45.3
2.	RENAL	12	12.3
3.	RETROPERITONEAL	10	10.3
4.	LYMPH NODES	09	9.2
5.	OMENTUM	06	6.1
6.	PELVIC MASS	06	6.1
7.	LEFT ILIAC FOSSA MASS	03	3.1
8.	PANCREAS	03	3.1
9.	SPLEEN	02	2.06
10.	INGUINAL REGION	02	2.06
	TOTAL	97	100

Malignant lesions were present in 49 cases (50.5%) out of 97 cases; these cases were categorised as the majority. The cases that followed were 24 (24.7%) with inflammatory/non-neoplastic lesions, 14 (14.4%) with benign lesions, and 10 (10.3%) with subpar smears due to either acellular or blood element restriction. (Table 2).

Table 2. Distribution of cases according to their categories

Sl. no.	Site	Non-neoplastic/ inflammatory	Benign	Malignant	Inconclusive
1.	Hepatobiliary (44)	06	03	28	07
2.	Renal (12)	02	02	06	02
3.	Retroperitoneal (10)	02	04	04	--
4.	Lymph nodes (09)	04	00	04	01
5.	Omentum (06)	02	02	02	--
6.	Pelvic mass (06)	02	02	02	--
7.	Left iliac fossa mass (03)	02	01	--	--
8.	Pancreas(03)	--	--	03	--
9.	Spleen (02)	02	--	--	--
10.	Inguinal region (02)	02	--	--	--
	Total (97)	**24**	**14**	**49**	**10**

Out of the 24 cases of inflammatory/non-neoplastic lesions (summarised in table 3), the majority of lesions originated from the hepatobiliary region and included 03 cases of cirrhosis, 02 cases of abscess, and 01 case of fatty liver. The second most prevalent site, with 04 cases-03 of granulomatous lymphadenitis and 01 of reactive lymphadenitis was the intra-abdominal lymph nodes. There were two cases of renal cyst, two cases of endometriosis, one case of acute suppurative lesion from the pelvic region, two cases of abscess in the left iliac fossa, two cases of inflamed omentum, one case each of extramedullary hematopoiesis and reactive hyperplasia of the spleen, and two cases of abscess in the inguinal region.

Table 3. Inflammatory/Non Neoplastic Lesions

Site	Non-neoplastic/ inflammatory	Total no. Of cases
1. Hepatobiliary	• Cirrhosis- 03 • Abscess- 02 • Fatty Liver- 01	06
2. Renal	• Cyst- 02	02
3. Retroperitoneal	• Abscess- 02	02
4. Lymph Nodes	• Granulomatous lymphadenitis- 02 • Reactive lymphadenitis- 01	03
5. Omentum	• Inflammatory-01	01
6. Pelvic Mass	• Acute Suppurative Lesion- 02 • Endometriosis- 01	03
7. Left Iliac Fossa Mass	• Abscess- 03	03
8. Spleen	• Reactive hyperplasia- 01 • Extramedullary hematopoiesis- 01	02
9. Inguinal Region	• Abscess- 02	02

Table 4 summarises 14 cases of benign lesions, of which the majority were located in the retroperitoneal area. These cases included 1 case of leiomyoma, 1 case of neurofibroma, and 2 cases of lipoma. The hepatobiliary region, which included one case of hemangioma and two cases of hepatobiliary cystadenoma, was the next prevalent site. There were two cases in each of the pelvic, omental, and renal regions. These cases included two cases of omental lipoma, two cases of mucinous cystadenoma of the ovary, and one case each of renal angiolipoma and renal oncocytoma.

Table 4. Benign Lesions

SITE	BENIGN CONDITIONS	TOTAL CASES
1. Hepatobiliary	• Hemangioma- 01 • Hepatobiliary Cystadenoma- 02	03
2. Renal	• Angiomyolipoma- 01 • Oncocytoma- 01	02
3. Retroperitoneal	• Lipoma- 02 • Neurofibroma- 01 • Leiomyoma- 01	04
4. Omentum	• Lipoma-02	02
5. Pelvic Mass	• Mucinous Cystadenoma Of Ovary- 02	02
6. LEFT ILIAC FOSSA MASS	• Spindle Cell Lesion- 01	01

Table 5 summarises the majority of the 49 cases (50.5%) of malignant lesions that were found in the liver. Of these, 28 cases were found to be related to HCC (hepatocellular carcinoma), 10 cases of metastatic adenocarcinoma deposits, 02 cases of neuroendocrine carcinoma metastatic deposits, 02 cases that tested positive for malignancy, and 01 case of intrahepatic cholangiocarcinoma. The kidneys, which included 04 cases of renal cell carcinoma and 02 cases of metastatic adenocarcinoma deposits, were the next most prevalent place. The retroperitoneal area, which included 02 cases of lymphoma and 02 cases of metastatic adenocarcinoma deposits, came next. There were 04 cases of intra abdominal lymph nodes, with 02 cases of metastatic adenocarcinoma deposits and 02 cases of metastatic squamous cell carcinoma deposits. There were three cases of pancreatic adenocarcinoma. One case each of malignant spindle cell lesion and prostatic adenocarcinoma, were among the pelvic region, exhibiting malignant lesions.

Table 5. Malignant Lesions

SITE	MALIGNANT CONDITIONS	TOTAL CASES
1. Hepatobiliary	• Hepatocellular Carcinoma – 13 • Positive for malignancy- 02 • Metastatic Deposits Of □ Adenocarcinoma – 10 □ Neuroendocrine Carcinoma - 02 □ Cholangiocarcinoma- 01	28 (%)
2. Renal	• Renal Cell Carcinoma – 04 • Metastatic Deposits of Adenocarcinoma – 02	06 (%)
3. Retroperitoneal	• Lymphoma- 02 • Metastatic Deposits of Adenocarcinoma – 02	04 (%)
4. Lymph Nodes	• Metastatic Deposits of Adenocarcinoma -02	02 (%)
5. Omentum	• Metastatic Deposits of Adenocarcinoma -01 • Mucinous Adenocarcinoma- 01	02 (%)
6. Pelvic Mass	• Malignant spindle cell lesion-01 • Prostatic adenocarcinoma-01	02 (%)
7. Pancreas	• Adenocarcinoma Pancreas - 03	03 (%)

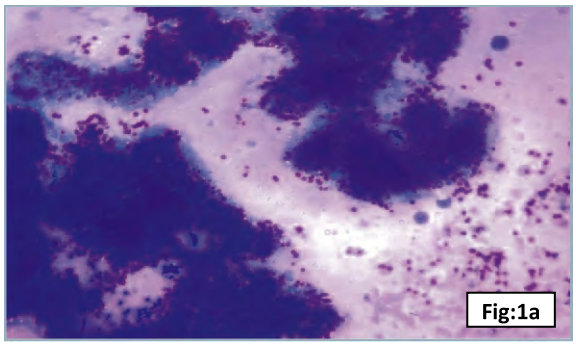
There were 97 intra-abdominal and pelvic lesions in our investigation. Forty-one of them had available histologic correlation. Of the 49 cases of malignant tumours, 27 had available histopathological correlation (Table 6). They included 10 cases of hepatocellular carcinoma (Fig.1), 8 cases of adenocarcinoma with liver metastases (Fig.2), 2 cases of renal cell carcinoma (Fig.3), 1 case of

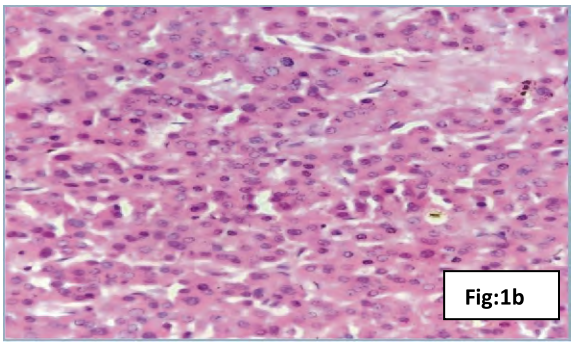
lymphoma (Fig. 4), 1 case of mucinous and metastatic adenocarcinoma in the omentum, and 1 case of prostatic adenocarcinoma. Histopathology validated the cytological diagnosis in 01 case of metastatic deposits of adenocarcinoma in the lymph node (Fig. 5) and 02 cases of pancreatic adenocarcinoma (02). Histopathological correlation was available in 9 out of the 14 cases of benign lesions. Each of the following conditions has one case: endometriosis (Fig. 8), mucinous cystadenoma of the ovary, oncocytoma, lipoma, neurofibroma (Fig. 7) of the retroperitoneal region, and hepatobiliary cystadenoma. Histopathological correlation was obtained for 02 instances (inflammatory/non-neoplastic lesions), 01 case (fatty liver), and 01 case (granulomatous lymphadenitis) out of 24 cases. Out of the 10 cases with unsatisfactory smears, four cases were found to be in the hepatobiliary area (hepatobiliary adenoma, hepatocellular carcinoma, metastatic deposits of adenocarcinoma, and cavernous hemangioma), and one case was found to be at the renal site (renal cell carcinoma).

Table 6. Cytohistopathological Correlation Of Cases

FNAC DIAGNOSIS	HISTOPATHOLOGY DIAGNOSIS
HEPATOBILIARY	
• Fatty Liver (01) • HepatobiliaryCystadenoma (01) • Hepatocellular Carcinoma (10) • Metastatic Deposits Of Adenocarcinoma (08) • Unsatisfactory (04)	• Fatty Liver (01) • HepatobiliaryCystadenoma (01) • Hepatocellular Carcinoma (10) • Metastatic Deposits Of Adenocarcinoma (08) • Hepatobiliary Adenoma (01) • Hepatocellular Carcinoma (01) • Metastatic Deposits Of Adenocarcinoma (01) • Cavernous Hemangioma (01)
RENAL	
• Angiomyolipoma (01) • Oncocytoma (01) • Renal Cell Carcinoma (02) • Unsatisfactory (01)	• Angiomyolipoma (01) • Oncocytoma (01) • Renal Cell Carcinoma (02) • Renal Cell Carcinoma (01)
RETROPERITONEAL	
• Lipoma (01) • Neurofibroma (01) • Lymphoma (01)	• Lipoma (01) • Neurofibroma (01) • Non-Hodgkin's Lymphoma (01)
OMENTUM	
• Metastatic Deposits Of Adenocarcinoma -01 • Mucinous Adenocarcinoma- 01	• Metastatic Deposits Of Adenocarcinoma -01 • Mucinous Adenocarcinoma- 01
PELVIC MASS	
• Endometriosis (01) • Mucinous Cystadenoma Of Ovary (01) • Prostatic Adenocarcinoma (01)	• Endometriosis (01) • Mucinous Cystadenoma Of Ovary (01) • Prostatic Adenocarcinoma (01)
LYMPH NODE	
• Granulomatous Lymphadenitis (01) • Metastatic Deposits Of Adenocarcinoma (01)	• Granulomatous Lymphadenitis (01) • Metastatic Deposits Of Adenocarcinoma (01)
PANCREAS	
• Pancreatic Adenocarcinoma (02)	• Pancreatic Adenocarcinoma (02)
TOTAL: 41	

In 41 of the 97 cases where cytohistopathological correlation was available, the current study found a sensitivity of 90%, specificity of 100%, positive predictive value of 78.5%, and diagnostic accuracy of 92.6%.





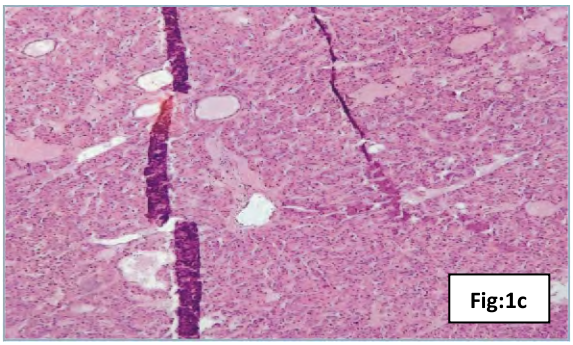
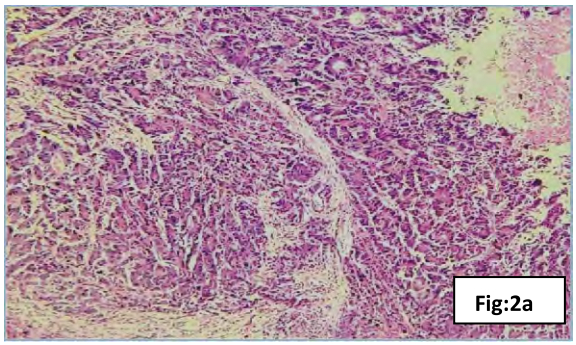


Fig. 1a, 1b, 1c. FNAC of Hepatocellular carcinoma showing sheets of neoplastic cells having high N:C ratio and granular vacuolated cytoplasm (10X Leishman stain). Corresponding histopathological pictures showing tumor cells arranged in solid sheets and trabecular pattern (40X and 10X H&E stain)



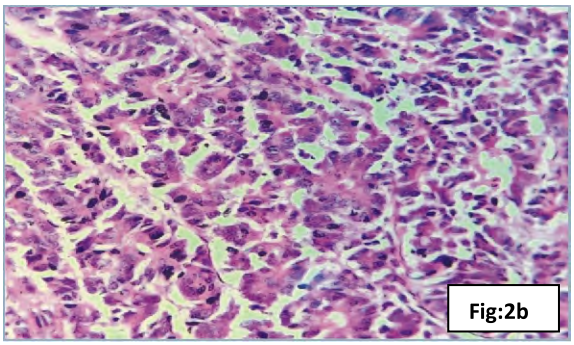
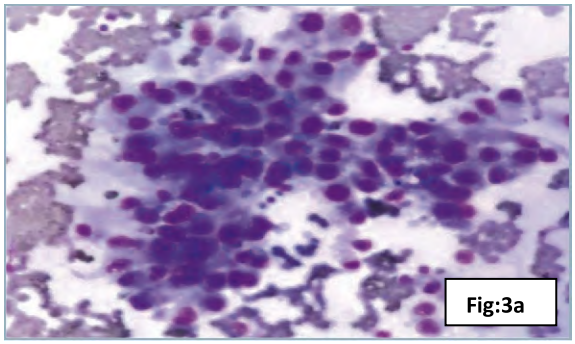


Fig. 2a & 2b. Metastatic Adenocarcinoma Deposits In Liver (10X and 40X H&E)



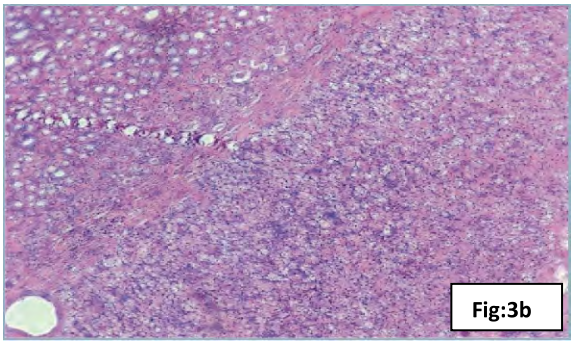
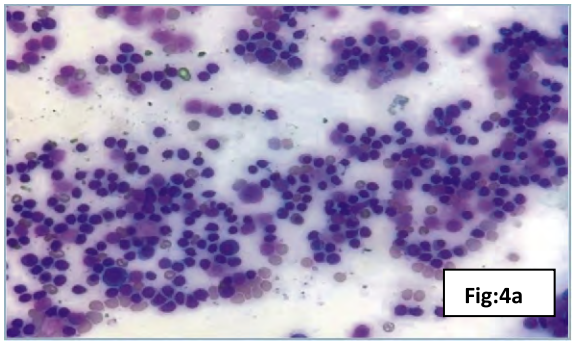
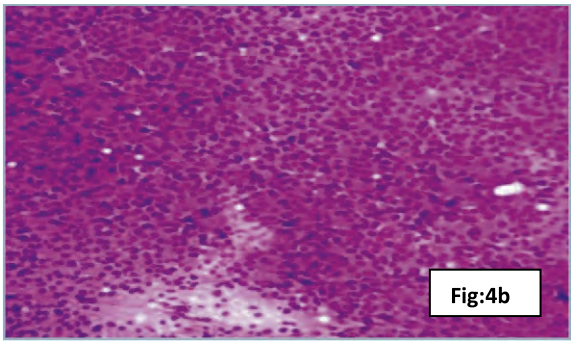


Fig. 3a, 3b. FNAC of Renal Cell Carcinoma showing poorly cohesive tumor cells, abundant fragile cytoplasm, moderate nuclear enlargement and anisokaryosis (40X Leishman stain). Corresponding histopathological picture showing solid nests of tumor cells having round to polygonal cells with clear or granular cytoplasm (10X H&E).





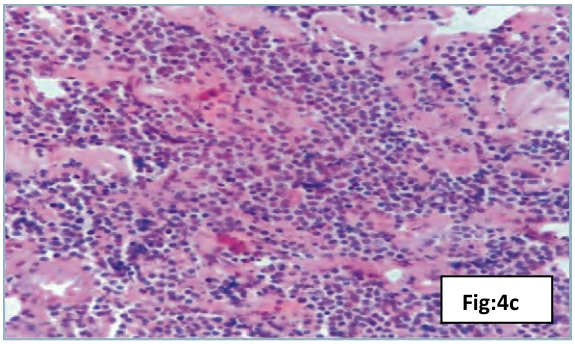
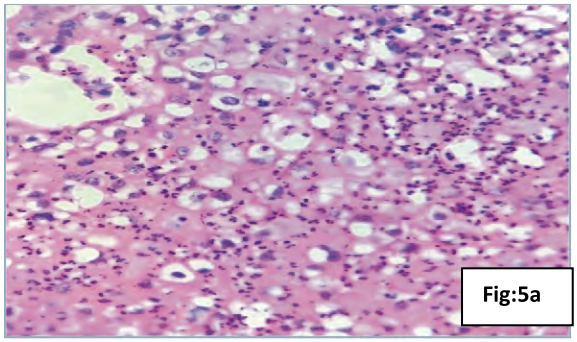


Fig. 4a,4b & 4c. FNAC of Non- Hodgkins Lymphoma showing monomorphic population of atypical lymphocytes arranged in diffuse sheets (10X & 40X Leishman stain). Corresponding histopathological picture showing similar features.



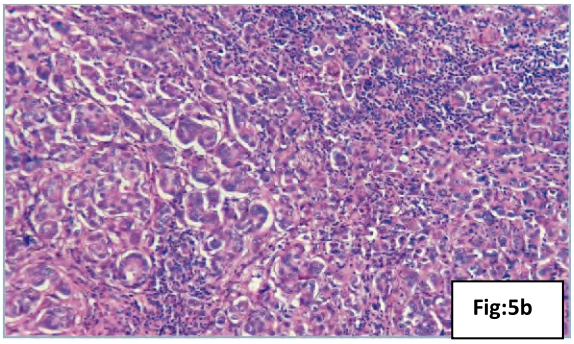
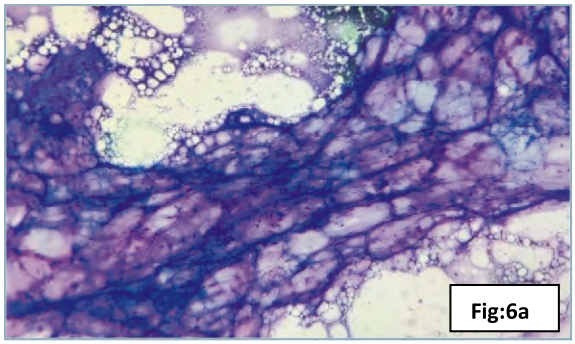


Fig. 5a & 5b. Metastatic adenocarcinoma deposits in Lymph Node.



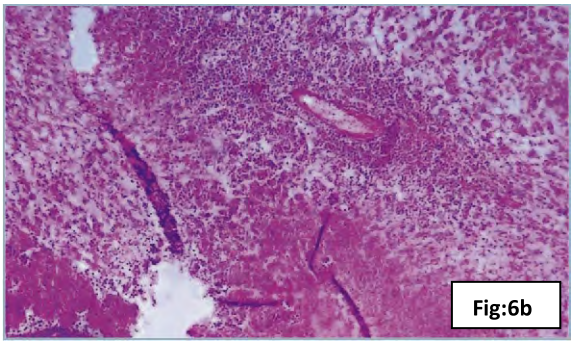


Fig. 6a & 6b. FNAC of Angiomyolipoma of kidney (40X Leishman stain). Corresponding histopathological picture showing similar features.(10X H&E) z

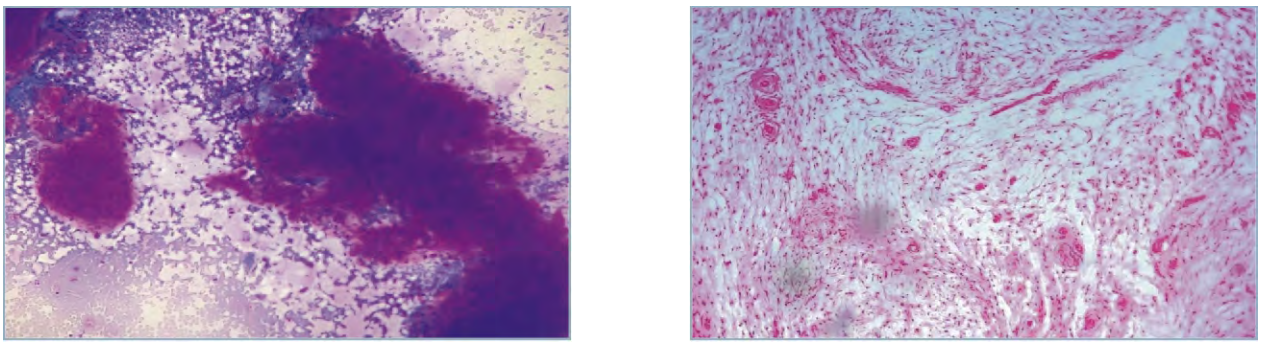


Fig.7a&7b. FNAC of Neurofibroma of (40X Leishman stain). Corresponding histopathological picture showing similar features.(40X H&E)

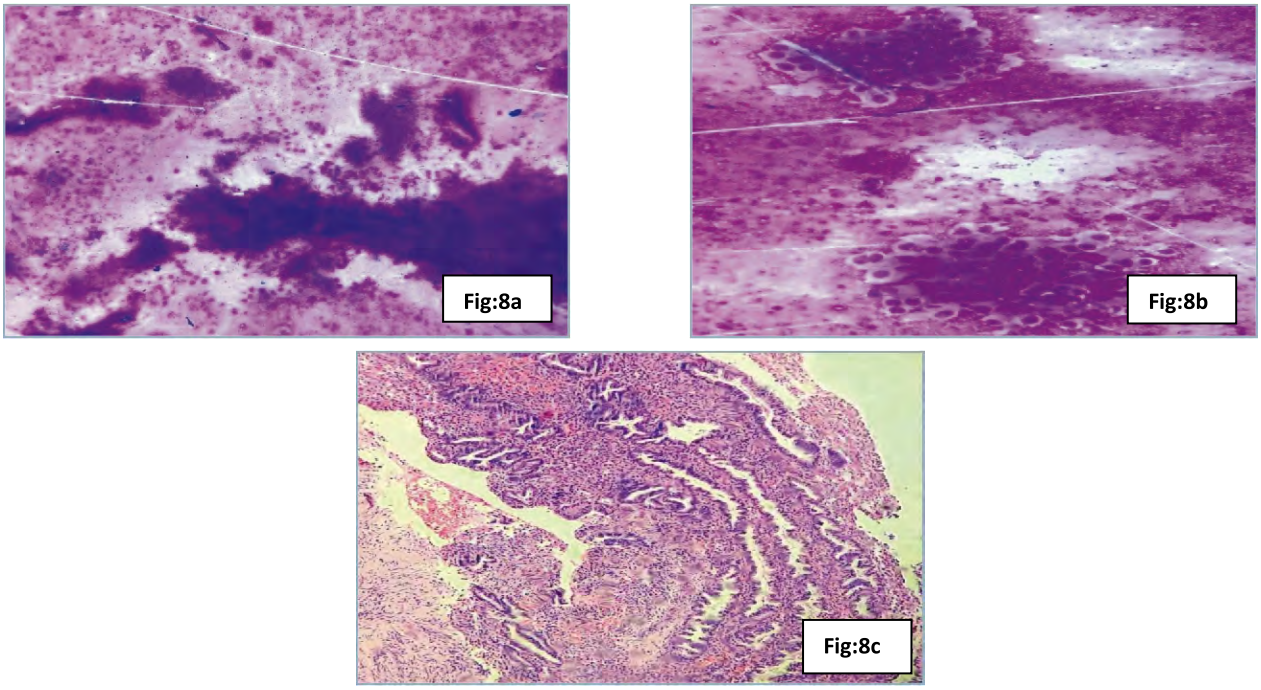


Fig. 8a,8b & 8c. FNAC of scar endometriosis (10X &40X Leishman stain). Corresponding histopathological picture showing similar features.(10X H&E)

Discussion:

More precise targeted sampling of non-palpable lesions is made possible by ultrasound guided FNAC[6]. In order to obtain cellular material, previously unreachable locations such as the intra-abdominal lesions are now frequently aspirated under imaging guidance.

The accuracy rate of collecting a good sample is very high when both the radiologist and the pathologist are supervising the procedure. The technique's adequacy rate is increased by the on-site cytopathologist's quick evaluation of the specimen and further passes as needed.

In our study's, The majority of patients were between the ages of 40 and 60, which was found to be comparable to research conducted by Rahul et al.[7], Vikas Yedshikar[8], and Dr. Momota Naiding et al.[9].

As in all the investigations, there were more male patients than female patients overall. The current study's male to female ratio of 1.71:1 is consistent with research conducted by Vikas Yedshikar[8], Rahul et al[7], and Tasleem Ahmad Reyaz et a[15].

In our investigation, as well as those conducted by Tasleem Ahmad Reyaz et al.[5], Mrinalini Singh et al.[10], Nipun Madhav et al.[11], Kolla et al.[12], and Rahul et al.[7], the liver was the most frequently aspirated location.

Of the 49 malignant cases, metastatic adenocarcinoma deposits accounted for 17 cases (36.1%), while hepatocellular carcinoma of the liver accounted for 13 cases (27.6%). These findings are comparable to those of studies conducted by Kothari et al. (2013) and Nipun Madhav et al. (2011), which similarly reported 37 cases (64.91%) and 69 cases

(58.4%) of metastatic adenocarcinoma deposits, respectively, and 10 cases (14.93%) and 34 cases (33.05%) of hepatocellular carcinoma.

The remaining groups in our analysis were 10 instances (10.5%) that were inconclusive, 14 cases (14.7%) of benign lesions, and 24 cases (25.2%) of inflammatory/non-neoplastic lesions. Different authors' studies have revealed varying incidences of these lesions (Table 7).

Of the 97 patients, 41 had available cyto-histological correlation. The study's high diagnostic accuracy (92.6%) of ultrasound-guided FNAC with no false-positive malignancy diagnosis was noted, making it equivalent to the majority of previous research (Table: 8).The diagnosis accuracy reported in these investigations ranged from 80% to 98.5%.

The current study's radiologically guided FNAC's sensitivity and specificity for abdominal cancers are similar to those reported by Dr. Momota Naiding et al.[10], Rahul et al.[7], Vikas Yedshikar[8], Sidhalingreddy et al.[16], and Rahul et al[7].

Table 7. Categories of final cytologic diagnosis- comparative analysis by various authors

Authors	Total no. of FNAC	Inflammatory	Benign	Malignant	Inconclusive
Present study	95	24	14	47	10
Kolla et al.[12]	120	10	01	80	09
NipunMadhav et al.[11]	164	37	03	118	06
Mrinalini Singh et al.[10]	125	37	03	76	05
Hemalatha A.L et.al[14]	90	20	15.5	64.5	0
Stewart CJR et al.[15]	141	7.8	0	78.2	13.5

Table 8. Comparative analysis of statistical results

Sl. No.	Study	Total no. Of FNAC	Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)
1.	Present study	95	90	100	92.6
2.	Kolla et al.[12]	120	88.9	83.3	87.5
3.	Rahul et al.[7]	204	97.01	100	96.08
4.	Vikas Yedshikar [8]	217	98	100	98.3
5.	Sidhalingreddy et al.[16]	245	94.1	100	96.5
6.	Dr.MomotaNaiding et al.[9]	57	95	100	91.2

Conclusion

The OPD-based, image-guided FNAC approach is a straightforward, economical, precise, fast and safe way to diagnose pelvic and intra-abdominal lesions. Even though we looked at a wide range of organs in our study, more extensive research on each organ is still required to draw firm conclusions. Under the supervision of a radiologist, a pathologist can perform image-guided FNAC, which allows for precise anatomical imaging and lesion targeting. It also carries little to no risk during the process and aids in selecting the best course of treatment.

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[ORIGINAL ARTICLE]

Influence of obesity on cognitive functions in 9th-grade children – A cross-sectional study.

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ABSTRACT :

Background: Nowadays obesity is becoming more common even among children. More than 340 million children and adolescents aged 5-19 were overweight and obese in 2016 which has risen dramatically from just 4% in 1975 to more than 19.3% in 2016.

Aim: To study the influence of obesity on cognitive functions in 9th grade children from high schools in a city.

Methodology: The study was conducted by including 9th-grade school children, boys and girls, from two cities. After obtaining their consent, data were collected by measuring their height, weight, Waist circumference (WC), Hip circumference (HC), and average skin fold thickness. Utilising a certified app that records the time (in seconds), the performance of children in Trail Making Test (TMT) -A and B were also recorded. The longer it takes for the children to complete the task, the poorer their performance during the task. Descriptive statistics were used for continuous and categorical data. Pearson Correlation coefficient, Chi-square test, binomial test, and Mann-Whitney test were used to analyse the data.

Results: The findings from the data analysis showed a contrast with our expected outcome stated in the research proposal earlier. There was an absence of correlation found between obesity and cognitive functions. It indicates that cognitive functions are not influenced by Body mass index (BMI). However, in subgroup analysis, among obese, there was a positive but insignificant correlation r = 0.136 found between obesity and cognitive functions. The prevalence of obesity in 9th-grade children was found at 16% in this study.

Conclusion: Though there was a weak and statistically insignificant correlation found; the findings of this study implies that childhood obesity needs to be addressed appropriately.

Key-words: *TRAIL MAKING TEST (TMT), adolescence obesity, correlation, cognitive functions, Body Mass Index (BMI), Waist Hip ratio (WHR)*

Introduction:

Childhood obesity refers to a child who is significantly overweight for his or her age and height. In 2016, the prevalence of childhood overweight and obesity in India was reported to be 19.3%.[1]

Cognition is the ability to think, recognize, and analyse one's surroundings through visuospatial orientation, attention, and memory.[2] Poor self-esteem, reduced attention, altered peer group and sleep apnea are all plausible physiological and psychosocial causes underlying the relation between obesity and cognition.[3]

There are contrasting pieces of evidence linking childhood obesity and cognitive outcomes.[3] Therefore, it was aimed to assess the influence of obesity on the cognitive functions of children.

Subjects and methods:

Study Design: A high school-based cross-sectional study. *Study Centre and population:* The study was designed to include 9th grade children from two private high schools in a city in southern India during the academic year 2021-22.

Sample size: A total of 161 children were recruited to participate in the study. The duration of the study was 2 months.

Eligibility Criteria: Inclusion Criteria: With written informed consent, boys and girls aged 13-14 years from 9th grade have been included in this study.

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Exclusion Criteria: It was planned to exclude children with physical disabilities and metabolic causes of obesity from this study. But no such child was found during data collection.

Sample size calculation and justification: Many published literature reported both significant and not significant findings about the correlation coefficient. Therefore, the sample size was calculated based on the prevalence of obesity. The estimated proportion (p) of obesity was taken at 19.3%.[1] Considering the absolute precision of 7% and the desired confidence level of 95%, 2-sided; the required sample size was 125. The data collection was completed for 161 students from 9th grade to deal with missing data and errors. Sample size calculation was done using nMaster (2.0) Licences software. *Sampling frame:* To study the influence of obesity on cognitive functions, two private schools in a city from southern India were selected. The permission of the school principal was taken to start the study with children (participants). The written informed consent was obtained from the parents of the children as well as an assent form from the children a day before. As per inclusion and exclusion criteria, 161 children were recruited for this study. Ethical approval for the study protocol had been obtained from the Ethical Review Committee, no. IEC/2020/1/8 before the data collection.

Data Collection and Study Procedure:

The measure of Obesity: Body mass index (BMI), waist circumference (WC) and hip circumference (HC), triceps skin fold thickness. Each child's weight was measured using a portable standard weight floor scale and a Stature Meter (Generic brand) was used to measure the height. These measurements were used to calculate the body mass index, BMI = Weight (In Kgs)/ Height (In Meters) ^2. Waist (in cm) and Hip Circumference (in cm) were measured by using standardised tape. Skin fold calliper was used to assess the skin fold thickness.

The measure of Cognitive Functions: Trail Making Test (Part A and Part B):

In this study, the Android app-based method was used to measure the cognitive functions of the children (participants). The score (time in seconds) was measured accurately and saved by the app (default) which helped to reduce the measurement bias and participants' valuable time.

About Trail Making Test (TMT)[4]:

The Trail Making Test (TMT) is a short and convenient assessment of cognitive functions, principally attention and working memory. There were two parts to this test: Trail Making Tests A and B. Both parts of the Trail Making Test consisted of 25 circles distributed over the screen. In Part A, the circles were numbered 1 – 25, and the child had to connect the numbers in ascending order. In Part B, the circles include both numbers (1–13) and letters (A – L); the child had to connect the circles in an ascending pattern along with the task of alternating between the numbers and letters (i.e., 1-A-2-B-3-C, etc.). The child was instructed to connect the circles as quickly as possible. If the child makes an error, it was pointed out immediately and the child was allowed to correct it. The total time was measured including the time taken for errors and corrections.

TMT Method: Using Android-based APP for TRAIL MAKING TEST 1.3

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It has been developed for the quantitative evaluation of visuospatial working memory. The participants are required to make use of their eyes and dominant fingers, thus aiming to measure the time for coordinated movement, sustained attention, and set-shifting. Guidelines were given in the app to explain to the participants.[6]

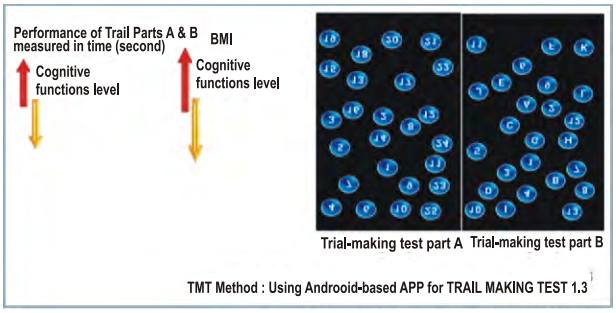


Fig 1. Understanding variables for correlation and illustration of app-based TMT Part A & Part B.

Statistical Analysis: The collected data was entered into the Microsoft Office Excel worksheet. After cleaning and compiling, it was imported to SPSS software for data analysis. Mean, Standard deviation, Frequency and Percentages were used to describe the continuous and categorical data respectively. Karl Pearson's correlation coefficient was calculated to find the relation between BMI values (defines obese/nonobese) and TMT -part A and B scores (measures cognitive functions). A Chi-square test was used to find the association of obesity (based on

BMI values) with gender, age groups, Waist-Hip ratio (WHR) and average skinfold thickness. A binomial test was used to test the equality of proportions between obese and non-obese groups. A non-parametric Mann-Whitney test was used to find the difference between the performance of children in TMT scores for Part A and B. The statistical significance level was considered at $p < 0.05$. Scatter diagrams and bar graphs were presented using Microsoft Excel (10.0). The statistical analysis was done by using IBM SPSS (version 21.0).

Results:

In this cross-sectional study, there were 90 boys and 71 girls out of a total of 161 ninth graders. All of the children were between the ages of 13 and 14, with a mean age of 14 years and a standard deviation of 4.8 months.

Descriptive statistics for all continuous variables under study are presented in Table 1 below. Some interesting findings are explained in the discussion section which helped to understand the unbiasedness of data measurements while understanding the correlation between the cognitive functions of children assessed by TMT-part A and TMT-part B with BMI values.

Table 1. Descriptive Statistics for continuous variables in the study

Characteristics	Age (years)	Height (m)	Weight (kg)	BMI (kg/m^2)	WHR	AST (mm)	TMT A (seconds)	TMT B (seconds)
Sample size (n)	161	161	161	161	161	161	161	161
Mean	13.8	1.6	56.4	21.9	0.8	23.6	50	154
S E of Mean	0.0	0.0	1.0	0.4	0.0	0.7	2	8
Median	14.0	1.6	54.0	21.2	0.8	22.0	47	128
Mode	14	1.65	64	18.7	0.87	22	47	68
Std. Deviation	0.4	0.1	12.9	4.6	0.1	9	23	103
Minimum	13	1.4	30	13.7	0.7	6	20	31
Maximum	14	1.8	96	34.8	1.0	60	169	687
25	14	1.5	47	18.6	0.8	18	36	85
Percentiles 50	14	1.6	54	21.2	0.8	22	47	128
75	14	1.7	64.5	25.1	0.9	29	59	183

RTST - Right triceps skinfold thickness, LTST- Left triceps skinfold thickness, AST- Average Skinfold Thickness

The study characteristics were presented as frequency and proportions in Table 2.

Table 2. Descriptive statistics for categorical data in frequency and percentages.

Characteristics	Category	N= 161
Gender	Girls	71 (44%)
	Boys	90 (60%)
BMI	Underweight	6 (4%)
	Normal (Non-obese)	83 (52%)
	Overweight	46 (28%)
	Obese	26 (16%)
Waist:Hip ratio	Normal	138 (86%)
	Obese	23 (14%)
Average skinfold thickness	Lean	1 (0.6%)
	Ideal	23 (14.4%)
	Average	59 (37%)
	Overfat	78 (48%)

In Figure 2, the scatter plot showed that there was almost no correlation between study outcomes TMT-part A performance and BMI values. The blue and red circles represented boys and girls respectively.

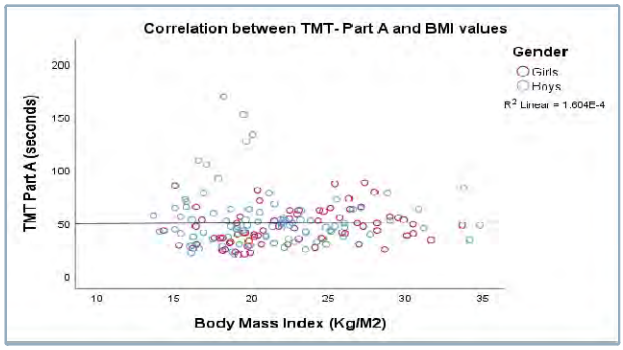


Fig 2. The scatter diagram shows almost no correlation (r= 0.013, p=0.873) between Trail-Making test performance (in seconds)– part A and BMI values in 9th grade children. (n=161)

In Fig 3, absolutely no correlation was found between study outcomes TMT- part B performance with BMI values, presented in the scatter diagram.

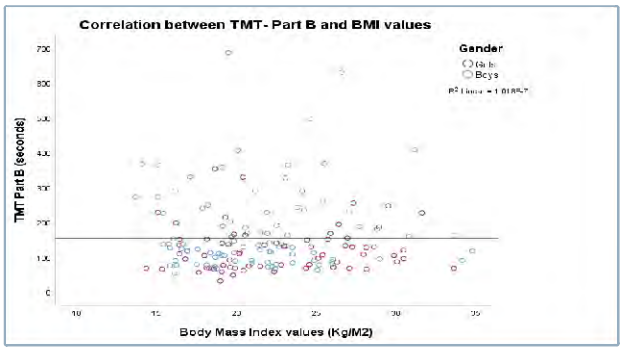


Fig 3. The Scatter diagram shows no correlation (r= 0.00, p=0.997) between Trail-Making test performance (in seconds)– part B and BMI values in 9th grade children. (n=161)

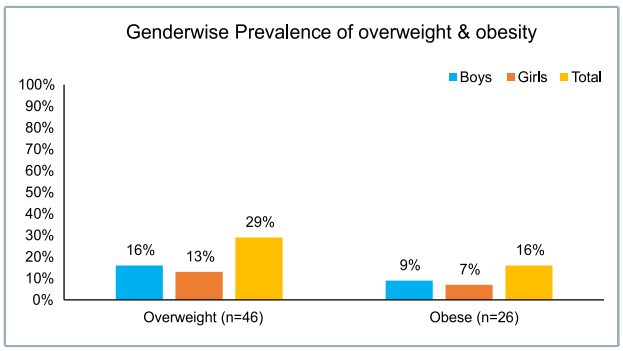
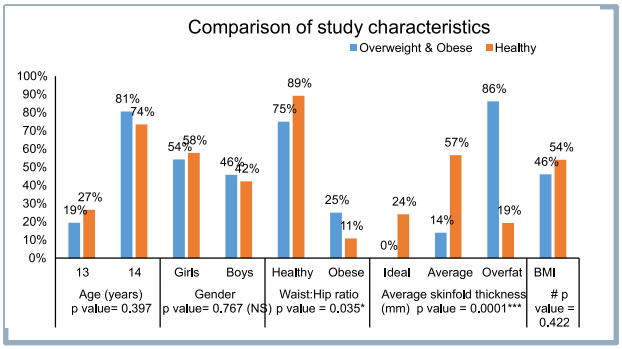


Fig. 4. depicts a multiple bar diagram, comparing the prevalence of overweight and obesity between genders. The prevalence of obesity was found more among boys than girls.

Fig 4. A multiple bar diagram shows the gender-wise comparison of the prevalence of overweight and obese (n=72) out of the total study participants (N=161)

Subgroup Analysis for overweight & obese, non-obese (based on BMI values classified using WHO criteria):

Pearson's Chi-square tests showed an insignificant proportion in age and gender, while the Waist: Hip ratio (WHR) showed a highly significant proportion between the overweight & obese and normal (non-obese) groups. Excluding five cases of malnourished children, the binomial test was used to determine whether the proportions between the overweight & obese and the normal group (based on BMI cutoffs) were equal. There was no statistically significant difference between the overweight & obese group and the normal group at p = 0.422 (Fig. 5).



*# Binomial test for BMI class, NS= Not Significant at p> 0.05, *** Highly significant at p <0.0001*

Fig 5. A multiple bar diagram shows the comparison between categories of study characteristics with p values (Chi-square test used with continuity correction). A binomial test was used for BMI classification.

In Table 3, a non-parametric Mann-Whitney test was used to compare the average performance of children in TMT-parts A and B in the comparison groups of overweight & obese and normal. Only the variable of weight revealed a statistically significant difference. age, height, TMT-part A, and TMT-part B were all variables found to remain statistically insignificant in this study.

Table 3. The difference in TMT-part A and TMT-part B performance and other characteristics between overweight & obese and normal groups.

Table 3. The difference in TMT-part A and TMT-part B performance and other characteristics between overweight & obese and normal groups.

Characteristics	Groups (Based on BMI)	Mean Rank	Mann-Whitney U Test	Z score	p-value	Effect size
TMT-A (Seconds)	Overweight & Obese (n= 72)	84.99	2485	-1.807	0.071(NS)	-0.145
	Normal (n=83)	71.93				
TMT-B (Seconds)	Overweight & Obese (n= 72)	81.18	2759	-0.822	0.411(NS)	-0.066
	Normal (n=83)	75.24				
BMI (Kg/m2)	Overweight & Obese (n= 72)	119.12	28	-10.622	0.0001***	-0.853
	Normal (n=83)	42.33				
Waist-Hip Ratio	Overweight & Obese (n= 72)	96.39	1664	-4.751	0.0001***	-0.382
	Normal (n=83)	62.05				
Weight (Kg)	Overweight & Obese (n= 72)	116.27	233	-9.892	0.0001***	-0.795
	Normal (n=83)	44.80				
Height (M)	Overweight & Obese (n= 72)	77.10	2923	-0.233	0.815 (NS)	-0.019
	Normal (n=83)	78.78				
Age (years)	Overweight & Obese (n= 72)	80.93	2777	-1.035	0.301 (NS)	-0.083
	Normal (n=83)	75.46				

****p<0.0001- highly significant, NS- Not Significant.*

There was no evidence to support the difference in TMT A and TMT B performance between the overweight & obese and normal groups. (TMT A- p = 0.071, Effect size = -0.145) and (TMT B- p = 0.411, Effect size = -0.066). TMT A and TMT B effect sizes were found to be -.0145 and -0.066, respectively, indicating a small effect. (According to Cohen's classification of effect sizes which is 0.1 (small effect), 0.3 (moderate effect) and 0.5 and above (large effect)).

It is shown that there was no correlation found between children's performance on TMT-parts A and B and their BMI values. However, a statistically significant correlation was found between WHR and TMT-part B in obese children. (Table 4)

Table 4 . Correlation between BMI values and performance of children for TMT- part A and TMT- part B. (n= 161)

Correlation coefficient r	TMT- Part A	TMT-part B
BMI in overweight & obese children	0.136	0.00
BMI in non-obese children	-0.025	-0.045
Total Children	0.013	0.00
WHR in obese children	0.08	0.22**

***p<0.001 very significant.*

The scatter diagram in Fig. 6 illustrates the positive correlation between TMT-part A and BMI values in the obese group, but it was found statistically insignificant. The straight trend line shows a little positive correlation. The blue and red circles distinguished boys and girls, respectively.

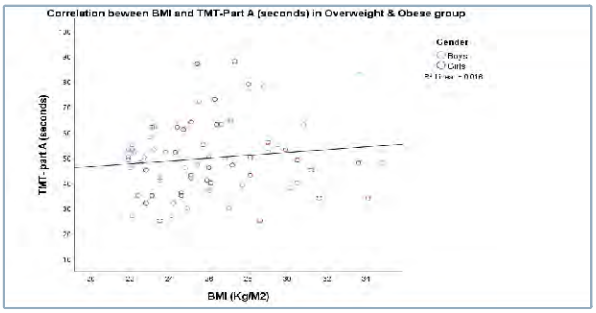
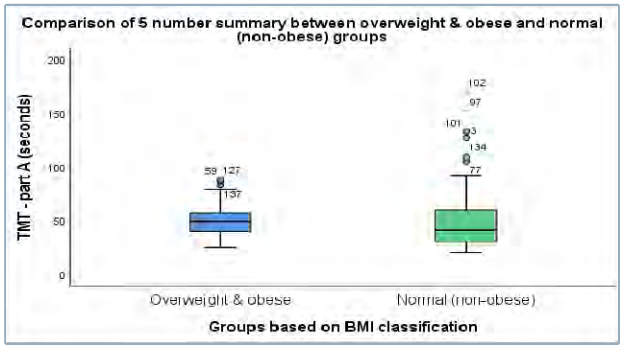


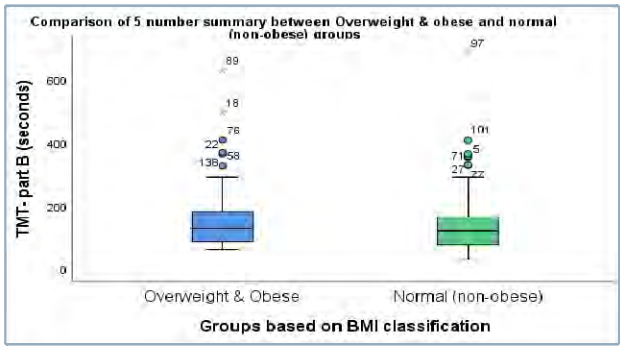
Fig. 6. The Scatter diagram shows a positive but statistically insignificant correlation (r = 0.136, p=0.271) between Trail Making Test performance (TMT in seconds) – part A and the Overweight and obese group in 9th grade children. (n=72)

Box-Whiskers plots in Figs. 7 and 8 show the dispersion of cognitive function in both groups for TMT parts A and B. Outliers were found to stretch the normal distribution positively skewed and weaken the correlation between BMI and cognitive function (TMT performances) of study participants. The numbers at outliers show the case numbers of the study.



Numbers shown as Outliers are the cases (students ID) numbers

Fig. 7. Box-Whisker's plot shows the dispersion of cognitive function (TMT performance) in both groups for TMT part A



Numbers shown as Outliers are the cases (students ID) numbers

Fig. 8. Box-Whisker's plot shows the dispersion of cognitive function (TMT performance) in both groups for TMT part B

Discussion:

In this cross-sectional study, conducted for a total of 161 ninth-grade children, the linear Pearson correlation between Trail Making Test-part A & B scores in seconds (using a mobile app that measures children's cognitive functions) and BMI values did not produce any statistically significant results.

In light of conflicting results from previous studies stating a positive or negative correlation, this study was undertaken to assess the influence of obesity on cognitive functions in 9th grade children. The descriptive continuous data and categorical data are presented in Table 1 and Table 2.

To assess the cognitive functions in children, performance scores in TMT- parts A and B were collected (by using an app). The longer it takes to complete the task, the lower the cognitive level. A negative correlation was expected between obesity and cognitive functions (i.e. the higher BMI, the lower cognitive levels, Fig 1). However, this study found no correlation between BMI and the TMT-part A and B performance scores. (Figure 2 and Figure 3).

In our study, the prevalence of obesity among children was found to be 16% (figure 4). An increase in the prevalence of obesity among children (9% in India, 20161) might be due to the strict public health measures and lockdown strategies that were adopted during the COVID-19 pandemic in the year 2020-21 as stated by Hourani HA et al[7].

Our study also highlights that boys have a higher prevalence of obesity than girls. One Indian study found the age-adjusted prevalence of obesity was 2.9% in boys and 1.5% in girls.[8]

In Fig. 5, the statistically insignificant results for BMI values, age groups and gender proved that participants were equal in proportions for the same variables in this study. It helped to rule out the bias to compare the obese and non-obese groups. Statistical significance in WHR indicates generating a hypothesis which has been explained at the end of this discussion part.

Since neither of the variables in TMT-A nor TMT-B were normally distributed, the nonparametric Mann-Whitney test was applied to compare the performance of the overweight & obese and normal groups in Table 3. The result was statistically insignificant with a small effect size.

One logical explanation suggested by researchers to support our findings is that obesity takes a long time to exert a detrimental effect on cognitive functions. It is also possible that the psychosocial effects of self-esteem, peer relationships, and discrimination intensify with age and are more influential in college students and adults than in children.

Afzal AS et al also stated that it is quite normal for children to fluctuate in and out of their BMI status during their childhood due to the dynamic nature of growth.3 While addressing the relation between BMI and cognition, Liang et al. opine that there may be a new threshold at a specific BMI value where an individual's weight strongly influences cognitive functioning.[9]

While employing a battery of tests to assess cognitive development, Mond JM et al observed strikingly similar performance from obese and normal (non-obese) children.[10]

In Table 4, the correlation analysis showed that there was

no correlation found between children's performance on TMT-parts A and B and their BMI values at p>0.05 in total children as well as obese and normal groups. However, a statistically significant, positive correlation (r=.22) was found between WHR and TMT-part B in obese children. That is those with high WHR, spent more time in TMT-part B. To explore more about obesity and cognitive functions in school children, a subgroup analysis was performed.

In this subgroup analysis, based on BMI values, the children were assigned to three categories: malnourished, non-obese (normal), and overweight & obese. Excluding the group of five malnourished children, the non-obese (n = 83) and overweight & obese (n = 72) groups were analysed to figure out the correlation between BMI and TMT-part A & B scores in each group. Fig.6 showed that TMT-part A performance in the overweight & obese group (n=72) was negatively impacted by elevated BMI values (obesity) (r=.13). Despite being statistically insignificant, this weak correlation can be viewed as good evidence for explaining the negative correlation between obesity and cognitive function. Confounding factors (age and gender) were ruled out because they were found in equal proportion (no significant difference) in the overweight & obese as well as non-obese groups. Furthermore, there was no significant difference in binomial test results between the overweight & obese and non-obese groups (Figure 5). The correlation between TMT-part B and elevated BMI values was found absolutely zero. (Table 4). Future studies with a large sample size may provide a clear picture supporting these findings.

Similarly, in the non-obese group (n = 83), there was a negligible negative correlation obtained for both TMT scores (parts A and B), which reflects the good performance of non-obese children during the given task (TMT Parts A and B). To support our above findings, Khan NA et al. suggested that further studies need to be conducted to ascertain the susceptibility of cognitive processes to the effects of overall adiposity and fat distribution while explaining the weak, negative association of obesity with cognitive functions.[11]

However, many research studies conducted at various locations with varying sample sizes, discovered that obesity affected cognitive functions[2,12,13]. Therefore, in future studies, a large sample size of the obese group may prove statistical significance.

In Fig. 7, the dispersion of TMT-part A values was compared in both groups based on BMI classification. The overweight & obese group showed the normal distribution, ranging the TMT score performance between 25 seconds and 75 seconds excluding three outliers. It was interesting to note that, the normal (non-obese) group showed a little positively skewed distribution with four outliers, ranging up to 175 seconds. It interprets that, non-obese children spent more time completing the task. Altogether, the data distribution of these two groups supports the statement that obesity does not influence cognitive functions.

In Fig. 8, the dispersion of TMT-part B values was compared in both groups based on BMI classification. Both groups showed a positively skewed distribution, ranging the TMT score performance up to 650 to 700 seconds including many outliers. It was again compelling evidence to note that, children from both groups spent more time completing the task on TMT-part B. These two data distributions also support the same statement that obesity does not influence cognitive functions.

Literature supporting this study's main findings (no evidence of correlation): Gunstad et al. (2008) were unable to establish any association between obesity and cognitive function in children aged 6–19 years. This study included 478 children and was designed to assess body mass index and study on children and observed that obesity had no bearing on standard academic tests A 6-year longitudinal study involving children aged 2–8 years done in the United States by Leblanc et al. in 1963 found no link between childhood obesity and cognitive abilities. Using an individual fixed effect (FE) approach, Palermo and Dowd (2012) demonstrated that obesity has no remarkable effect on cognitive achievement among children and adolescents. The Child Development Supplement (CDS) waves I–III data were used in this study to investigate whether overweight and obesity are associated with cognitive and non-cognitive skills. Kaestner and Grossman (2009) noticed that obese students aged 5 to 12 had math and reading test scores comparable to their normal-weight peers. The author attempts to prove here that an elevated BMI status has no impact on educational achievement.

Literature supporting the negative correlation between obesity and cognitive functions: In the systematic review, Taras and Potts-Datema (2005) reviewed nine studies and found that each one evidenced a negative relationship between obesity and school performance, yet this wasn't a uniform finding of this research. Furthermore, the quality and size of these studies varied, ranging from a study of 65 obese children aged 8–13 in Brazil to 60,000 Finnish adolescents to 12,537 people aged 23 or older in England and Scotland. Edwards and Grossman (1979) noted that obese children aged 6–11 had lower scores on the Wechsler Intelligence Scale for Kids (WISC) and the Wide Range Achievement Test (WRAT) than their normal-weight counterparts. Calvo, D., Galioto, R., Gunstad, J.,

and Spitznagel, M. B., deduced that adolescents with a higher BMI had increased reaction times on the Continuous Performance Test (CPT) than their normal-weight peers. Additionally, obese subjects with increased uncontrollable eating behaviour performed poorly in inhibitory control and working memory tests.

The following studies explain academic performance in boys and girls, exploring the effect of obesity on cognitive functions indirectly. Datar and Sturm (2006) highlighted those girls with higher BMI had lower math and reading test scores than normal-weight girls. However, there was no such association for boys. Averett and Stifel (2007) concluded that obese children had lower reading scores but not lower math scores than normal children. They also studied underweight children and showed that they had lower math scores but not lower reading scores.

Black et al. stated in their explanation of childhood obesity and cognitive achievement that there are many potential explanations for the disparities in results, including geographical and age differences within the study population, choice of control variables, and differences in methodology.

The relationship between childhood obesity and cognition needs to be thoroughly researched due to the empirical challenges in determining the causal effects coupled with the inconsistencies in the existing literature. To help with policy development, it is critical to comprehend the precise nature of the connection between childhood obesity and skill attainment.

A Thought to generate a hypothesis, is waist-hip ratio better than BMI?

This present study showed that there was a statistically significant difference in WHR and BMI values in the comparison of Obese and non-obese groups. An Indian study found more than one-third of adolescents with central obesity do not meet obesity BMI standards. This emphasises the importance of measuring waist circumference in addition to BMI when assessing obesity.[14] According to the Harvard Report, BMI is not a perfect measure because it does not directly assess body fat. Since muscle and bone are denser than fat, BMI can overestimate body fat in athletes with high bone density and muscle mass while underestimating it in elderly people with low bone density and muscle mass. WHR (waist-hip ratio) can better reflect the accumulation of intra-abdominal fat compared to BMI.[15]

Yet, since the direct measurements of body fat require special equipment and are expensive, BMI is a still fairly reliable method of determining high body fat.[15]

Hence, further research is required on BMI criteria and WHR to assess obesity.

Recommendations:

Besides discrepancies in results across studies, it is critical to prevent obesity in the early stages of life to circumvent the adverse effects of excess fat on our health. To combat obesity, all parties, including parents, teachers, health practitioners, the private sector, and the government, must join hands and develop effective policies.

Strength of study: The data collection was undertaken in schools in an organized and planned way, including obtaining permissions from higher authorities and their cooperation, as well as participants' cooperation and using standard equipment to measure the parameters, resulting in mostly bias-free data collection. It is reflected in the results after data analysis, which helped to draw a reliable conclusion.

Limitations: The expected outcome for the obese group revealed a weak and insignificant correlation. This result might become statistically significant with a larger sample size, increasing the study's power. The small sample size of this study may affect the generalisability of this cross-sectional study. There were restrictions during data collection regarding iliac skin fold measurement because it was not permitted to measure in light of the pandemic COVID-19. The absence of correlation in the desired variables limited the application of regression methods in data analysis in the study.

Conclusion:

In this cross-sectional study, no correlation was found between obesity and cognition functions. However, among the obese group, a negative correlation was found between obesity and cognition functions. Obesity was found to be more prevalent in boys than in girls. To get reliable results on the relationship between obesity and cognitive functions, more studies must be conducted rigorously with a good study design.

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Conflicts of interest: None

ICMR STS-2020-Reference ID: 2020-06970

Classification of BMI and Waixc-Waist-hip reshow have done based on the WHO growth chart and guideline given by the manufactures of skinfold callicer respectfully[16-18]

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ORIGINAL ARTICLE

Assessment of Knowledge Regarding Occupational Health Hazards and its Precautionary Measures-A Cross Sectional Study Among Dal Millworkers

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ABSTRACT :

Introduction: Kalaburagi is the major pulse producing and processing district in Karnataka. Dal mill workers are exposed to dal dust leading to skin allergies, musculoskeletal disorders, irritation of eyes, etc.

Objectives-

1) To assess the knowledge related to occupational health hazards among dal mill workers

2) To determine prevailing occupational health hazards among the workers

3) To assess preventive and control measures taken for occupational health hazards among the workers

Methodology- This is a cross sectional study conducted in Kapnoor industrial area, Kalaburagi, where in 4 dal mills each with 25 workers, were included in the study. After seeking permission from the Dal mill owner, the study details were explained to the participants and face to face interview was conducted after obtaining their oral consent. SPSS (Version 28) was used for data analysis.

Results- Out of 63 participants, 85% were males and 15% were females. The knowledge of workers regarding various diseases such as occupational dermatitis, musculoskeletal disorders & allergic conditions were found to be 42%, 65% and 52% respectively and the study showed prevalence of occupational dermatitis (25%), musculoskeletal disorders (48%) and allergic disorders (44%) respectively. About 33.3% were found to be trained in use of personal protective equipment's [PPE]

Conclusion- Occupational hazards among dal mill workers can be prevented by pre-periodic and periodic (annual) medical examination, prevention is by daily use of personnel protective equipment's (PPE) like mask, gloves, goggles and ear muffs.

Keywords: *Dal mill workers, Musculoskeletal disorders, occupational hazards, Personal protective equipment's (PPE)*

Introduction

About half of the world's population is made up of workers, who also serve as the main forces. The suffering and hardship brought on by illnesses and deaths at work affect both the employee and their family. [1]

The risks connected to working in particular occupations are therefore known as occupational hazards[2]. Total 17% is contributed by India to occupational diseases when compared to 11% contributed by world[3]

Dal milling is one of India's most important processing industries. One of the top producers of pulses worldwide is India. Among the many pulses grown in the country are lentils, Bengal gram, pigeon pea, green gram, and black gram. [4]

In Karnataka, production and processing is more, Kalaburagi is known as mass producer of tur dal which has more than 300 registered dal mill which are operating in whole district of Gulbarga[5]

The people who work in the dal mill units are exposed to a wide range of physical, chemical, and environmental health problems, including noise disturbances, contamination of air and dust. The employees of dal mills may experience breathing difficulties, skin allergies, musculoskeletal disorders, eye and nose irritation[6]

Personal protective equipment for dal mill workers is

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being implemented primarily to lessen health risks and disorders associated with dust allergies at work[6]. Therefore, the current study was carried out to evaluate the level of knowledge about the occupational health hazard they faced, to identify the prevalence of occupational diseases among the workers, and to assess KAP regarding PPE kits.

Objective:

1) To assess the knowledge related to occupational health hazards among dal mill workers
2) To determine prevailing occupational health hazards among the workers
3) To assess preventive and control measures taken for occupational health hazards among the workers

Materials and Methods

This is a cross sectional study conducted in Kapnoor industrial area, Kalaburagi, Karnataka for a period of 3 months (June to August 2023).

Sample size and sampling procedure:

In Gulbarga city, there are 40 dal mills[7], 10% of 40 is 4 By using simple random sampling, four dal mills (Nadar, Birbitte, Nandi and VKM dal mill) were selected. Each dal mill containing 25 workers, 63 workers were present during data collection, so the sample size is 63. Due permission was obtained from owners of Dal mill. Oral Consent was taken from the study participants and confidentiality was assured.

Inclusion criteria: Workers who indicate their willingness to participate and those who were present at the time of data collection were included in the study.

Exclusion criteria: The workers who are absent at the time of data collection and those who are not willing to participate are excluded from the study

Data analysis: Tabulation and statistical data were calculated using Excel and SPSS (Version 28) with graphical representation.

Ethical clearance: Ethical clearance was obtained from Institutional ethical committee (ESICMC/GLB/IEC/16/2023)

Data collection: Pre-tested & pre-validated questionnaire was used in the study for obtaining data from the workers. The questionnaire consists of socio-demographic profile, knowledge about occupational hazards among workers and knowledge about use of personal protective equipment [PPE].

Statistical methods: Data was entered in Excel Sheet and socio-demographic variables were described as frequency and percentage.

Results

Table 1 shows Sociodemographic profile of study participants. The study population comprised of 63 workers among whom 86% were males. Among 63 workers, most of them belong to 31-45 years (41.2%), Hindu religion 59 (93.65%), illiterate 27 (42.8%), married 54 (86%). Prevalence of co-morbidities among workers were 6.35%.

Fig. 1 depicts prevalence of occupational health hazards among dal mill workers. 82% of workers had one or more illnesses. Based on symptoms found in dal mill workers, occupational health hazards were classified into musculoskeletal disorders, allergic disorders and occupational dermatitis. Prevalence of musculoskeletal disorders, allergic disorder and occupational dermatitis was found to 48%, 44% and 25% respectively. Most common symptoms found among workers were Headache (44%), joint pain (48%), backpain (48%), neck pain (36%) and itching (25%).

Fig. 2 depicts about the knowledge of the dal mill workers regarding occupational health hazards. It is observed that majority had awareness regarding musculoskeletal disorders (65%) followed by allergic disorder (52%) and occupational dermatitis (42%). None had knowledge regarding occupational injuries

Table 2 indicates preventive and control measures taken for workers in dal mill and it is observed that 33.3% of the workers have received training on how to use personal protective equipment's [PPE]. 67.6% of the workers knew about PPE. PPE was provided to 33.3% of the workers. It is observed that most common used PPE was mask (68.2%) followed by cap (31.7%). Usage of ear muff, gloves and apron was not observed. Only 9% of workers were aware about regular medical checkup that is organised in factory.

Table 1. Sociodemographic profile of the study participants

Sociodemographic Factors	Parameters	Frequency [n=63]	Percentage (%)
Age Groups (years)	1-15	4	6
	16-30	20	31.7
	31-45	26	41.2
	46-60	10	15.8
	61-75	3	4.7
Sex	Male	54	86
	Female	9	14
Religion	Hindu	59	93.65
	Muslim	3	4.76
	Christian	1	1.58
Education	Illiterate	27	42.8
	Primary school	10	15.8
	Middle school	3	4.7
	High school	15	23.8
	Intermediate school	7	11.1
	Graduate	1	1.5
Marital status	Married	54	86
	Unmarried	9	14
Co-morbidity (HTN,DM, Asthma)	Yes	4	6.35
	No	59	93.65

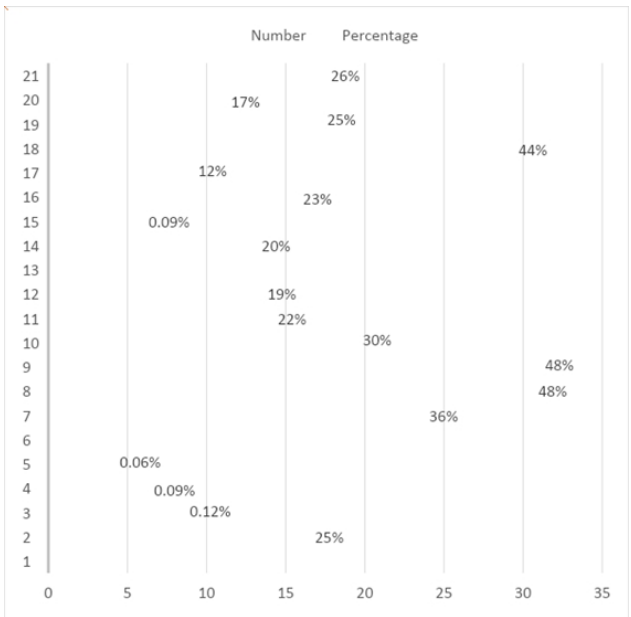

Fig. 1. Prevalence of Occupational health Hazards among dal mill workers

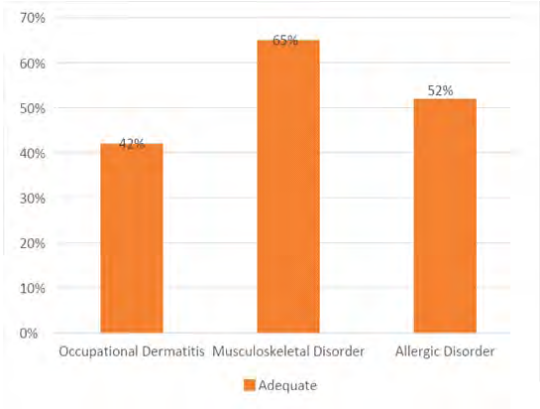

Fig. 2. Knowledge regarding Occupational Health Hazards among Dal mill workers

Table 2. Preventive and control measures taken for workers in Dal mill

		Frequency [n=63]	Percentage %
Training workers for PPE	Yes	21	33.3
	No	42	66.6
Awareness for using PPE	Yes	44	67.6
	No	19	32.4
PPE provided	Yes	21	33.3
	No	42	66.6
Usage of PPE	Cap	20	31.7
	Mask	43	68.2
	Ear muff	0	0
	Gloves	0	0
	Apron	0	0
Medical services available at work	Yes	20	31.7
	No	43	68.2
Frequency of medical checkup	No	57	90.4
	Once a year	3	4.7
	Twice a year	3	4.7

Discussion

Currently, In India there are 52 crore workers[8] working in factories. Safety and health of the workers is important. The present study focus on problems faced by dal mill workers. Male members comprised majority in study (86%) which was similar to Sudha et al4 were males comprised 73.3% in their study.

Illiteracy was found to be prevalent in the study population (i.e) 42.8% when compared to Deepak et al[9] study where majority was found to be in Intermediate school. This may be due to geographic location.

In present study knowledge regarding musculoskeletal disorders, allergic disorders and occupational dermatitis among the worker were found to be 65%, 52% and 42% respectively. The findings were different from Suda et al[4] study, they had 70%, 40%, 60% respectively.

In the present study, prevalence of musculoskeletal disorders was 48% which is equivalent to study conducted by Someshwari et al6 (45%). In the study conducted by Deepak et al9 prevalence of musculoskeletal disorders (60%) was found to be commonest disorder prevalent among workers.

Among the dal mill workers, 33.3% of the workers were provided and trained with PPE. Whereas in a study conducted by Sudha et al4, no PPE were provided and the workers were not trained in using PPE. Because there was insufficient health education about the use of PPE, the use of PPE was restricted in our study.

Limitations of study

1) We were not able to achieve adequate sample size, hence uncertainity was high.
2) As the finance was limited, the study couldn't be done in larger scale.
3) The workers were not provided proper training regarding the use of PPE kits, hence they

couldn't know the importance of occupational diseases. In our study they lagged the use of PPE, which was negatively impacted.

Conclusion

Industrial workers are at higher risk of developing occupational health hazards due to unsafe working environment. The study showed that most of the workers were not aware about the occupational diseases and personnel protective equipments (PPEs) which brings about the negligence and negative impact. Hence health education was needed. Health education was given to increase knowledge of the workers. Regular periodic health checkup and health education should be given periodically to prevent occupational health hazards.

Acknowledgement: We would like to thank the Dal mill workers of Kapnoor Industrial area (Nadar, Birbitte, Nandi and VKM dal mill) who participated in the research.

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CASE REPORT

The Rubber That Bleeds – A Case Report

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ABSTRACT :

Blue Rubber Bleb Nevus Syndrome (BRBNS) is a rare disorder characterized by multiple venous malformations of the skin and visceral organs. In this article, we present the case of a 16-year-old girl who was diagnosed with BRBNS at the age of 5 years due to the presence of cutaneous, gastrointestinal, and muscular hemangiomas. She presented to us with severe iron deficiency anemia and was found to have new hemangiomas on endoscopy during her current admission. Sirolimus therapy was initiated. We discuss the clinical manifestations, pathogenesis, and treatment options for BRBNS by reviewing the relevant literature.

Keywords : *Blue rubber bleb nevus syndrome , hemangiomas , gastrointestinal bleeding , iron deficiency anemia, sirolimus.*

Introduction

Blue Rubber Bleb Nevus Syndrome (BRBNS), also known as Bean syndrome, is a rare congenital disorder associated with venous malformations of the skin and visceral organs, commonly involving the gastrointestinal tract. Patients usually present with chronic iron deficiency anemia due to gastrointestinal blood loss. In this case report, we present a patient who was diagnosed with BRBNS in childhood and came to us with symptoms of severe anemia. Endoscopy revealed new hemangiomas in the gastrointestinal tract that precipitated her anemia. Sirolimus therapy was initiated. We aim to highlight this rare cause of chronic anemia and discuss the clinical presentation and management with a review of the literature.

Case Report

A 16-year-old girl presented to us with a history of easy fatigability and New York Heart Association class III dyspnea of 1 month's duration. She had no other cardiac symptoms or pedal edema. She had a normal menstrual cycle with no abnormal bleeding in the recent past, and her diet included non-vegetarian foods. On examination, she had pallor and bluish, non-tender lesions noted in the right palm and bilateral plantar aspects of the foot, as well as a bluish, rubbery, non-tender swelling over the right deltoid region [Fig. 1].

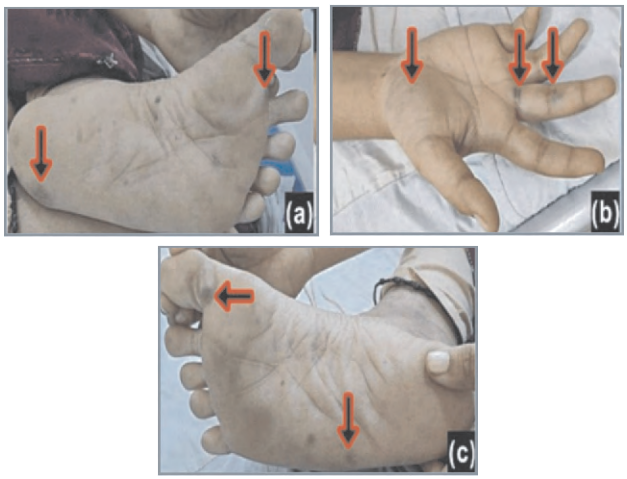

Fig. 1. Cutaneous Lesions.

Bluish-brown raised lesions suggestive of cutaneous hemagiomas noted in (a) Left foot (b) Right Palm and (c) Right foot

The rest of the clinical examination was unremarkable. The skin lesions had been present since early childhood. At 5 years of age, she was admitted to another hospital for melena. Upper GI endoscopy was normal, but colonoscopy revealed multiple hemangiomas of 0.5 to 1 cm throughout the colon, with normal intervening mucosa. She was

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screened for vascular malformations in other organs by Magnetic Resonance Imaging (MRI), which revealed a large, well-defined, hyperintense mass lesion seen in the deltoid muscle belly (5.2*5.4*4.6 cms), suggestive of an intramuscular hemangioma. An intermuscular hemangioma in the left lower lateral chest wall extending into the extrapleural space (3.7*2 cms) and a small intramuscular hemangioma in the left paraspinal muscle at the L4 L5 level (2.1*1.1 cms) were also noted. [Figure2]

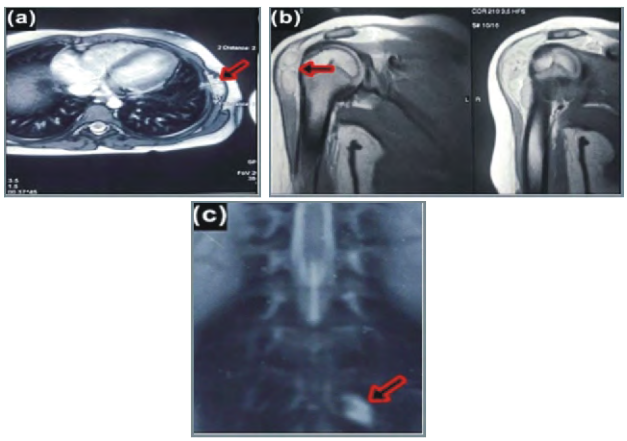

Fig. 2. Magenetic Resonance Images showing muscular hemangiomas

a) An intermuscular hemangioma in left lower lateral chest wall. b) Intramuscular hemangiomas seen in right deltoid and c) left paraspinal muscle

MRI brain was normal. In view of multiple cutaneous and visceral hemangiomas, she was diagnosed with Blue Rubber Bleb Nevus Syndrome. She was started on iron supplements and propranolol, but the patient defaulted in due course. Since then, she had been admitted four times for blood transfusion in a different hospital. She did not have any family history of a similar illness. In the present admission, she had severe iron deficiency anemia with hemoglobin 2.4 mg/dl (12-14 mg/dl), iron 44 mcg/dl (32-104 mcg/dl), total iron-binding capacity of 508 mcg/dl (250-450 mcg/dl), and ferritin 5.1 ng/ml (7-8.4 ng/ml). Fecal occult blood was positive. Her hemoglobin rose to 8 mg/dl after three packed red cell transfusions and 1000 mg of Ferric carboxy maltose. Upper GI endoscopy revealed new hemangiomas in the mid-esophagus and the second part of the duodenum without any stigmata of recent or active bleed. Colonoscopy reiterated the previous findings and did not show any signs of active or recent bleed.

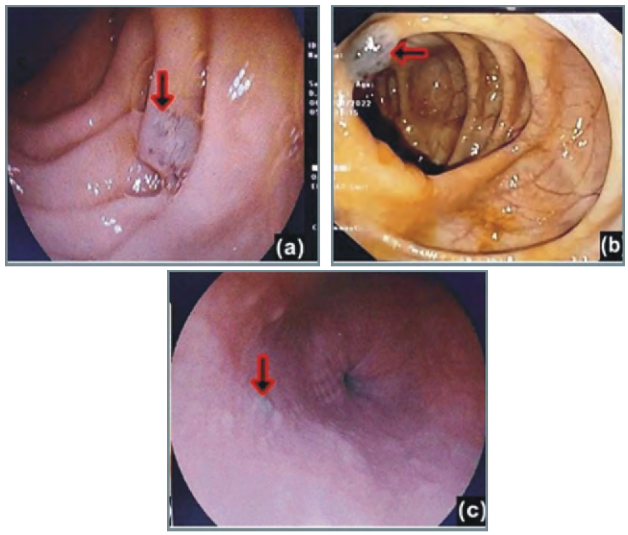

Fig. 3. Endoscopic images of gastrointestinal hemangiomas.

a) Upper gastrointestinal endoscopy showing hemagiomas in second part of duodenum b) Colonoscopy showing hemangioma in large bowel and c) esophagus

In view of the requirement for multiple blood transfusions and the formation of new visceral lesions, she was started on sirolimus therapy and Iron supplementation. She is kept under follow-up.

Discussion

Blue Rubber Bleb Nevus Syndrome is a rare disorder characterized by discrete venous malformations of varying size and appearance on the skin, within the gastrointestinal (GI) tract, and less often, in other organ systems. It was first reported by Gascoyen in 1860 and was later described in detail by William Bennet Bean, who coined the term "Bean syndrome". Only around 350 cases have been reported in the literature with varied clinical presentations. Of the reported cases, 21% are from the USA and 7% are from India[1]. The condition does not have a sex predilection. The oldest patient reported was 82 years old, and the youngest was an unborn baby (shown by B-ultrasound in an antenatal examination). Onset of lesions was noted in 30% since birth, 9% in infancy, 48% in childhood, 9% in adolescence, and 4% in adulthood[2]. The disease is mostly sporadic, but rarely, an autosomal dominant mode of inheritance is reported. Recently, two somatic activating mutations on the same allele (double CIS mutations) of the TEK (TIE2) gene have been discovered to cause this disorder[1]. The TEK gene encodes a protein called the TEK receptor tyrosine kinase, which is involved in multiple steps of angiogenesis. When the TEK receptor is activated, it triggers the release of

chemical signals that facilitate cell-cell communication between endothelial cells and smooth muscle cells. This communication leads to new blood vessel formation and safeguards the structure and integrity of these blood vessels. The TEK receptor is constitutively active in BRBNS due to somatic activating mutations, which leads to unregulated angiogenesis.

The clinical presentation of Blue Rubber Bleb Nevus Syndrome includes both cutaneous and visceral hemangiomas and their associated complications. Cutaneous lesions are present in more than 94% of patients and are characterized by rubbery, soft, occasionally tender, and hemorrhagic nodules that are easily compressible and refill promptly after compression. The size of these lesions can range from small papules to large disfiguring nodules, and they often involve the extremities[2,3]. Gastrointestinal (GI) system involvement is the next most commonly observed symptom, present in nearly 76% of patients [3].The lesions tend to appear predominantly in the small intestine, but they can occur anywhere from the mouth to the anus. These vascular malformations can be polylobulated, nodular, sessile, pedunculated, ulcerated, or submucosal protrusive lesions, and they can lead to chronic blood loss causing iron deficiency anemia [4,5]. Sudden massive hemorrhage is rare[6]. The other organs that can be involved include the central nervous system(13%), muscle (9%), and liver[7]. Literature review shows that vascular malformations can be seen in almost every organ system, and single or multisystem involvement can be seen[2]. The Size and number of lesions grew with time.

Patients can also present with complications such as intussusception, gangrene, intestinal volvulus, or infarction[8]. Serious complications such as central nervous system hemorrhage or infarction can occur in cases of hemangiomas in the brain or spinal cord compression in the case of hemangiomas in the vertebrae. Rare complications of BRBNS have been reported, such as blood coagulation disturbance (4 cases), thrombocytopenia (3 cases), and disseminated intravascular coagulopathy (2 cases), and the reasons for these complications are unclear 2. Malignant transformation has not been reported to date.

The evaluation typically reveals iron deficiency anemia, and fecal occult blood testing may also be positive. Endoscopy is considered the gold standard for diagnosing lesions associated with BRBNS, and it can help identify the location, size, and extent of the lesions. Capsule endoscopy is a non-invasive technique that can be useful for diagnosing venous malformations involving the GI system, especially in the small intestine. Endoscopic ultrasound reveals hypoechoic lesions with luminal structures, predominantly involving the mucosa and submucosa. Computed tomography (CT) and magnetic resonance imaging (MRI) can also be useful in locating lesions and determining the extent of the disease[4,8]. Histopathological examination revealed cavernous venous dilatations with a thin wall of smooth muscle lined by a single layer of endothelial cells, surrounded by delicate connective tissue. Biopsy is not routinely necessary. The differential diagnosis of BRBNS includes Osler-Weber-Rendu syndrome, Klippel-Trenaunay syndrome, and Maffucci syndrome [2].

There is currently no curative treatment for BRBNS. Skin lesions do not necessarily require treatment. However, laser photocoagulation, sclerotherapy, and surgical resection may be performed for aesthetic or functional reasons. GI lesions tend to cause chronic iron deficiency anemia, and iron supplementation and packed red cell transfusion may be necessary depending on the severity of anemia. Endoscopic treatment is less invasive and can fully preserve the entire length of the bowel. Endoscopic treatment is indicated for lesions that are endoscopically accessible, as well as for cases with diffuse GI involvement. Good clinical outcomes have been reported with endoscopic laser photocoagulation, band ligation, sclerotherapy, submucosal dissection, or polypectomy[9]. In cases of localized disease or massive hemorrhage, or complications such as volvulus or intussusception, surgical treatment is necessary [10]. For lesions located in other organs, the aim is to control bleeding or compression. If conservative therapy does not provide relief, surgical resection is often required.

Pharmacological therapies such as steroids (which inhibit endothelial cell migration), interferon alpha (which inhibits secretion of vascular endothelial growth factor - VEGF), propranolol (which decreases VEGF activity), and vincristine (which inhibits tubulin polymerization) as anti-angiogenic agents have not shown satisfactory results. Octreotide has been used in some cases to reduce gastrointestinal bleeding by reducing splanchnic blood flow [6].

Sirolimus (rapamycin), an inhibitor of mammalian Target of Rapamycin (mTOR), has shown promising results in treating BRBNS. Yuksekkaya et al. reported the first use of sirolimus in an 8-year-old child with BRBNS. Sirolimus was initiated at a dose of 0.05-0.1 mg/kg, and the blood trough level was maintained between 1-5 ng/mL. Although the lesions did not completely regress, their size and number were reduced. Hemoglobin levels improved, and the need for blood transfusions decreased. It was observed that if sirolimus was stopped or its trough level was below 2 ng/mL, old lesions regrew and new lesions appeared, leading to blood loss[6]. The upregulated TIE2/TEK receptor in BRBNS due to somatic mutations tends to cause unopposed angiogenesis via the PI3/AKT pathway, resulting in endothelial cell survival. The PI3 pathway in turn activates mTOR, a key regulator of angiogenesis. VEGF is also an upstream activator of mTOR. Sirolimus exerts its effects in BRBNS by inhibiting mTOR, thereby suppressing angiogenesis [10].

According to a literature review, nearly 30 cases have been successfully treated with sirolimus since its first use. Although the drug dosage and trough level varied in each case, the frequency of gastrointestinal bleeding was significantly reduced, and patients were no longer dependent on blood transfusions [12,13].The recommended dose is 1.6 mg/m2/day, with a trough level to be maintained between 10-15 ng/mL. However, successful management of BRBNS has also been reported with lower trough levels. Consensus regarding the dose and trough level to maintain has not been established yet 1. Sirolimus has the potential to adversely affect renal function, bone marrow, and cholesterol metabolism. Regular monitoring of these parameters is recommended to detect and manage any potential side effects.

Our patient, a 16-year-old girl, presented with a one-month history of easy fatiguability and dyspnea, and was found to have severe iron deficiency anemia. She also had cutaneous lesions since childhood and was diagnosed as BRBNS with multiple GI hemangiomas at the age of 5 years. Further imaging revealed additional muscular hemangiomas in the right deltoid, left lateral chest wall, and left paraspinal muscle. There was no family history of similar illness. In the recent Upper GI endoscopy, new GI hemangiomas were found. The patient was treated with intravenous iron and blood transfusions, and sirolimus therapy was initiated due to the formation of new visceral lesions and the need for multiple transfusions. She is currently under follow-up to monitor her response to treatment and assess her prognosis.

Conclusion

Blue Rubber Bleb Nevus Syndrome is a rare cause of chronic iron deficiency anemia, and its endoscopic or surgical management is often complicated and ineffective due to diffuse lesions. Sirolimus therapy has shown promising results in reducing the size and number of visceral lesions and the requirement for blood transfusion. However, due to the rarity of BRBNS, large-scale randomized controlled trials with sirolimus could not be conducted. Consensus on the optimal dose and trough level of sirolimus for the treatment of BRBNS should be established through further studies.

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CASE REPORT

Mucormycosis – An Uninvited Resident Evil in The Post Covid Era: A Case Series

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ABSTRACT :

Mucormycosis is a rare opportunistic fulminant fungal infection caused by saprophytic fungi belonging to the family Mucoraceae, the principal pathogens being Rhizopus, Lichtheimia, Apophysomyces, and Rhizomucor.Incidence of Mucormycosis has been drastically increased in post Covid-19 era. Medical conditions like diabetes milletus, hypertension are also to be considered as risk factors and are found to be associated with disease progression. Outcome of the affected patients are usually poor due to destructive and progressive nature of the disease. Here we present a series of four cases of Mucormycosis with their clinical presentation, diagnosis, treatment course and follow up data.

Keywords: *Rhizopus, fungal infection, post Covid-19,*

Introduction

Mucormycosis is a opportunistic fungal infection caused by saprophytic fungiof the family Mucoraceae, the principal pathogens being Rhizopus, Lichtheimia, Apophysomyces, and Rhizomucor.[1,2]

The risk factors predisposing patients to mucormycosis are uncontrolled diabetes, neutropenia, haematological malignancies, organ transplantation, trauma and burn, and use of immunosuppressants such as corticosteroids. Mortality rate ranges between 50-80%.Higher mortality is associated with intracranial involvement, disseminated disease and presence of underlying comorbidities. (Fig.1)

Case series

We report four cases of Rhino-orbital mucormycosis from January 2022 to August 2023 admitted at ESIC Medical College & Hospital, Hyderabad. All the patients presented with headache, facial pain, puffiness of face and loss of vision seen in one patient. Mean age of the patients was 43 years. Among them 2 patients had a history of Covid 19 infection and one of them presented with uncontrolled diabetes with mean HbA1C of 12.7. CT scan and MRI showed fungal sinusitis with osteomeatal complex occlusion in all the 4 cases. KOH mount showed broad pauciseptate hyaline ribbon like fungal hyphae with obtuse angled branching. Histopathology showed necrotic debris with refractile aseptate branching fungal hyphal structures in 3 cases. Fungal culture showed growth of Rhizopus species in 3 cases which were further confirmed by MALDI-TOF MS. Functional endoscopic sinus surgery was done in 3 cases and patients were treated with Liposomal Amphotericin B except one case who could not survive following enucleation.[Table 2]

Discussion

Rhino-orbital-cerebral Mucormycosis is associated with a mortality rate of 25-60%.[3] Incidence of Mucormycosis surged during the COVID-19 pandemic due to usage of Corticosteroids with sinuses being the most common site to be affected. They exhibit overlapping features with Bacterial orbital sinusitis or Rhinocerebral aspergillosis or Scedosporiosis.[1,4] Microscopy and Culture of clinical specimens are the cornerstones of early diagnosis of Mucormycosis. Majority of Rhino-orbital-cerebral Mucormycosis were caused by Rhizopus arrhizus.High index of clinical suspicion along with early evaluation of risk factors can help in early diagnosis and recovery.In cases of resource limited hospitals, consideration for a combination of

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Amphotericin B and Posaconazole has similar efficiency thereby reducing the need for high dosage of Amphotericin B and thereby reducing its toxicity.[3,4,5]

Early Surgical debridement and initiation of Antifungal therapy decreases the mortality of these patients.

Table 1. Clinical details of all the four patients

Case Series	Patient -1	Patient -2	Patient -3	Patient -4
Age	42years	33years	48years	47 years
Sex	F	F	M	M
Comorbidities	CKD, T2 DM, Coronary artery disease(Recent MI) , Hypertension	T2 DM	Nil	AKI, Uncontrolled Diabetes
HbA1c	7.7	8.2	-	12.7
Covid 19 history	Post-Covid	Post-Covid	No history	No history
H/O Steroid intake	Present	Not present	Not present	Not present
Clinical Features	Sinusitis, headache, facial pain	Headache, facial pain, Sinusitis	Headache, facial pain, Left Chronic Maxillary Sinusitis	Orbital cellulitis with loss of vision with sinusitis, headache
Surgery	**FESS**	**FESS**	**FESS**	**No Surgery**
Antifungal treatment	IV LAB-150 mg X 14 days PCZ-100 mg TID X 21 days	IV LAB-150 mg X 14 days PCZ-100 mg TID X 21 days	IV LAB-150 mg X 14 days PCZ-100 mg TID X 21 days	IV LAB-150 mg X 14 days
Outcome	Discharge	Discharge	Discharge	Succumbed to Death
Fungal culture Report MALDI-TOF	*Rhizopus homothalicus*	*Rhizopus arrhizus*	Organism could not be cultured. KOH showed Fungal elements	*Rhizopus arrhizus*

CKD→Chronic kidney disease; T2 DM→Type 2 Diabetes milletus; AKI→Acute Kidney Injury; LAB→Liposomal Amphotericin B ; PCZ→Posaconazole; FESS→Functional endoscopic sinus Surgery; MI→Myocardial infection.

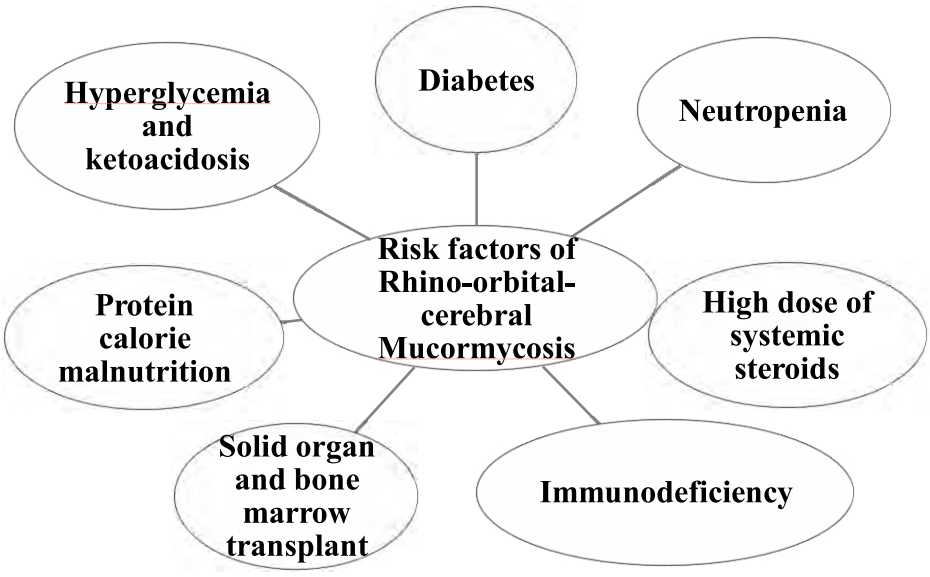


Fig. 1. Risk factors of Mucormycosis

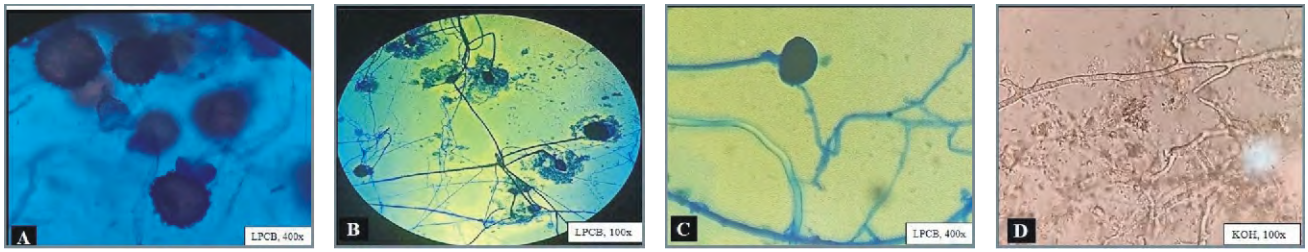


Fig. A. to C. Lactophenol cotton blue stain shows (A) Rhizopus homothallicus (B) - (C) Rhizopus arrhizus; (D) Broad, ribbon-like, non-septate hyphae with wide angle branching seen in wet mount(KOH X400).

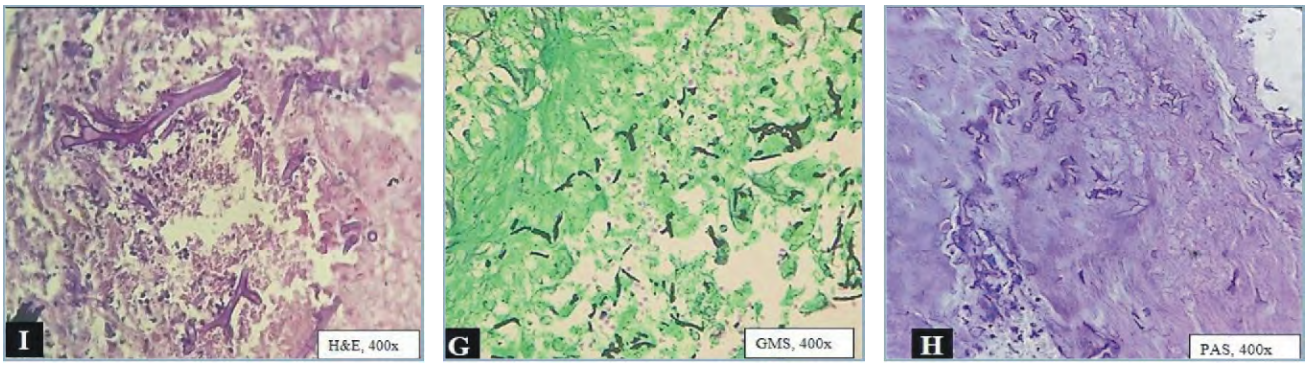
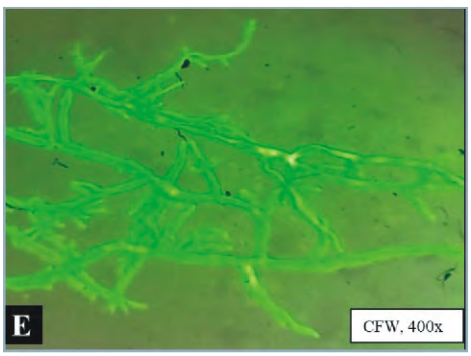


Fig. G, H, I. Broad non-septate fungal hyphae with wide angle branching in tissue sections. (GMS, 400x; H&E, 400x; PAS, 400X).



(E) Broad, ribbon-like, non-septate hyphae with wide angle branching stained with Fluorescent brightener (CFW X 400)

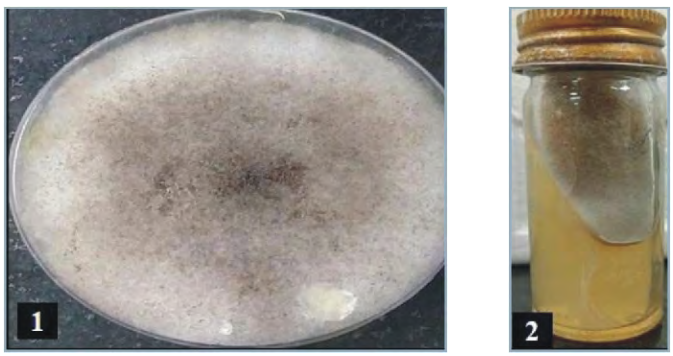
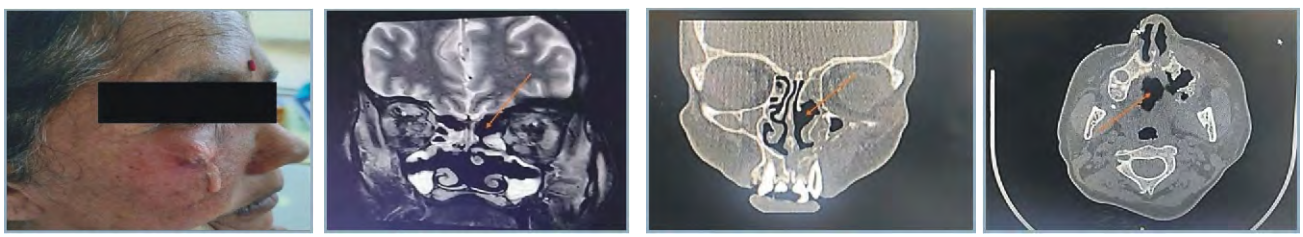


Fig.1&2. Cottony growth on Sabouraud Dextrose agar with Antibiotics which are white at first and then to grey or brown.



Radiological investigations like MRI and CT-scan of nose with paranasal sinuses shows erosion of maxillary sinuses

Conclusion

Patients with poorly controlled diabetes and COVID-19 living in hot climates, which contribute to Mucorales proliferation, are at greater risk of developing Mucormycosis. Despite aggressive medical therapy and surgical interventions, the condition has a high mortality rate and worse outcome. Therefore, identification of risk factors, early detection of the infection, surgical debridement & prompt anti-fungal therapy are mainstay of treatment to this lethal infection.

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CASE REPORT

Eumycetoma Caused by Cladophialophora bantiana: A Rare Clinical Entity

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ABSTRACT :

A 54-year-old farmer presented with painless subcutaneous swelling of the right thigh, multiple draining sinuses discharging black grains, and scarring. Biopsy revealed grains surrounded by a granulomatous reaction with a positive PAS stain, leading to the diagnosis of eumycetoma. Tissue fungal culture identified Cladophialophora bantiana, a dematiaceous fungus, as the causative agent. The patient was successfully treated with Itraconazole.

Keywords : *Eumycetoma, Cladophialophora bantiana, Itraconazole, Fungal infection, Subcutaneous mycosis, PAS*

Introduction

Mycetoma is a chronic, suppurative, and deforming granulomatous disease affecting subcutaneous tissues and bones, characterized by localized swellings with multiple sinuses discharging granules.[1] It is classified into eumycetoma, caused by fungi, and actinomycetoma, caused by bacteria. While eumycetoma is commonly attributed to organisms like Madurella mycetomatis, we present a unique case of eumycetoma caused by Cladophialophora bantiana. Cladophialophora bantiana is a dematiaceous fungus which is commonly seen in cerebral phaeohyphomycosis.[2]

Case Report

A 54-year-old farmer came to dermatology OPD of our hospital, with complaint of painless raised lesions and scarring over right thigh for many months. Approximately one year ago, the patient's health appeared to be normal. However, during this time frame, he began to experience a swelling in his right knee, accompanied by mild, non-progressive pain. After six months had passed, the patient observed a small lesion on his right thigh, which was associated with pus discharge. Subsequently, he developed multiple similar lesions in the surrounding areas. Remarkably, all these lesions healed spontaneously without any medical intervention, leaving behind scars. Additionally, the patient reported a recurrence of lesions in the same scarred areas.

The patient did not report any history of trauma at the site of these lesions and did not mention any lesions elsewhere in his body. Furthermore, the patient denied experiencing chronic cough, evening fever spikes, unexplained weight loss, or having a family history of tuberculosis. He also had no history of alcohol or tobacco use and did not suffer from diabetes or hypertension. Moreover, the patient was not taking any chronic medications.

Upon dermatologial examination a subcutaneous swelling, multiple draining sinuses, discharging black grains, and scarring on the right thigh were observed (Figure 1). Systemic examination was unremarkable, and X-ray of the right knee was normal. For further investigation, 5 mm punch biopsy was taken from the lesions for histopathological examination (HPE) and fungal culture.

The patient samples were placed on Sabaroud's Dextrose agar (SDA) supplemented with chloramphenicol and then incubated in a Biochemical Oxygen Demand (BOD) incubator at 25°C for over one week. The culture media displayed the growth of black, velvety colonies with a dark pigment on the reverse side (Figure 2).

Upon examination of a Lactophenol cotton blue (LPCB) mount, branched, segmented, septate

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hyphae were observed. (Figure 3).

Biopsy material stained with H&E showed grains surrounded by a granulomatous reaction, with a positive PAS stain.

Taking into consideration both the clinical and laboratory findings, we confirmed that the case was indeed eumycotic mycetoma caused by Cladophialophora bantiana.

Following the initiation of treatment with Itraconazole for a period of two months, the patient showed significant improvement. However, regrettably, the patient did not adhere to further follow-up appointments.

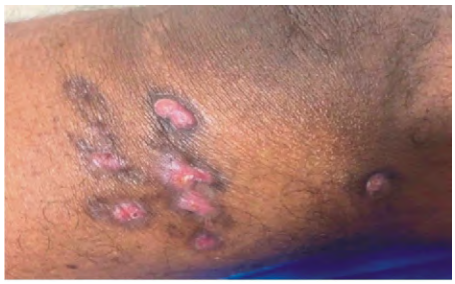

Fig. 1. Right thigh showing subcutaneous swelling with multiple draining sinuses and scarring

Fig. 2. SDA culture medium shows black velvety growth

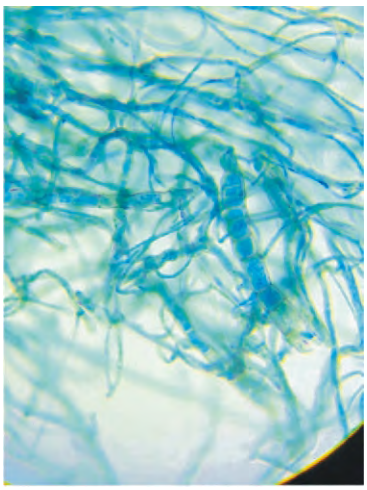

Fig. 3. Lactophenol cotton blue (LPCB) mount

Discussion

Mycetoma, characterized by its chronicity and distinctive clinical features, remains a significant health concern in regions with limited resources, particularly in tropical and subtropical climates. The disease significantly impacts the quality of life of affected individuals, especially those engaged in agricultural activities, who are at a higher risk of exposure to the causative agents.[3] In this context, understanding the diverse range of pathogens responsible for mycetoma, is of paramount importance for accurate diagnosis and effective management.

Mycetoma is a disease that can be induced by both fungi (known as eumycetoma) and bacteria (referred to as actinomycetoma), and it presents with similar clinical characteristics. The ailment is thought to commence following minor injuries that introduce the responsible microorganism into the subcutaneous tissue.[4]

The most common organism of eumycetoma is Madurella mycetomatis. It can also be caused by Madurella grisea, Scedosporium apiospermum, Leptosphaeria senegalensis, Curvularia lunata, Neotestudina rosatii, Acremonium, Fusarium. The prevalence of these species varies depending on geographic location and climatic conditions. M. mycetomatis typically generates black grains and is predominantly found in tropical regions, while S. apiospermum forms white grains and is more commonly observed in temperate regions.[4]

In the early stages, mycetoma may appear as a papule, a nodule, or induration without clear boundary. The lesions eventually rupture into sinus tracts, discharging fluid with grains. This process involves cycles of healing and breakdown, leading to progressive swelling and deformity. Patients might not recall minor traumas triggering these symptoms. The exact incubation period remains unknown, but the time from infection to seeking medical help varies widely, from few months to several decades. Vital structures like tendons and nerves are generally preserved until later stages due to adequate blood supply. Enlarged regional lymph nodes may occur due to secondary infections or immune complex deposition. Patients often delay seeking care until they display the classic triad: a painless subcutaneous mass, multiple sinus tracts, and grain-containing discharge. This delay results from the slow, painless progression of the disease, limited access to health

education, and low socio-economic status.[5]

Histopathologically, eumycetoma is characterized by chronic inflammation, the presence of granulomas aimed at containing the infection, and the formation of neutrophilic abscesses. Additionally, scattered giant cells and fibrosis within the affected tissues reflect the chronic nature of the disease. Grains, a hallmark of eumycetoma, can be visualized through staining techniques such as hematoxylin and eosin (H&E) as well as specialized methods like Periodic-acid-Schiff (PAS) and Grocott-Gomori silver staining. The grains exhibit a distinctive pattern with clusters of branched hyphae arranged radially, occasionally forming vacuoles.[4]

Modern fungal infection diagnostics, rely on molecular techniques like polymerase chain reaction (PCR) and DNA sequencing for swift and accurate species identification. However, these methods should complement rather than replace conventional diagnostics due to non-standardized techniques and cost considerations.

Various imaging methods, such as X-rays, ultrasound, MRI, and CT scans, are employed to assess the extent of lesions.

In our case, the isolation and identification of Cladophialophora bantiana from tissue culture were critical in confirming the causative agent. This dematiaceous fungus, characterized by its dark-walled, septate hyphae, is a rare but emerging pathogen in cases of eumycetoma.

Typically, Cladophialophora bantiana is notorious for its predilection for causing cerebral phaeohyphomycosis, a severe and often fatal central nervous system infection.[6] Its infection outside the central nervous system have been reported sporadically, with a limited number of cases in humans and animals.[7] While central nervous system infections are associated with a grim prognosis, subcutaneous infections, as seen in our case, are generally more amenable to treatment.[8]

Our patient responded well to therapy with Itraconazole, a broad-spectrum antifungal agent commonly used in the treatment of eumycetoma. This favourable outcome is consistent with reports in the literature where patients infected with Cladophialophora bantiana in various clinical scenarios have shown positive responses to antifungal therapy.[9]

Research into the genomics and virulence factors of Cladophialophora bantiana is ongoing and may shed light on the mechanisms underlying its pathogenicity and adaptation in different host environments.[10] This knowledge could potentially inform the development of more targeted therapeutic strategies and enhance our understanding of the interactions between fungi and the host immune response.

Conclusion

This unique case of eumycetoma caused by Cladophialophora bantiana underscores the clinical diversity of fungal infections in endemic regions. Healthcare providers must remain vigilant and consider uncommon etiological agents when diagnosing and managing mycetoma. Early diagnosis and appropriate antifungal therapy are crucial for successful outcomes. Continued research into the genetics and virulence of dematiaceous fungi such as Cladophialophora bantiana holds promise for improved treatment strategies and a deeper understanding of this pathogen.

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CASE REPORT

Oral submucous fibrosis, a premalignant condition, managed with nasolabial flap and buccal fat pad flap-A case report.

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ABSTRACT :

A 45-year-old female presented to ESIC dental college and hospital, Rohini New Delhi with chief complaint of reduced mouth opening and inability to eat food since many years. On examination the patient had mouth opening of 12 mm and fibrous bands were palpable bilaterally extending from canine to retromolar area (more on right side). The findings were consistent with history of tobacco chewing (last 22 years). After investigation and clearance from anesthesia, surgical management was done under general anesthesia. Bilateral fibrotomy, extraction of all 3rd molar, and reconstruction with nasolabial flap and buccal fat pad on right side and buccal fat pad alone was done on left side. Intraoperative maximal mouth opening of 35 mm was achieved. Postoperative physiotherapy was advised to prevent recurrence.

Keywords: *Oral submucous fibrosis; fibrotomy; buccal fat pad; nasolabial flap*

Introduction

Tobacco chewing is common practice in India, which leads to premalignant condition (submucous fibrosis) and consequently malignant condition (oral carcinoma)[1]. Oral submucous fibrosis (OSMF) is chronic condition characterized by limited or nil mouth opening due to progressive stiffening of oral mucosa[2]. Varied treatments are available to manage OSMF. Starting from corticosteroids, hyaluronic acid injection to bilateral fibrotomy, extraction of all 3rd molar, and reconstruction with buccal fat pad and/or nasolabial flap[3]. Postoperative physiotherapy plays a crucial role in preventing relapse and maintaining mouth opening. This case report highlights a report of OSMF managed with surgical approach and importance of postoperative physiotherapy.

Case Presentation

A 45 year old female presented to ESIC dental college and hospital, Rohini New Delhi with chief complaint of reduced mouth opening and inability to eat food since many years. On examination the patient had mouth opening of 12 mm and fibrous bands were palpable bilaterally extending from canine to retromolar area (Fig. 1).

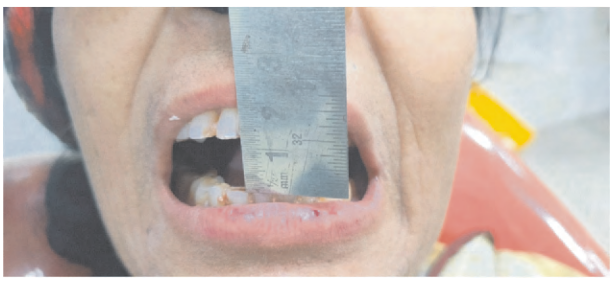

Fig. 1. Preoperative mouth opening of 12 mm.

Blanching of bilateral buccal mucosa was present with no definitive malignant lesion. The patient gave a history of tobacco chewing (almost 22 years). History of tobacco chewing combined with clinical examination indicated a diagnosis of oral submucous fibrosis. Orthopantomogram and all routine examination was done followed by preanesthetic check-up. The patient was planned for bilateral fibrotomy, extraction of all 3rd molars, and reconstruction with buccal fat pad and/or nasolabial flap after taking consent. Intraoperative a maximal incisal opening of 35 mm was achieved after fibrotomy and extraction of 3rd molars (Fig. 2).

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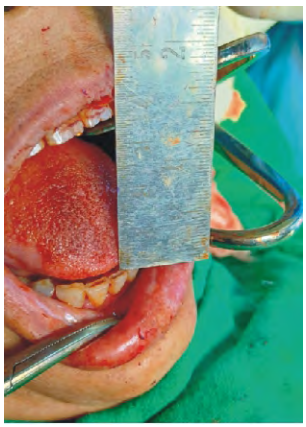

Fig. 2. Intraoperative picture showing maximal incisal opening around 35 mm.

On right side, fibrous bands were present from corner of mouth to retromolar area and reconstruction was done combine buccal fat pad and nasolabial flap (Fig. 3).

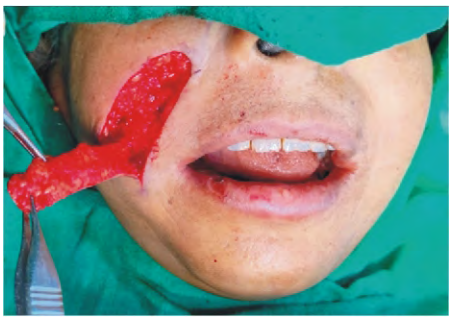

Fig. 3. Harvesting of nasolabial flap on right side.

On left side, fibrotic bands were palpable posterior to canine to retromolar area. Hence, the surgeons were able to reconstruct with buccal fat pad only. Postoperative mouth opening exercise was reinforced. At follow up of 15 days, the patient had a mouth opening of 33 mm.

Discussion

OSMF is a chronic irreversible disease associated with functional morbidity and risk of being transforming to malignancy. The causative factors are varied. Few of them are areca nut chewing, genetic processes, nutritional deficiencies, and immunological process. A long-term study demonstrated that this areca nut chewing is followed by oral submucous fibrosis. The present case had the habit of areca nut chewing along with tobacco since 22 years.

Areca nut chewing suppresses the appetite and considered to have a psycho-stimulating factors. OSMF is a premalignant condition, and an associated finding of oral carcinoma have been observed in 5.2% cases.[4] Paymaster have described an occurrence of carcinoma in one-third cases of OSMF.[5] This mandates the immediate treatment of the condition. In the present case report, the patient was counselled for quitting the habit and motivated about the need of surgical treatment combined with medical therapy (vitamin B, antioxidants, and iron supplements) and most importantly about the need of physiotherapy in postoperative time-period. A satisfactory mouth opening of 35 mm was achieved. The patient was kept on follow up and at the recent follow up maximal mouth opening of 33 mm was observed.

Conclusion

Surgical excision of fibrous band, reconstruction with buccal fat pad or nasolabial flap, if required and physiotherapy in postoperative period is vital in management of oral submucous fibrosis.

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CASE REPORT

Neonatal Alloimmune Thrombocytopenia-A Case Report

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ABSTRACT :

Neonatal alloimmune thrombocytopenia (NAIT) is a disorder linked to maternal antibodies and immune incompatibility between the unborn baby and the mother.

A female baby weighing 2.8 kgs at birth was referred from a district hospital on day 3 of life with presenting complaints of lethargy, not accepting the feeds, bleeding per vagina, and no urination for 24 hours. A provisional diagnosis of neonatal alloimmune thrombocytopenia was made since there was a worsening of platelet count even after transfusion of 2 units of random platelet. The baby was started on intravenous immunoglobulin (IVIG) with a dose of 1gm/Kg for 3 days. The platelet count was repeated after 3 days and had increased to 1.66 lakhs /mL

Administration of compatible platelet transfusion is the treatment of choice in case of severe thrombocytopenia or active bleeding. Random platelets can also be administered to gain time until matched platelets are available. If there is no response to transfusions resulting in persistent thrombocytopenia, IVIG 1.0-2.0g/kg can be administered. In our case, the newborn responded to the IVIG and there was an increase in the platelet count on day 3.

A thrombocytopenic fetus or newborn is at risk of intracranial hemorrhage that may result in lifelong disability or death. Further research is required to define standard treatment protocols and explore new treatment options, such as anti-HPA-1a prophylaxis, anti-neonatal Fc receptor (FcRn), and anti-NK therapies.

Keywords- *neonatal alloimmune thrombocytopenia; Human platelet alloantigens; Pregnancy;*

Introduction-

Antibody-mediated disease arises from incompatibilities between the mother and the unborn child. Maternal antibodies produced in the blood cross the placenta to the baby and cause the lysis of erythrocytes, neutrophils, and platelets. Neonatal alloimmune thrombocytopenia (NAIT) is a disorder linked to maternal antibodies and immune incompatibility between the unborn baby and the mother.[1] NAIT occurs due to the passive transfusion of maternal antibodies that act against fetal platelet alloantigens.[2-4]

Antibody-mediated disease arises from incompatibilities between the mother and the unborn child. Maternal antibodies produced in the blood cross the placenta to the baby and cause the lysis of erythrocytes, neutrophils, and platelets. Neonatal alloimmune thrombocytopenia (NAIT) is a disorder linked to maternal antibodies and immune incompatibility between the unborn baby and the mother.1 NAIT occurs due to the passive transfusion of maternal antibodies that act against fetal platelet alloantigens.[2-4]

Fetal and neonatal alloimmune thrombocytopenia (FNAIT) was first reported in the medical literature in 1953. The antigens, or targets for the immune system on platelet cells, were first described in the 1950s and 1960s. As of 2022, 35 different platelet-specific antigens in FNAIT have been described. FNAIT is the leading cause of severe thrombocytopenia in newborns.[5]Thrombocytopenia is defined as platelet levels below 150,000/uL, with severe thrombocytopenia being less than 50,000/uL. Pathogenesis is typically due to HLA-Ia incompatibility between the mother and fetus. This can occur when a newborn's father is HLA-Ia positive, but the

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mother is not. Maternal anti-HLA-Ia antibodies cross the placenta reaching the fetus, causing a Coombs positive reaction.[5]

Patient information :

A female baby weighing 2.8 kgs at birth was referred from a district hospital on day 3 of life with presenting complaints of lethargy, not accepting the feeds, bleeding per vagina, no urination since 24 hours.

The history revealed that the newborn was a firstborn of non-consanguineous marriage and there is no history of significant antenatal illness. It was a full-term normal delivery with a birth weight of 2.8 kgs On physical examination child was sick-looking and irritable, with no pallor or icterus. Skin showed extensive petechiae and purpura. Capillary filling time was prolonged (>3 seconds)

A provisional diagnosis of sepsis was made, and a sepsis screening was carried out (CBC, CRP, Culture sensitivity) The child was treated with IV fluids and parenteral antibiotics.CBC on the day of admission showed WBC-23,000/mL, hemoglobin 18.6 gm/dl, Platelet count-14,000/mL and the mother's platelet count was normal. The ultrasound abdomen report revealed the presence of retroperitoneal hemorrhage. The neuro sonogram was normal and due to non-availability, fetal sonogram was not done.

Septic screening was negative and hence antibiotics were stopped. A transfusion of random platelets was done because of thrombocytopenia, but the count was reduced to 4000 /mL after an infusion of 2 units. A provisional diagnosis of neonatal alloimmune thrombocytopenia was made since there was a worsening of platelet count. The baby was started on intravenous immunoglobulin (IVIG) with a dose of 1gm/Kg for 3 days. The platelet count was repeated after 3 days and had increased to 1.66 lakhs /mL

The investigations to prove NAIT such a anti HPA antibody of the mother, and HPA genotyping of the father, mother, and newborn have been sent to Pune and the results are awaited.

The child was hemodynamically stable and the skin manifestations had disappeared at the time of discharge. [Fig. 1]

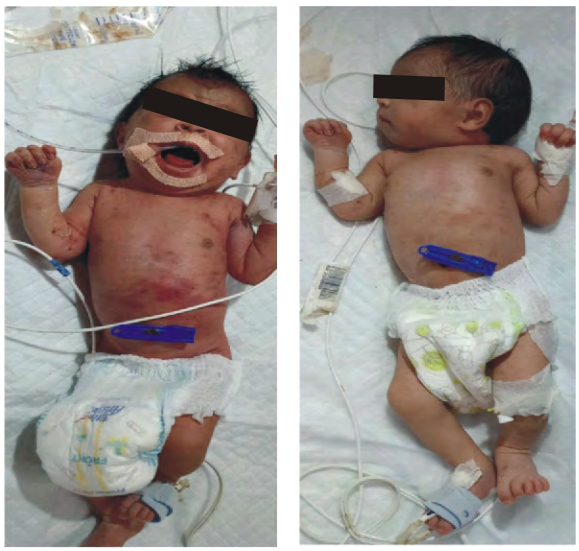

Fig. 1. Newborn baby with NAIT before and after the intervention

Discussion-

NAIT is a rare severe condition and must be suspected if clinical manifestations such as skin or gastrointestinal bleeding or intracranial hemorrhage on ultrasound and severe thrombocytopenia are present.[6] In our case, there were no signs of intracranial hemorrhage.

The difference between autoimmune thrombocytopenia and alloimmune thrombocy-topenia is that the mother's platelet count will be low in autoimmune thrombocytopenia, which was not seen in our case. A severe thrombocytopenia with the presence of retroperitoneal bleeding is seen only in Alloimmune thrombocytopenia.

Administration of compatible platelet transfusion is the treatment of choice in case of severe thrombocytopenia or active bleeding. Random platelets can also be administered to gain time until matched platelets are available. If there is no response to transfusions resulting in persistent thrombocytopenia, IVIG 1.0-2.0g/kg can be administered.[7] In our case, the newborn responded to the IVIG and there was an increase in the platelet count on day. [3]

However, it is currently unclear whether IVIG has equal efficacies for all anti-HPAs or other platelet antigens such as CD36.[8] Further research is required to define standard treatment protocols and explore new treatment options, such as anti-HPA-1a prophylaxis, anti-neonatal Fc receptor (FcRn), and anti-NK therapies.

FNAIT is not routinely screened for during pregnancy and is thought to be underdiagnosed. The

babies are screened for FNAIT when they have older siblings who have had it. In the case of firstborn children with FNAIT, diagnosis is made after the newborn baby has developed widespread skin petechiae and thrombocytopenia.

A screening program to detect pregnancies at risk is not being implemented in any country and the diagnosis is established in the post-natal period when the child is born with symptoms.[9] Life-threatening complications include ICH, IUGR, and neurological sequelae. A thrombocytopenic fetus or newborn is at risk of intracranial hemorrhage that may result in lifelong disability or death.[10] There is a need to implement a screening program for diagnosing FNAIT to prevent the development of life-threatening complications in newborn babies.

Conclusion-

In our case, the newborn showed improvement in the platelet count after the administration of IVIG and random platelet infusion was not useful in improving the count.

Conflict of interest- None

Author contribution- All authors have contributed equally.

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REVIEW ARTICLE

Artificial Intelligence and Machine Learning in Diagnostic Pathology – An Overview

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ABSTRACT :

Artificial intelligence and machine learning (ML) are recently gaining wide importance and acceptance in the field of diagnostics. The introduction of digital pathology has enabled the acquisition of scanned slide images that are essential for the application of AI. The AI is commonly used in screening for dysplasias, diagnosis, grading and prognosis of tumours. Till date predominant work of AI has been done cancers of the cervix, breast, prostate, ovary, brain, and lung and stomach carcinomas. Artificial intelligence assisted methods show promising results in improving the diagnostic accuracy and efficiency, especially in identifying novel biomarkers and predicting treatment outcomes. Several Deep learning techniques are employed like multilayer perception, recurrent neural network and convulsion neural network, which are subsets of Artificial intelligence models and Machine learning techniques. This brief review discusses the advancements in the various sections of Diagnostic Pathology.

Key words: *Artificial intelligence, CellaVision, Deep learning, Spotlearn, Digital Pathology*

Introduction

Artificial intelligence (AI) is the training of the computer in the cognition functions like learning, reasoning, and perception. Artificial intelligence and machine learning (ML) are recently gaining wide importance and acceptance in the field of diagnostics. The applications of AI and ML methods in diagnostic laboratory services are growing day by day. Cancer is the leading cause of death throughout the world. Morbidity and mortality due to cancer can be preventable if diagnosed and treated early. The currently used screening methods are not sensitive enough to detect the cancer in the early stage. Hence AI is a promising tool early detection of cancer. The introduction of digital pathology has enabled the acquisition of scanned slide images that are essential for the application of AI. The first documentation of AI in the cancer screening and diagnosis is way back in 1959 for the cervical cancer screening by pap smear[1,2].

The AI is commonly used in screening for dysplasias, diagnosis, grading and prognosis of tumours. Till date predominant work of AI has been done cancers of the cervix, breast, prostate, ovary, brain, and lung and stomach carcinomas.[2]

In hematology and clinical pathology, morphology is still the accepted mode of diagnosis for initial screening before genetic and molecular confirmatory tests. AI is rapidly evolving field of science that provides us the computational programs and systematic algorithms which mimics human intelligence1.[3] Hematology and cytology diagnostics primarily depend on the cell characteristics, cell size, abnormal hemoglobinisation and intra-nuclear or intracytoplasmic inclusions for the diagnosis of various conditions.

Artificial intelligence assisted methods show promising results in improving the diagnostic accuracy and efficiency, especially in identifying novel biomarkers and predicting treatment outcomes. AI has been in use to detect the various hematological conditions like leukemias, thalassemias based on the customized algorithms since 1994. Machine learning is a subset of artificial intelligence which deals with pattern detection, classification etc. and has major subdivisions like supervised ML, unsupervised ML, and reinforcement ML.[1,3] Deep learning is a type of

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Machine Learning with refers to creating learning models using raw data. Several Deep learning techniques are employed like multilayer perception, recurrent neural network and convulsion neural network. These machine learning techniques, artificial neural networks and multilayer perception techniques are the foundations of all AI systems used in hematology. These models are used for interpretation of blood cell morphology and analysis of peripheral blood smears, bone marrow aspirates, lymph node aspirates etc. which aid the hematologists and cytologists in accurate diagnosis.

1. Histopathology and AI models:

i. Cervical cancer and AI:

Bostrom et al.[3] first utilized the technique for the screening of the cervical cancer, in their study on 1000 pap smears using a cyto-analyser which classified the cells into normal or abnormal based on nuclear size and absorption. The smear is then classified into normal or abnormal depending on the fraction of cells having abnormal characteristics. The result was promising among the screened 1000 smears, 65 per cent of the premenopausal smears and 35 per cent of the post menopause smears were properly identified. Tanka et al.[4] in their study using CYBEST 4 instrument for screening of the pap smears, observed 27.9% of cases of false positive and 2.8% were false negative. Wu M et al.[5] in their study on ovarian tumour classification observed an accuracy of 78.2%, Steiner et al[6] in their study on using deep learning technique documented 91% sensitivity for lymph node metastasis detection in breast cancer patient. However Breen et al[7] on a study on ovarian tumours observed that many models were available for ovarian tumours classification, diagnosis and prognosis but none of the models were satisfactory for implementation. In an another study on endometrial cancer by Erdemoglu et al.[8] using Phyton model observed an accuracy was 0.94 for predicting a precancerous disease. Precision, recall, and F1 scores for the test group were 0.71, 0.50, and 0.59, respectively.

ii. Prostatic cancer grading systems and AI:

With respect to male genital System AI is used for Gleason grading, Aravanti E et al.[9] on automated screening of the Gleason grading observed a kappa value of 0.75% agreement between pathologist and screening model. Chuluunbaatar et al.[10] used the technique of AI in counting the Tumour infiltrating lymphocyte, they observed a sensitivity of 89% and F-score of 0.88 compared to manually annotated TILs.

iii. Gastrointestinal malignancies and detection using AI models:

AI model has been widely applied in the diagnosis and prognostication of the gastric malignancy. A DL algorithm to classify gastric biopsy images into negative for dysplasia, tubular adenoma and carcinoma has the, the sensitivity and specificity for diagnosis were 100% and 97.49%, respectively. Various authors have incorporated the AI technique in the routine screening of the lymph node metastasis they observed that DL model is very effective in diagnosis of the primary gastric malignancy but also helped in predicting the lymph node micro metastasis which was difficult to pick by naked eyes. It was also incorporated in counting of the mitosis in cases of GIST for accurate grading and for analysing the PDL-1 immunoscoring and HER 2 new scoring.[2]

iv. AI in neuropathology:

The use full ness of the AI model was also tested in neuropathological specimens, Ertosun and Rubin in their study on automated screening of the glioma grading using CNN observed, 96%of accuracy for sub typing of the glioma for glioblastoma over the low grade gliomas[11]. In an another study by Chung et al[12] concluded that AI models developed, SVM offered the highest accuracy of 93.5% and attained 86.95% and 99.73% of sensitivity and specificity respectively for the diagnosis of the Glioblastoma.

2. Peripheral blood/Bone marrow analysis

i. Automated cell differentiation using morphology:

Review of peripheral blood smears stained using one of the Romanowsky stains like Leishman stain or Giemsa stain has been the most commonly used simple, reliable diagnostic tool in the field of hematology. For diagnosis of iron deficiency anemia, thalassemia which have similar peripheral smear images, pathologists rely on additional parameters like RDW and certain indices to make a final diagnosis, apart from the confirmatory tests. Similarly, identifications of leukemic blast cells by analyzing the cell morphology and detection of malignant cells in effusion cytology forms the basis of cytological diagnosis.

Certain systems which incorporate AI and ML for diagnostic hematology, include CellaVision and Morphogo, which are approved by the FDA.[13-15]

These are connected to an automated hematology analyzer and a peripheral smear staining unit which capture images and classifies the cells as WBC & RBCs automatically. Numerous images are captured from the barcoded labelled slide with the detection camera attached to the hematology analyzer and representative images on different morphological types of cells are created. According to the authors Lealem Gedefaw et al in their review, CellaVision demonstrated a 100% sensitivity and 94% specificity in identifying atypical cells and for identification of nucleated RBCs.[1]

RBCs are identified and classified based on morphological features like size, pallor, borders and abnormal inclusion bodies. Specific AI programs for identification of sickle cells, stomatocytes, target cells and various other poikilocytes are available and these can identify and classify RBCs in to 21 morphological categories. Customized programs using AI and ML are developed to identify the abnormal cells in low proportions including schistocytes thus reducing the TAT require for manual screening of peripheral smears for making a diagnosis of Microangiopathic hemolytic anemias. Thus, AI in hematology has an undeniable potential in that it reduces the turnaround time and improves the accuracy in the morphological diagnosis of various entities[15,18].

ii. Cell phenotype analysis using digital images:

Scopio and Mantiscope are FDA approved high throughput hematology digital cell morphology platforms, which use advanced computational photography imaging tool with AI support. These can be used to detect abnormalities in RBCs, WBCs, and platelets including platelet clumping[13,16,17].

iii. Immunophenotyping using AI:

Diagnosis of lymphoma is made easier by integrating AI based models in interpreting smears or sections stained with immunohistochemical markers. ImmunoGenius is a ML based mobile application developed to predict various lymphomas, based on the expression profiles of several immunohistochemical markers. This system develops algorithms which help to narrow down the diagnosis of lymphomas[13,15,19].

iv. Abnormal phenotype detection:

Inclusion detection is also possible with AI based image analysis of RBCs and WBCs. Diagnosing conditions like Hb-H inclusion disease, a subtype of Alpha thalassemia is crucial screening test and classically done using staining of cells by supravital stains like Brilliant Cresyl Blue or new methylene blue. This AI based detection enhances the accuracy ad also shortens the TAT for diagnosing these conditions.

3. Genomic testing in Hematology using AI

i. AI in chromosomal abnormality detection:

Cytogenetic karyotyping and Fluorescence in situ hybridization are techniques routinely used for diagnosis of various chromosomal abnormalities in hematological conditions like myeloid leukemias. DNA & RNA FISH detection techniques using AI algorithms like SpotLearn and DeepSpot, respectively, aim to accurately detect the FISH signals.[20] These also are employed for detection of Minimal Residual Disease in patients with multiple myeloma and acute leukemia in cases which are limited by the minimal number of cells required for flow cytometry.

ii. Chromoenhancer model[13,15] is an AI based model used for improving the accuracy and efficiency of diagnosis by cytogenetic karyotyping. In this technique, the images of karyogram taken from a cytogenetics state-of–the-art system are fed into the cycleGAN model and then the enhanced Karyogram images are interpreted, thereby improving the accuracy. The extended applications of AI based models in hematology include its use in enhanced interpretation of Whole genome sequence and Single cell sequence analyses.

Conclusion:

Artificial intelligence has varied applications in diagnostic pathology which has to be explored for enhanced accuracy of diagnosis. By leveraging the power of AI and ML, there can be significant advancements in the various diagnostic fields of Pathology.

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REVIEW ARTICLE

Review of Occupational Diseases, Occupational Safety and Health in India

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Background : Indian scenario and burden

India has a large and diverse workforce of about 500 million people, employed in various sectors such as agriculture, industry, services, and informal economy[1,2]. The majority of workers are in the informal sector, which is characterized by low wages, poor working conditions, lack of social security, and limited access to OHS services.[4] OHS is important for the economic and social development of a country, as it reduces the burden of occupational diseases and injuries, improves productivity and quality of work, and enhances workers' satisfaction and morale.[3]

Occupational health and safety (OHS) is the discipline that deals with the prevention and control of hazards at the workplace, as well as the promotion and protection of workers' health and well-being[1].

The main occupational hazards and diseases in India are related to exposure to vapour, dust, gas and fumes, chemicals, noise, heat, radiation, biological agents, ergonomic factors, psychosocial stress, and accidents. Some of the common occupational diseases are silicosis, asbestosis, byssinosis, coal workers' pneumoconiosis, chronic obstructive lung diseases, noise-induced hearing loss, pesticide poisoning, and musculoskeletal disorders[4,5]. The risk factors which causes most deaths according to WHO

1. long working hours
2. industrial air pollution , gases and fumes
3. injuries

The work related health conditions that cause most deaths according to WHO are

1. COPD
2. Stroke
3. Ischemic heart disease

The world of work and work patterns is changing rapidly. The main features of the future are as follows

1. Fragmented industry (with materials sourced globally)
2. Hybrid working- work and home
3. Smaller work forces
4. More mobile employees such as gig workers
5. Waning influence of organized labour
6. Multiskilled workers
7. Greater use of sub-contracted task
8. Less job stability and security
9. More part-time and more flexible work hours
10. More mechanized (possibly more dehumanized work places)

Therefore, occupational physicians see more of occupation-related illness rather than occupational diseases. Few examples are

1. Stress related disorders
2. Chronic fatigue syndromes
3. Post-traumatic stress disorders
4. Diffuse pain syndromes
5. Chronic somatisation disorders
6. Multiple chemical sensitivity
7. A combination of psychological, neurological and immunological issues.

The legal framework for OHS in India is based on the constitutional provisions, which mandate the state to ensure the welfare and safety of workers, and to enact laws and policies for that purpose. There are several acts and rules that regulate OHS in different sectors and occupations, such as the Factories Act, 1948, the Mines Act, 1952, the Dock Workers (Safety, Health and Welfare) Act, 1986, the Building and Other

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Construction Workers (Regulation of Employment and Conditions of Service) Act, 1996, and the Occupational Safety, Health and Working Conditions Code, 2020.

The implementation and enforcement of OHS laws and standards in India is the responsibility of various central and state agencies, such as the Directorate General of Factory Advice Service and Labour Institutes (DGFASLI), the Directorate General of Mines Safety (DGMS), the Central Labour Commissioner, the State Labour Departments, and the State Factory and Boiler Inspectorates.

Even though there is a political will and a legal framework for occupational health and safety in Indian constitution, there is a need to a constantly re-prioritize different aspects according to the changing scenario.

The challenges and gaps in OHS in India include the low coverage and quality of OHS services, the inadequate infrastructure and manpower, the lack of awareness and compliance among employers and workers, the insufficient data and research, the fragmentation and duplication of OHS legislation and administration, and the emerging issues of new technologies, globalization, and climate change[4].

The opportunities and strategies for improving OHS in India, the strengthening and integration of OHS institutions and systems, the promotion and participation of social dialogue and tripartism, the development and dissemination of OHS information and education, the enhancement and expansion of OHS services and programs, the fostering and support of OHS culture and leadership, and the collaboration and coordination of national and international stakeholders[4].

To conclude, Occupational Safety and Health is not just a legal obligation or a corporate responsibility; it is a moral imperative. We spend a significant portion of our lives at work, and we all deserve to go home safe and healthy. By prioritizing OSH, we not only protect the lives and well-being of our workforce but also enhance productivity and reduce costs for businesses.

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BOOK REVIEW

Current Diagnosis & Treatment: Occupational & Environmental Medicine, 6th Edition (A & Lange series) edited by Joseph LaDou and Robert Harrison.

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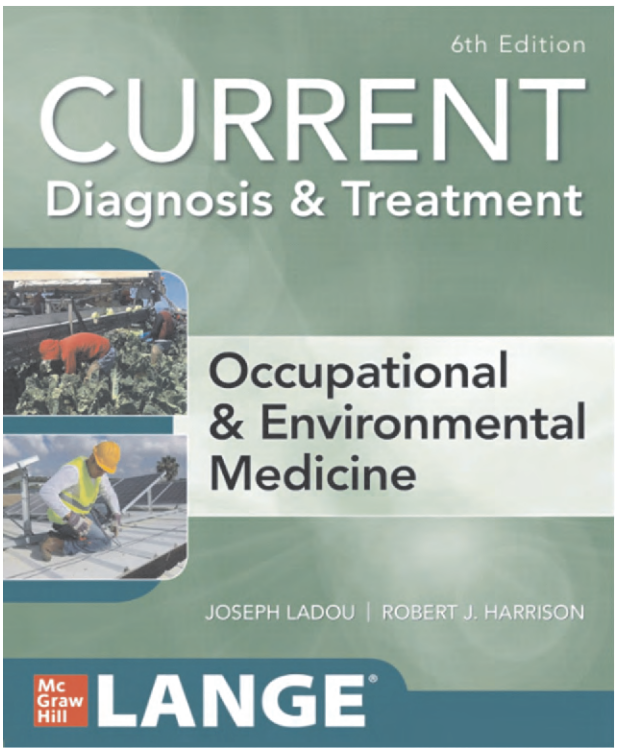

Introduction

Occupational and Environmental health has got a mention in regular medical curriculum but practical exposure on this aspect to majority of medical fraternity is minimal. Medical practitioners, due to less exposure to this aspect sometime mis-diagnose the condition viz. Silicosis lesions as Cured TB with refractory lesions, necessitating need of basic orientation to Occupational and Environmental Health. Sixth edition of Current Diagnosis & Treatment: Occupational & Environmental Medicine serves as a comprehensive and concise guide on orientation to this aspect of medical science. in the field. The book aims to provide a practical and evidence-based approach to the diagnosis, treatment, and prevention of occupational and environmental injuries and illnesses, as well as to address the ethical, legal, and social aspects of occupational health and safety practice.

Summary

The book is divided into six section named Occupational Health, Occupational Injuries, Occupational Illnesses, Occupational and Environmental Exposures, Program Management and Environmental Health. Aspects of Biostatistics & Epidemiology are covered as a separate annexure. The sections are curated in a way to cater to need of the medical practitioner in a desired context of Human body or Industrial relevance or Environmental exposure. The topics comprehensively covers the epidemiology, pathophysiology, diagnosis, treatment, and prevention of various occupational and environmental diseases and disorders in the context of practice of Occupational and environmental medicine.

Each chapter provides an up-to-date overview of the main topics and issues, with a focus on clinical management, toxicology and prevention. It can be used as a text-book for toxic properties and clinical manifestations of industrial materials and environmental agents, such as metals, solvents, pesticides, radiation, and air pollutants, and provides guidance on the assessment and management of acute and chronic poisoning cases.

The book addresses the special needs and challenges of occupational and environmental health in different populations and settings, such as children, women, older workers, migrant workers, health care workers, and disaster responders, and provides recommendations on the design and implementation of occupational and environmental health programs and policies. The authors have explored the emerging topics and challenges in the field, such as the impact of climate change, the changing nature of work, the concept of total worker health, workplace violence, genetic toxicology, and responder safety and health, and highlights the current research and best practices in these areas.

The Sixth edition cover the Occupational and Environmental health in broader context by including

- New chapters on the impact of climate change on workers, the changing nature of work, Total Worker Health, workplace violence, pediatric environmental health, genetic toxicology and responder safety and health
- Latest approaches to prevent workplace-related injuries through the application of ergonomic principles
- Updated practical information on the toxic properties and clinical manifestations of industrial materials and environmental agents.
- Making it a ready reference guide for medical practitioner in field of updated information on the subject.

The specific references provided at end of each chapter area smooth sail for those who wish to explore more in this field. Each chapter concludes with self-assessment questions that summarily recapitulate the in-text material before moving to next section or chapter. The illustrations, diagram and pictures are more vivid making it a handy book to carry with.

Evaluation

The book is a valuable and authoritative ready reference guide not only for the Occupational Health Practitioner or factory Medical Officers but also serves as a good companion to medical practitioner providing specific information guiding them to the more accurate diagnosis incorporation the occupational aspect in details. It offers a comprehensive and updated coverage of the field, with a clear and concise presentation of the relevant information and evidence. The book is well-written and well-organized, with a logical and consistent structure, and a user-friendly format, featuring tables, figures, algorithms, case studies, key points, and references in each chapter, as well as appendices, glossary, and index at the end of the book. The book is well-referenced and well-supported, with a balanced and critical review of the literature, and a careful and rigorous use of sources and methods, reflecting the authors' expertise and experience in the field.

I find this book to be relevant and significant, as it provides practical and evidence-based guidance and recommendations for the health care professional and the occupational health and safety practitioner. The book the latest research and best practices in the field, and introduces new concepts and perspectives, such as the impact of climate change, the changing nature of work, the concept of total worker health, and the genetic toxicology of occupational and environmental exposures. However, the concepts provided in this book have to be adapted to occupational health practise in Indian settings. Ethical and legal issues have to be specifically understood in the Indian scenario.

Conclusion

The book is an excellent and comprehensive guide to multidisciplinary approach in Occupational and Environmental medicine. I find this book to be suitable for health care professionals of various specialties and levels of expertise, as well as for students, researchers, policy makers, and employers who are interested in occupational and environmental health issues.

Dr. Anjani Kumar has more than 20 years of experience in this field and has been associated with various industries before joining in his present position. He is also training head for Associate Fellow Of Industrial Health (AFIH) in RLI, Chennai, for 8 years.

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LETTER TO EDITOR

Unravelling the Significance of POU2F3 (OCT-11) Immunohistochemical Marker in Pathology

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In the realm of pathology, the quest for precise diagnostic tools is ceaseless. Among the array of techniques available, immunohistochemistry (IHC) stands out as a vital method for detecting specific proteins in tissue samples. Within this landscape, the POU2F3 immunohistochemical marker has emerged as a notable marker, offering insights into various pathological conditions.[1]

POU2F3, also known as Skn-1a or Oct-111, belongs to the POU domain family of transcription factors. It is required for the generation of a rare chemosensory cell type. These cells are known by a variety of names such as tuft, brush, microvillous, caveolated, or multivesicular cells, generally called as "tuft cells." Tuft cells, like neuroendocrine cells, respond to external stimuli by releasing bioactive chemicals that modulate local epithelial and immune cell functions. Tuft cells are not the same as neuroendocrine cells, despite having comparable activities and locations. These cells are found in various organ systems, including tongue, taste buds, intestinal epithelium, skin, pancreas, and bronchial epithelium.[2]

IHC staining for POU2F3 follows standard protocols, involving the use of specific antibodies targeting the protein of interest. Tissue sections are incubated with the primary antibody, followed by secondary antibody incubation and visualization using chromogenic or fluorescent detection systems. Interpretation of staining patterns involves assessing the intensity and distribution of POU2F3 expression within the tissue sample, often in comparison to normal tissue controls. It is expressed in the nucleus of the cells.[2]

In pathological conditions, alterations in POU2F3 expression have been observed, providing valuable diagnostic and prognostic information. Here are some key areas where POU2F3 IHC staining proves significant.

In respiratory tract malignancies, amongst small cell lung carcinomas (SCLC) when all the other conventional neuroendocrine markers were not expressed, POU2F3 was found to be positive, this subtype is called as tuft cell like variant of SCLC and is found to have worse prognosis.[1] POU2F3 can be used to differentiate thymic squamous cell carcinoma from thymoma and in subtyping thymoma.[3] POU2F3 expression patterns can aid in the diagnosis and classification of various skin disorders, including squamous cell carcinomas, basal cell carcinomas, and melanomas. Differential expression levels of POU2F3 have been identified in different stages of skin cancer progression, offering insights into disease aggressiveness and prognosis.[4] POU2F3 immunohistochemistry is utilized in the evaluation of gastrointestinal tumours, particularly in distinguishing between different types of colorectal carcinomas. Its expression profile can aid pathologists in assessing tumour differentiation and predicting patient prognosis in colorectal cancer cases.[5]

As research in molecular pathology continues to advance, the role of POU2F3 as an immunohisto chemical marker is likely to evolve further. Ongoing investigations aim to elucidate its molecular interactions and downstream signalling pathways, paving the way for the development of targeted therapies and personalized treatment strategies.[2]

In conclusion, POU2F3 immunohistochemistry holds promise as a valuable tool in the diagnostic armamentarium of pathologists. Its ability to discern subtle changes in protein expression patterns offers a deeper understanding of various pathological conditions, ultimately contributing to more accurate diagnoses and improved patient care.

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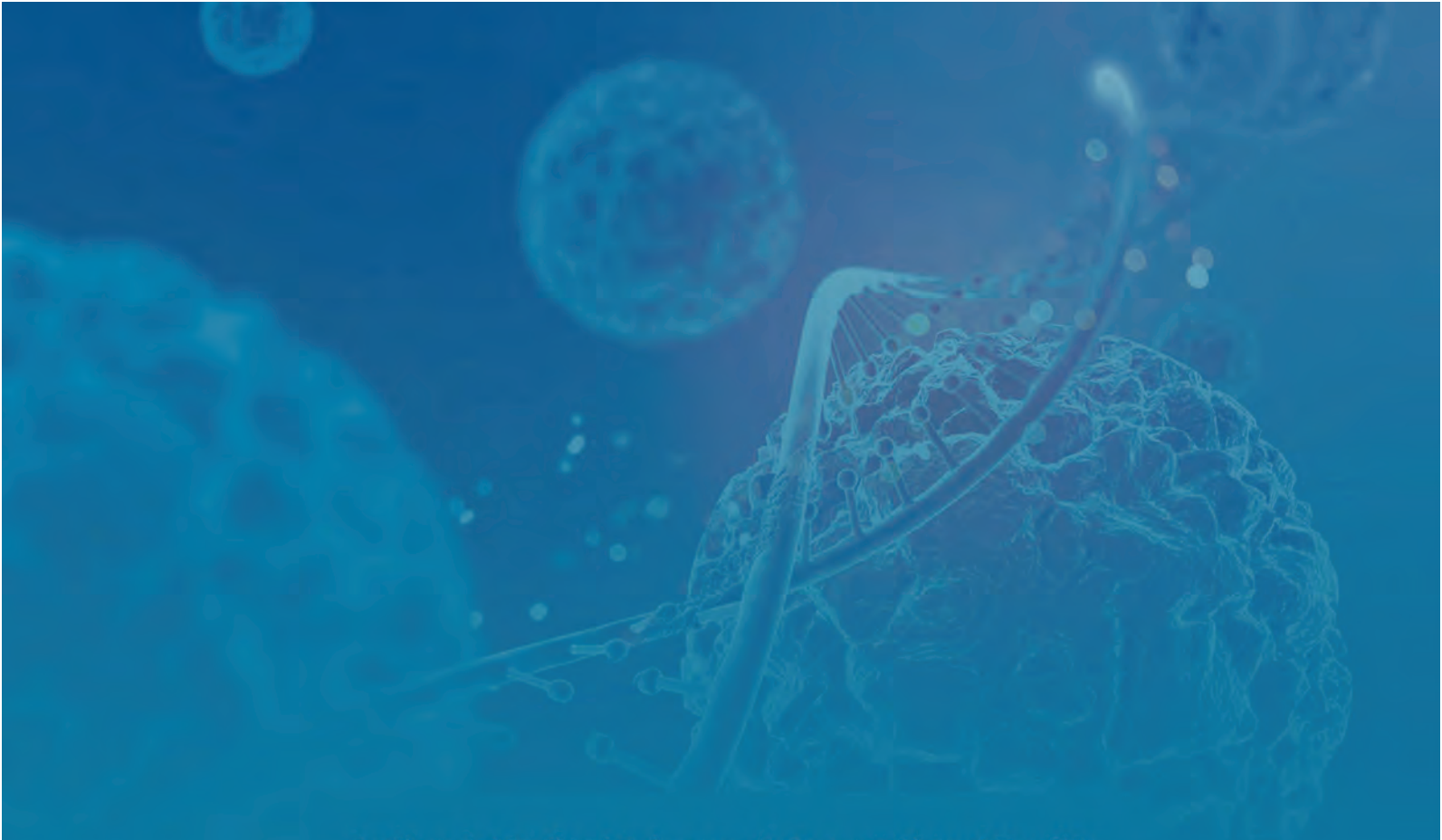

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