



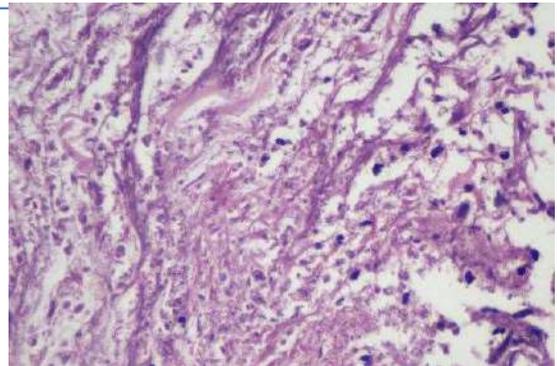
National Board of Examination (NBE) Journal of Medical Sciences

NBEJMS

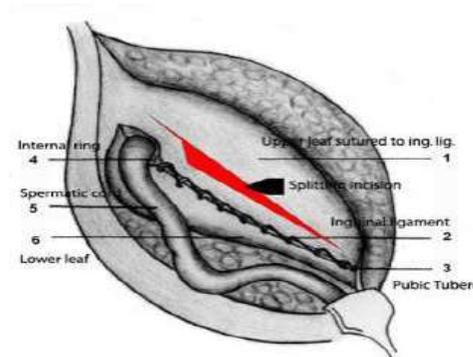
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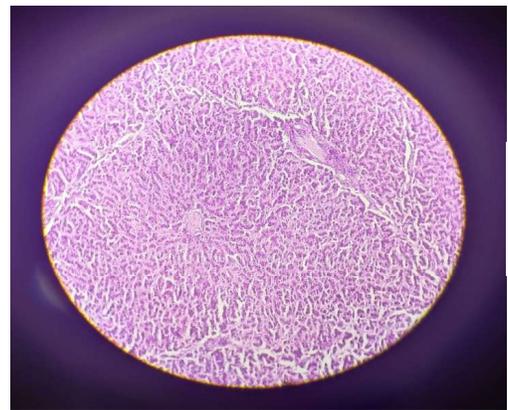
Image showing tip of drainage catheter



Muscle tissue with necrotising inflammation (H&E 40X)



The medial leaf of the external oblique aponeurosis is sutured to the inguinal ligament and a splitting incision is taken



Histopathological examination of liver (Photomicrograph)

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S

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**NATIONAL BOARD OF EXAMINATIONS –
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EDITORIAL

National Board of Examination–Journal of Medical Sciences (NBEJMS): Completing One Year of Consistent Publication & Marching Ahead

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The National Board of Examination in Medical Sciences (NBEMS) launched its Medical Journal entitled ‘National Board of Examinations–Journal of Medical Sciences’ (NBEJMS) on January 1st, 2023 and has been consistently publishing issues from January 2023 to December 2023 of volume 1.

The Journal has already achieved indexing by the **Directory of Open Access Journals (DOAJ)**. DOAJ is a unique and extensive index of diverse open access journals from around the world, driven by a growing community, committed to ensuring quality content is freely available online for everyone.

The NBEJMS also has received an **ISSN Number (2583–7524)**. The International Standard Serial Number (ISSN) is a unique identifier assigned to a periodical publication, such as a journal, to distinguish it from other publications.

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For permanent identification and citation accuracy the NBEJMS now has its own **Digital Object Identifier (DOI) Number**, separately for each article. The DOI is a unique alphanumeric string assigned to a document, such as an academic article, providing a permanent link to it.

The NBEJMS is online journal with free to read and download. Online free medical journals play a vital role in democratizing access to medical knowledge, fostering global collaboration, advancing medical science, and improving healthcare education and patient care.

Spreading awareness about NBEJMS, among the medical institutions and hospitals, which is essential for promoting equity in access to medical knowledge, fostering collaboration, supporting continuous learning, and ultimately contributing to advancements in healthcare on a global scale.

The NBEJMS will be instrumental in spreading awareness about reforms undertaken by NBEMS and the Government of India by providing a platform to disseminate information about the reforms, policy changes and updates to keep medical professionals, institutions and hospitals informed about the latest developments in medical science and healthcare sector.

Access to information through NBEJMS empowers healthcare professionals, administrators, policymakers, and the public to actively engage in discussions about healthcare reforms. Informed stakeholders are better equipped to contribute to the success of these reforms.

We would now be publishing special supplements in different super-specialties of medical sciences with the collaboration of different medical institutions under the aegis of NBEJMS, such as:

- Recent Advances in **Gastroenterology**
- Recent Advances in **Endocrinology**
- Recent Advances in **Nephrology**
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- Recent Advances in **Trauma**
- Recent Advances in **Anatomy**
- Recent Advances in **Medicine etc.**

We believe that, this approach can contribute significantly to the dissemination of cutting-edge research and advancements in various medical fields.

The NBEJMS will provide Guest-Editorship to Leaders in different super-specialties, thus, leveraging the expertise of renowned professionals. Such a collaboration would enhance the credibility and quality of the published content. Special supplements focused on recent advances provide a platform to share valuable insights and discoveries within specific medical fields. Eventually, this

would contribute to the dissemination of knowledge and in promoting awareness in the latest developments.

Collaboration with different medical institutions fosters networking opportunities. Building relationships with leaders in different super-specialties can lead to future alliances, research partnerships, and shared resources. Special supplements with contributions from esteemed professionals and institutions can elevate the visibility of NBEJMS. This can attract a wider audience, including researchers, practitioners, and students interested in specific medical specialties.

By covering a range of super-specialties, NBEJMS becomes a comprehensive resource for professionals across the medical spectrum. This diversity appeals to a broad readership and ensures relevance to various disciplines. Special supplements can serve as educational tools for medical professionals, students, and researchers. They provide in-depth insights into recent advances, best practices, and emerging trends in specific super-specialties.



ORIGINAL ARTICLE

Chronotype: Its effect on cognitive flexibility among medical students with Internet Gaming Disorder: A cross-sectional study

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Abstract

Introduction: The role of technology is intended to aid rather than distract. Gaming Addiction has been recognized by the World Health Organization (WHO) as a disorder in the ICD11, diagnosed when behavior significantly impairs crucial aspects of life for at least 12 months. Notably, the use of technological devices, particularly smartphones and computer screens, affects the endogenous circadian clock or chronotype. Chronotype classifies individuals into three groups: early, intermediate, and late types, each with distinct sleep patterns and preferences. Cognitive flexibility involves suppressing interference from automated tasks, a skill evaluated through the Stroop effect in task-switching designs.

Methodology: A quantitative cross-sectional survey was conducted over a 2-month duration on undergraduate students in a southern Indian medical college. Using convenient sampling, 600 Internet Gaming Disorder (IGD) Short Form questionnaires were distributed, achieving an 81.5% response rate across all three student phases. Google play store-based app 'App Usage Tracker (AUT)' was used to assess the amount of time spent by the individual on each application. Chronotype of medical students was assessed using, Morningness and Eveningness questionnaire (MEQ). Cognitive flexibility was measured using a) Stroop Colour and Word Test and b) Trail Making Test (TMT). **Results:** Among 489 participants, the prevalence of IGD was 4.9%, with 24 individuals meeting the IGD9-SF endorsement criterion. Subsequent assessments for chronotype and cognitive flexibility in IGD students showed no significant association with Chronotypes. Higher IGD scores correlated with elevated TMT (B-A) scores, indicating reduced task-switching ability. More hours spent on gaming correlated with higher IGD scores, while productive online hours exhibited a negative correlation.

Keywords: Chronotype, Cognition, Gaming addiction, smartphone addiction

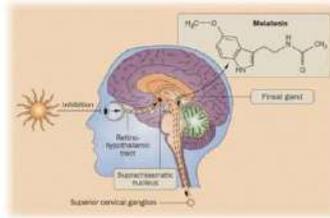
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Graphical Abstract

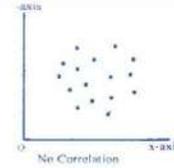


Internet Gaming disorder (IGD) among young adults



Chronotype

Chronotype- No correlation



4.9% prevalence of IGD in our study



Cognitive flexibility



Cognitive flexibility reduces

Introduction

The role of technology should be that of an aid, not a distraction. Unfortunately, people worldwide are increasingly being drawn away from their real-life responsibilities by the allure of mobile phones. The global escalation of nomophobia, or the fear of being without a mobile phone, serves as a testament to this phenomenon. Recognizing the potential harm associated with technology-related behaviors, the World Health Organization (WHO) has classified Gaming Addiction as a disorder in the ICD11. This disorder is diagnosed when the behavioral pattern results in significant impairment in personal, family, social, educational, occupational, or other essential areas of functioning, persisting for a minimum of 12 months [1]. A study conducted in South India revealed a prevalence of 4.25% of Internet Gaming Disorder (IGD) among medical students [2].

The impact of different technological devices, especially smartphones and computer screens, has been found to influence the endogenous circadian clock, known as chronotype [3]. Chronotype categorizes individuals into three groups: early-type or morning types, who wake up early but feel fatigued in the early evening; intermediate types, who fall between early and late types in terms of waking and sleeping patterns; and late-type or evening types, who stay up late at night and wake up late the next day.

Cognitive flexibility refers to the ability to suppress cognitive interference that arises from automated tasks when individuals are required to engage in novel or less automated tasks. This challenge in inhibiting the more automated process is commonly referred to as the Stroop effect, often assessed through a task-switching design [4]. Individuals with IGD tend to exhibit impaired cognitive flexibility compared to healthy controls [5]. This

cognitive skill is a fundamental aspect of executive function, reflecting an individual's capacity to swiftly transition between tasks. Moreover, cognitive flexibility influences academic achievement, cognitive abilities, and creativity in learners. In the context of IGD, gamers need to swiftly shift between tasks during gameplay.

Research on chronotype assessment has suggested that individuals with an evening-type preference are more susceptible to Internet Gaming Disorder (IGD) [6]. Among medical students, those who are active during phases that are either out-of-phase or in-phase with their circadian rhythm types (or chronotypes) may potentially impact cognition. In the context of circadian rhythms, being "in-phase" refers to being aligned with the typical 24-hour cycle, while being "out-of-phase" indicates a misalignment or deviation from this standard cycle. Comparatively, late chronotypes exhibit notably higher daytime sleepiness in contrast to early chronotypes and tend to perform less effectively in the morning across various cognitive and physical measures [7]. Neurobehavioral deficits, such as decreased alertness and an increase in unintentional sleep episodes due to disruptions in the circadian rhythm, are more pronounced in younger participants as opposed to older adults [8]. Although some studies have failed to establish a correlation between chronotype and academic performance [9], it remains an area of ongoing investigation.

Studies exploring cognitive flexibility have indicated that prolonged gaming can enhance brain synchronization in regions related to sensory-motor coordination and visual-spatial processing. However, several other studies have

highlighted impaired executive functions among individuals with internet addiction. Considering the contradictory findings, the assessment of cognitive flexibility among individuals with IGD was deemed necessary.

Despite existing research on internet addiction among medical students, there is a notable lack of literature specifically addressing the prevalence of IGD and chronotype within this population. This study aims to investigate the impact of chronotype on cognitive flexibility among medical students affected by IGD. Notably, based on our thorough literature search in PUBMED and Google Scholar up until February 2022, we found no published data from India that evaluated the relationship between IGD, chronotype, and cognitive flexibility in medical students. Hence, this novel study was initiated as a pilot project.

Aims & Objectives

To determine the prevalence of IGD among medical students

To correlate Chronotype and its association with IGD score

To correlate between Cognitive flexibility and IGD score

Materials & methods

The present research is a quantitative cross-sectional survey conducted at a medical college in southern India, targeting undergraduate medical students over a period of 2 months from July 2022 to September 2022.

The study was commenced after obtaining the Scientific Research Committee & Institutional Ethics Committee clearance. After explaining the purpose of the study, informed written consent was taken from all the subjects. Six hundred paper-and-pencil questionnaires of

Internet Gaming Disorder Scale 9– Short-Form (IGDS9-SF) were distributed in class using convenient sampling and data was collected from all three phases of students (MBBS phase I, II, III Part 1 & 2) within the same day. In (IGDS9-SF), out of 9 criterions, if 5 criterions are answered as very often (which is considered as endorsement of criterion), the participant was considered as disordered gamer. The overall response rate was 81.5%.

Internet Gaming Disorder Scale – Short-Form (IGDS9-SF) was used to assess the severity of IGD as proposed by the American Psychiatric Association in the latest edition of the diagnostic and statistical manual of mental disorders (DSM-5). It is a 9-item scale which assess the gaming activity in the past 12 months. Each item is scored from 1 to 5, higher scores indicating greater severity. Scores are summed to determine a total score, which ranges from 9 to 45, with higher scores indicating of higher degrees of gaming disorder. The participant is considered as disordered gamer, If he answers five out of nine criterions as very often (which is considered as endorsement of criterion) [10]. Its reliability and validity have been verified in Indian population. It assesses the degree of severity of IGD and its detrimental effects by accounting for both online and offline gaming activities. Higher scores were associated with greater severity of IGD (includes both online and offline gaming) among study participants.

In our institute 24 undergraduate student across all phases of MBBS were categorized as having Gaming disorder. All the students with IGD were included for the next part of the study. Participants with a history of any neuropsychiatric disorder or on medications for the same were excluded. Participant using an Android operating

system-based smartphone were asked to download Google play store-based free app “App Usage Tracker©” to objectively measure the average amount of time spent in gaming per week.

“App Usage Tracker©” is installed from Google play store

Google play store-based app ‘App Usage Tracker (AUT)’ was used to assess the amount of time spent by the individual on each application. Smartphone user can track the duration in minutes spent on all the apps by him/her. The app displays the duration of usage in minutes and seconds. AUT does not track any personal communications. The smart phone app does not store confidential data of users. Participants were shown the working of the app and were assured that their data would not be deleted or shared. Participants were advised to continue using their smartphone in a regular manner and were advised to follow-up after 7 days. During follow-up, readings from the “*App Usage Tracker©*” was recorded. Participants were then advised to uninstall the tracker app if they wished. For ease of analysis, the data obtained from AUT was categorized into number of hours per week spent on Gaming, Social networking and Productivity time. No monetary or special benefits was received from the smart phone app [11].

Chronotype was measured for all the 24 students with IGD using Morningness and Eveningness-Questionnaire (MEQ)

Chronotype of medical students was assessed using, Morningness and Eveningness questionnaire (MEQ) which is developed by James A. Horne and Olov Ostberg [12]. Institutional pre-validation was carried out before the administration of

MEQ. MEQ is a 19-item questionnaire with four to five options against each question and with specific score for each option and these scores are from zero to six. It evaluates individual's sleep pattern over the last month. Students should mark only one suitable option for each question. The total score on the overall MEQ items ranges between 16 and 86. Based on the total score, individuals can be divided into three behavioral categories: Evening-types (score = 16–41), intermediatetypes (score = 42–58) and morning-types (score = 59–86).

The Stroop colour and word test

This test consists of three cards (Card W, Card C, Card CW), with one

hundred stimuli in each card. In card W, stimuli are the written names of four colours (red, blue, green, yellow). The subject reads the word loudly. Card C shows coloured squares (red, blue, green, yellow) and the subject is asked to name the colours of the squares. Cards CW display words referring to the names of the above colours, printed in a conflicting ink colour. The number of correct responses in the fixed time of 45s is recorded. The correct answers achieved in the first 45s for each table, generating three scores, namely word items (W), color items (C), and color word items (CW) (Figure 1) [4].

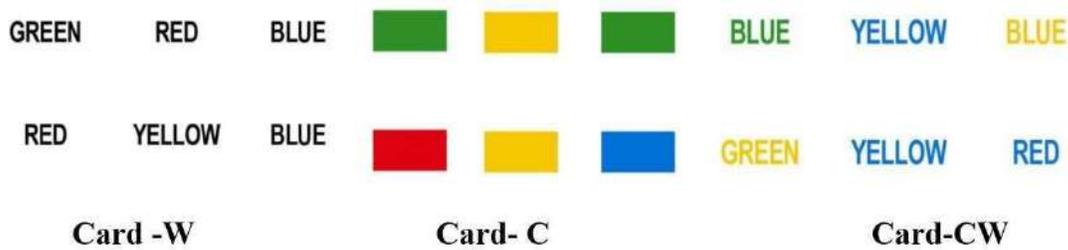


Figure 1. Cognitive flexibility was measured for all the 24 students with IGD using a) Stroop Colour and Word Test and b) Trail Making Test

Trail Making Test (TMT)

TMT assesses visual scanning, numeric and alphabetic sequencing, motor speed, and cognitive flexibility. TMT consists of two parts. In TMT-A subject has to draw lines connecting 25 encircled numbers sequentially which are randomly distributed on a sheet of paper as fast as possible. Similarly in TMT-B, the subject has to connect numbers and letters instead (e.g., 1, A, 2, B, 3, C) and it evaluates mental flexibility. Demonstration of the test to the participant was done using the sample

sheet (Trail Making Part A& B) before the start of test proper. The score on each part represents the amount of time required to complete the task. Time taken by the participant on each test without lifting up pen or pencil in ascending order was noted. If he/she made an error, mistakes were pointed out and asked them correct it. Time to correct mistake was also included in completion time for task. Time was limited to 480 s in this study. Trail making test B-A score is considered as a better indicator of task switching ability [13].

Results

Out of the 600 students approached, 489 provided responses to the IGD9-SF questionnaire. Among the respondents, 223 (45.60%) were male and 266 (54.39%) were female, resulting in an overall

response rate of 81.5%. The prevalence of IGD was 4.9% (24 participants), with 20 males (83.3%) and 4 females (16.6%) meeting the IGD9-SF criteria, as outlined in Tables 1-4.

Table 1: General characteristics of participants

	IGD (n=24)	No IGD(n=465)
Prevalence	4.9%	95.9%
IGD score	40.38±1.28	13.29±4.77
Gender		
Male	83.3% (n=20)	43.6% (n=203)
Female	16.6% (n=4)	56.3% (n=262)
Age	20.2±1.84	20.14±2.46
Nature of stay		
Hosteller	62.5% (n=15)	13%(n=61)
Days scholar	37.5% (n=9)	86.88% (n=404)

All data are represented as mean ±SD, Frequency is expressed in percentage %, IGD- Internet Gaming Disorder

Table 2: Association of various types of chronotype with IGD score:

Variable (Type of Chronotype)	r value	F	P
Evening type(E) (n=13)	-0.4779	3.256	0.0986
Morning type (M) (n=3)	-0.5000	0.3333	0.6667
Intermediate type (I) (n=8)	-0.6255	3.857	0.0972

No statistically significant difference was noted between IGD score among different Chronotype individuals

Table 3: Correlation of Cognitive flexibility test score with IGD score

Variables	Mean \pm SD	r	F	P value
TMT-A	30.04 \pm 5.97	- 0.1234	0.3404	0.5655
TMT-B	68.04 \pm 12.90	0.0228	0.0114	0.9159
TMT(B-A)	38 \pm 9.95	0.1036	0.2388	0.6299
Stroop color task (W) @ 45secs	84.95 \pm 5.87	0.1871	0.7979	0.3814
Stroop color task (C) @ 45secs	73.66 \pm 9.35	0.0437	0.0421	0.8393
Stroop color task (CW) @ 45secs	44.62 \pm 8.90	0.1100	0.2692	0.6090
All data are represented as mean \pm SD, TMT – Trail Making Test, W- Word, C – Color, CW- Color Word				

A Pearson correlation coefficient was computed to assess the linear relationship between Trail Making Test scores, Stroop colour task scores with IGD score. Negative correlation was found ((r- 0.1234) between TMT – A and IGD score but the difference was not significant p -value 0.6299.

Table 4: Correlation between the number of hours spent per week and IGD score

	IGD (n=24)	r value
Game time (hrs/week)	34.43 \pm 11.48	0.0258*
Social networking time(hrs/week)	40.42 \pm 13.78	-0.0699
Productivity time (hrs/week)	14.67 \pm 5.14	-0.0452

All data are represented as mean \pm SD, *P- value <0.05 was considered significant, IGD- Internet Gaming Disorder

Discussion

The main objective of this research was to examine the frequency of Internet gaming disorder (IGD) and its connection to chronotype and cognitive flexibility, measured using Stroop color task and TMT (Trail Making Test) scores among undergraduate medical students. Our study revealed a 4.9% prevalence of IGD (24 out of 489) among medical students as

displayed in Table 1. No significant association was observed between the IGD score and various chronotypes, nor was there any connection between the IGD score and cognitive flexibility.

Numerous studies have examined the occurrence of IGD in various groups. In our research, the prevalence of IGD among medical students was 4.9% (24 out of 489), In a study by Swarndeeep Singh et al., the

prevalence of IGD was 3.6% among medical students [14]. Similarly, another study demonstrated a prevalence of 4.25% in a south Indian medical college [2]. These findings are consistent with a recent meta-analysis that reported the prevalence of IGD in India to be between 2.7% and 5.5% [15]. Notably, a study conducted in north India among medical and dental students revealed a prevalence of 9%, with a higher prevalence among males, despite the greater number of female participants [16]. In our study, IGD was found to be more prevalent in males than in females. The combined prevalence of IGD among medical students from different countries was 6.2%, approximately double the prevalence in the general population [15].

In our research, the male population constituted 83.3%, indicating a notably high prevalence of IGD among males. Research has elucidated the variance in internet addiction rates between genders by emphasizing that males are inclined towards gaming [15], while females tend to favor the use of social networking sites. The meta-regression analysis indicated that the male gender was not a substantial moderator and did not explain the considerable heterogeneity in the combined prevalence of IGD [15]. The diverse cultural roles and expectations for males and females are evident in the content of video games, which are primarily tailored for males in the form of action games, while female participants often lean towards simulation games [17].

In our investigation, no correlation was identified between the IGD score and individuals of different Chronotypes. Among the IGD subjects, the distribution of Chronotypes was as follows: Evening type (n=13 out of 24), Intermediate type (n=8), and Morning type (n=3) as shown in Table

2. Several studies have reported an association between evening Chronotype and internet addiction, along with other addictive behaviors [18,19]. As part of an individual's personality, preferences for morningness-eveningness differ. Previous research has extensively explored the relationship between Chronotype and internet addiction. However, the association of IGD, a subtype of internet addiction, with Chronotype, has not been thoroughly examined. In this study, the lack of a significant association may be attributed to the limited sample size of IGD.

The cognitive flexibility of individuals is evaluated through the Trail Making Test and Stroop color task. TMT-A primarily assesses visuo-perceptual abilities, while TMT-B primarily reflects working memory and, to a lesser extent, task-switching ability. On the other hand, B-A minimizes the demands on visuo-perceptual and working memory, serving as a relatively pure indicator of executive control abilities and task-switching ability [20]. In our study, a positive correlation was observed between TMT-B, TMT B-A scores, and Stroop color task scores, except for TMT-A. Additionally, a higher IGD score was positively associated with higher TMT (B-A) test scores, as demonstrated in Table 3. The increasing TMT B-A score with a rise in the IGD score suggests reduced task-switching ability among IGD subjects. These findings align with other studies that indicate the frequent Internet Gamer group shows improved multitasking efficiency when assessed using a more natural task but not when evaluated using a conventional laboratory multitasking task [21].

In our research, a positive correlation was observed between the weekly hours spent using smart phones for

gaming and the IGD score, indicating a higher likelihood of Internet gaming disorder among individuals who dedicate more time to online gaming compared to social networking, as depicted in Table 4. Conversely, the number of hours spent online on productive activities per week exhibited a negative correlation with the IGD score, suggesting the detrimental impact of excessive gaming on academic performance.

The prevalence of IGD among medical students corresponded to that observed in young adults. Consequently, based on the prevalence results in the medical student population, counselling sessions were administered by a psychiatrist. Students with IGD were advised on various available cognitive-behavioural treatment strategies, such as implementing new schedules to disrupt internet usage patterns and setting limits on the amount of time spent online, with a specific focus on gaming. The utilization of an application for tracking screen time provided students with insights into their gaming habits. Moreover, a proposal was made to the Medical Education Unit to organize awareness programs for MBBS students regarding the adverse effects of Internet addiction.

A notable strength of our study is the notably high response rate for the IGD9-SF questionnaire, with no dropouts during the subsequent stages of the study. The use of a mobile application for objectively assessing the number of hours spent on online games offered students a clear understanding of the amount of valuable time consumed by gaming rather than productive activities. However, the results cannot be extrapolated to the general population as the study was conducted solely among medical students.

Additionally, due to the small sample size, the representation of chronotype and cognitive flexibility reports is limited. Furthermore, variations in prevalence might arise based on the subjects' urbanization and socioeconomic status, impacting the affordability of gaming setups, factors that were not accounted for in this study.

Conclusion

The observed prevalence of IGD among medical students is a cause for concern, emphasizing the urgency for timely intervention and early identification of affected individuals. There is a pressing need to raise awareness about Internet addiction and Internet gaming disorder. A positive correlation was observed between the weekly hours spent and the IGD score. Further research is imperative to delve into the diverse factors influencing addiction, its impact on cognition, and to identify effective intervention strategies for addressing gaming addiction among young individuals. Furthermore, exploring the potential benefits of concept-based academic internet games could be an avenue worth investigating.

Summary

Among 489 participants, the prevalence of IGD was 4.9%, with 24 individuals meeting the IGD9-SF endorsement criterion, of which 20 were males (83.3%) and 4 were females (16.6%). Further assessments of students with IGD were conducted for chronotype and cognitive flexibility. Notably, no significant association was found between the IGD score and different Chronotypes. The study revealed a positive correlation between TMT-B, TMT B-A scores, and Stroop color task scores, except for TMT-

A. Higher IGD scores were positively correlated with elevated TMT (B-A) test scores, suggesting a reduced task-switching ability among IGD subjects. Additionally, a positive correlation was observed between the weekly hours spent using smart phones for gaming and the IGD score, signifying a heightened risk of Internet gaming disorder among individuals dedicating more time to online gaming than social networking. Conversely, the number of productive hours spent online per week showed a negative correlation with the IGD score, highlighting the adverse consequences of excessive gaming. Timely intervention measures are crucial for individuals affected by IGD among medical students. It is imperative to prioritize primary prevention by promoting awareness of internet addiction and internet gaming disorder. Moreover, further research is warranted to develop effective intervention strategies for addressing gaming addiction among the youth.

Statements and declarations

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Conflict of Interest

The authors declare that they have no competing interests.

Ethics approval, consent to participate, consent to publish, availability of data and material, code availability

Not applicable.

Author Contribution

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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ORIGINAL ARTICLE

A Prospective Study Comparing Subperiosteal Versus Subdural Drain After Burr-hole Drainage of Chronic Subdural Hematoma

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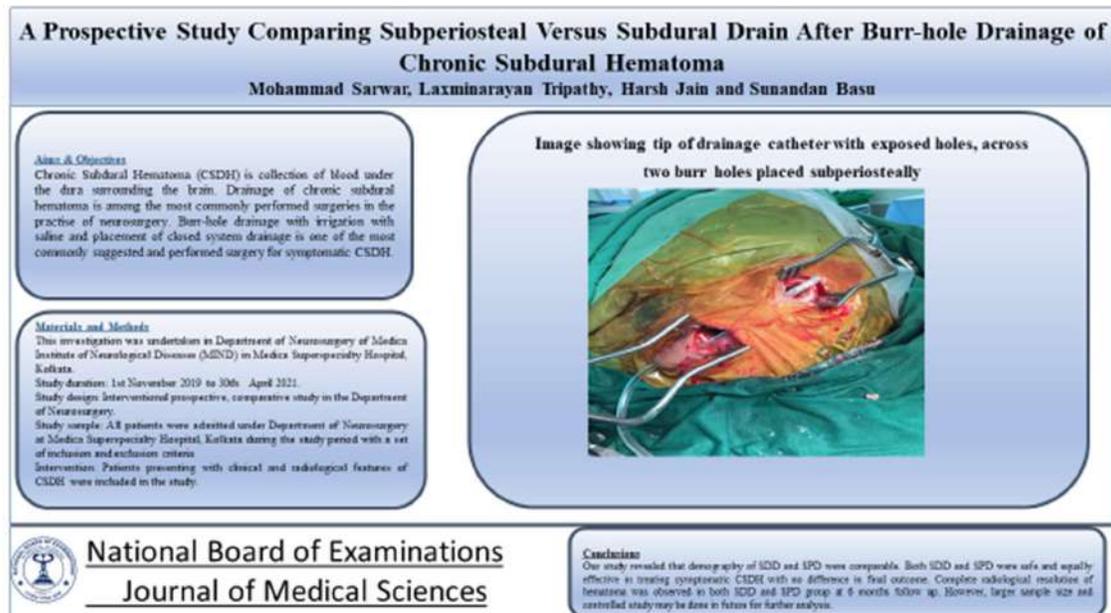
Abstract

Aims: The aim of our study was to perform a comparison between the efficacy of subperiosteal drain and subdural drain, and to evaluate any differences in terms of functional outcome in the treatment of symptomatic CSDH. **Materials and Methods:** The interventional, prospective, comparative study was undertaken in Department of Neurosurgery of Medica Institute of Neurological Diseases (MIND) in Medica Superspecialty Hospital, Kolkata, between 1st November 2019 to 30th April 2021, with set inclusion and exclusion criteria. Primary outcome was based on recurrence with 6 months. Secondary outcomes were incidence of re-operation and complications. 44 cases were distributed according to computer generated random numbers for the insertion of either drain following evacuation of CSDH. The data were analysed with SPSS software for windows version 21.0. **Results:** Our study has shown good outcomes in both groups at 3 months and 6 months. P values of Glasgow outcome score at discharge, 1 month, 3 months, and 6 months were 0.064, 0.39, 0.54 and 0.31; none of them were statistically significant. **Conclusion:** Our study revealed that both SDD and SPD were safe and equally effective in treating symptomatic CSDH with no difference in final outcome. Complete radiological resolution of hematoma was observed in both SDD and SPD groups at 6 months follow up. However, large sample size and controlled study may be done in future for further analysis.

Keywords: chronic subdural hematoma, CSDH, subdural drain, subperiosteal drain

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Graphical Abstract



Chronic Subdural Hematoma (CSDH) is collection of blood under the dura surrounding the brain. Drainage of chronic subdural hematoma is among the most commonly performed surgeries in the practise of neurosurgery. Burr-hole drainage with irrigation with saline and placement of closed system drainage is one of the most commonly suggested and performed surgery for symptomatic CSDH.

CSDH is commonly a disease of the geriatric population which is linked to significant morbidity and death. The occurrence of CSDH is approximately 19 per 1,00,000 population in the age group of 65-74 years, increasing to 47-153 per 1,00,000 population in patients older than 75 years [1].

The pathophysiology of CSDH was primarily theorised by Virchow [2] in 1857, when he first used the phrase “pachymeningitis haemorrhagica interna” that determined that dural inflammation was present and haemorrhagic elements.

McKissock et. al. [3] clinically defined CSDH as hematoma presenting after 20 days following trauma, resulting in the observation of dark crimson liquid blood encircled by a thin capsular membrane after surgery. Previously SDH was classified according to the appearance of density on computed tomography (CT) scans as hyperdense in acute SDH, as isodense on CT in subacute and hypodense in case of CSDH.

There are several surgical techniques used to treat this problem, including craniotomy, burr-hole craniostomy, and twist drill craniostomy. The gold standard of treatment, however, remains Burr-hole craniostomy and the hematoma's drainage and the installation of a drain. Patients without any symptoms and no radiological signs of a mass effects are managed conservatively with repeated CT scans and ongoing follow-ups. Spontaneous resolution of CSDH has also been described. Recent treatment modality

of refractory or recurrent middle meningeal artery embolisation as a persistent subdural hematoma has gained momentum. Al-Mufti (2021) [4] has studied on safety and efficacy of diluted n-butyl cyanoacrylate (n-BCA) for middle meningeal artery embolization.

Due to longer life expectancies, particularly in developing nations, there has been a noticeable increase in the number of patients presenting with symptomatic CSDH in recent years. (Baechli et al. 2004 [1]). Additionally, it is primarily diagnosed in elderly people who have concomitant medical disorders that may have a simultaneous role in its development. There aren't much class II evidence publications on the management of CSDH in the literature as of now. According to general consensus, burr-hole craniostomy together with irrigation and the installation of a closed drainage system is the preferred surgical procedure for symptomatic CSDH. (Weigel et al. 2003 [5]). Santarius et al. (2009) [6] found that after burr-hole evacuation of CSDH, the installation of a subdural drain was linked to a lower risk of recurrence and death. This was based on a randomised controlled experiment.

A significantly less invasive technique has been documented in more recent research, which involves using a subperiosteal drain rather than a traditional subdural drain (Gazzer et al. 2007 [7], Zumofen et al. 2009 [8], Bellut et al. 2012 [9]). This is because of implantation in a subdural drain on the cortical brain surface may result in problems like haemorrhage, seizures, and infection at the surgical site (e.g., Empyema).

The placement using a subperiosteal drain is advised for individuals who have a known high risk of problems, particularly

those who are older than 80 (Bellut⁹ et.al 2012).

We planned to investigate a sample size of 44 patients (22 in each group) using a prospective study design in order to show the variation in overall results and the rate of hematoma recurrence.

Material and Methods

This investigation was undertaken in Department of Neurosurgery of Medica Institute of Neurological Diseases (MIND) in Medica Superspecialty Hospital, Kolkata.

Study duration: 1st November 2019 to 30th April 2021.

Study design: Interventional prospective, comparative study in the Department of Neurosurgery.

Study sample: All patients were admitted under Department of Neurosurgery at Medica Superspecialty Hospital, Kolkata during the study period with a set of inclusion and exclusion criteria

Intervention: Patients presenting with clinical and radiological features of CSDH were included in the study.

The collected demographic and clinical variables included age, sex, co-morbidities like history of hypertension, diabetes mellitus, coagulopathy, hepatic, renal and cardiac diseases and medications (antihypertensive and antiplatelet or anticoagulant agents).

Blood pressure, pulse and respiration rate were recorded.

Glasgow Coma Score (GCS) was recorded.

Detailed history was obtained of any co-morbidities, history of trauma (exact date, significant or non-significant), previous brain surgeries.

Midline shift was noted on imaging.

Bilateral chronic subdural hematomas were considered as one case.

Routine investigation data such as haemoglobin, total leucocyte count, platelet count, PT, INR, blood sugar, serum urea, creatinine was collected.

Anaesthesia check-up was done in patients for surgery

Consent for surgery and anaesthesia was taken in each case.

Length of intensive care unit (ICU) stay and in the length of hospital stay was recorded.

Follow up period: The patient's clinical outcome was assessed by Glasgow Outcome Scale (GOS) on discharge, 1 month, 3 months, and 6 months follow up. Poor clinical outcome was defined as GOS <4. Mortality, morbidity and quality of life were recorded in follow-up clinic with a structured questionnaire.

Surgical Techniques

A proper informed permission form, outlining the indications and hazards of the research procedure, was obtained from the patient or their immediate family members or carers before to surgery. Anticoagulants and anti-platelet drugs used peri-operatively were excluded ahead of surgery, and FFP and vitamin K injection IM administered to establish normal clotting parameters. AEDs was given to all patient who presented with seizures as well as prophylactically to rest of the patients. In that case, IV Levetiracetam loading dose and maintenance dose given. Our preference of AED was Levetiracetam in all cases.

The following steps were taken during surgery:

The patient was given local anaesthesia (LA) / monitored anaesthesia care (MAC) during surgery.

With their head supported by a rubber horseshoe, the patient was put in a supine position headrest.

The area of incision was marked at level of maximum subdural collection at frontal and parietal region then covered with sterile surgical drapes after being cleansed with Povidone iodine.

A single shot of antibiotic prophylaxis 1.5 g of IV Cefuroxime (Supacef, Glaxo SmithKline Pharmaceuticals Ltd) and Local Anaesthetic (Lignocaine + Adrenaline) was given to each patient prior to skin grafting and Cefuroxime continued for 48 hours afterward (till drain was removed, whichever was later).

Two burr-holes were created at the maximum thickness of the clot, using a burr-hole craniostomy size that (measures at least 10mm x 10mm in diameter) around 6-8 cm apart.

Coagulation caused the dura mater to expand up widely in cruciate fashion according to the burr-hole's size.

Body irrigation was used during intraoperative subdural irrigation temperature when the discharge was clean, use regular saline.

The closed-system drainage was installed either with subperiosteal drain or subdural drain selected according to sequence of computer-generated random numbers.

When the SPD system was installed, a Romovac catheter (14 F) was positioned across the burr-hole in the sub-galeal plane. In case of placement of the SDD system, a Jackson-Pratt drain (flat) catheter was negotiated through the burr-hole and gently placed in the subdural space.

Either drain was attached to a collecting tube after being drawn through a

tiny skin incision posterolateral to the burr-hole bag (without any suction applied).

The bag was kept for gravity drainage below the patient's head level.

Before sealing the skin incision, body-temperature saline was poured into the subdural region to reduce pneumocephalus.

This parietal incision has closed first, and after filling the subdural space with warm saline, frontal incision is closed.

When treating patients of bilateral CSDH, the identical drain insertion technique was used on both sides.

Every patient received the typical post-operative treatment, including AED prophylaxis for 3 months.

Flat bed rest for 24 hours.

Removal of drain was done in 48 hours post-operatively in most cases, unless there was significant drainage.

A repeat CT scan was performed after removal of drain.

Additionally, we arranged for outpatient follow-up CT scans at three and six months.



Figure 1. Image showing tip of drainage catheter with exposed holes, across two burr holes placed subperiosteally.

Outcome measures (primary and secondary):

Primary outcome was based on recurrence within 6 months.

Secondary outcomes were incidence of re-operation and complications (both intra-operative and post-operative). When the mRS was 0-3, the clinical outcome was considered favourable, and when mRS was ≥ 4 , it was considered unfavourable.

Sample size

To calculate the sample size at 5% level of significance and 80% of power using the formula of $n = (Z_{\alpha/2} + Z_{\beta})^2 * \sigma^2 / E^2$

Where,

n= Sample Size

$Z_{\alpha/2}$ = Level of significance ($\alpha = 95\% = 1.96$)

Z_{β} = Desired power ($\beta = 20\% = 0.84$)

σ = Standard deviation ($\sigma = 1.00$)

E = Effect Size ($E = 0.45$)

At 95% significance level with 80% power value, the minimum sample size would be 44.

Version 21.0 of the SPSS programme for Windows was used to analyse the data. We analysed ICU stay and Hospital stay, age, GCS by non-parametric Mann Whitney test. For sex, midline shift and co-morbidities the Chi-Square test were used. We used the Mann Whitney test to make a comparison of the GOS across the 2 types of brain surgeries at the time of discharge, at 1 month, at 3 months, at 6 months. Chi-Square test is used to study mRS across SDD and SPD, hematoma density appearance in CT scan across SDD and SPD, hematoma thickness across SDD and SPD and clinical outcome across SDD and SPD. At a level of significance that was supposed to $P < 0.05$.

Ethical clearance obtained from Institutional Ethical Committee and Scientific Research Committee.

Results

Patient Selection

During the study period, total 44 cases were studied. Cases were distributed according to the computer-generated random numbers for the insertion of subdural drainage or subperiosteal drainage after burr hole evacuation for chronic subdural hematoma. Total 22 cases ($n=22$) were allotted in each group.

A class I evidence for lower recurrence rate with after a burr-hole, twist drill, or craniotomy, the installation of a closed drainage system was reported by Santarius et al. in 2009 [6].

Although various types of drains have been used, as reported in literature, there is no consensus in superiority of any particular type of drain so far. We performed a prospective comparative study

of sub-periosteal drain versus sub-dural drain following burr-hole craniostomy.

Discussion

CSDH is clinically defined as hematoma presenting commonly after a few weeks following trauma, resulting in the observation of dark crimson liquid blood encircled by a thin capsular membrane after surgery. CSDH is one of the most common clinical entities treated surgically in neurosurgery. It is more prevalent in geriatric population. The reported incidence [1] is 19 per 1,00,000 populations. Recurrence rates are high and range between 5 to 30 %.

Markwalder [10] has given a clinical grading scale to support the impartial evaluation of patients who arrive with CSDH. It is applied both before and after surgery to evaluate the patient's clinical score. Nakaguchi [11] has classified the radiological appearance of CSDH into four main types: Homogenous, Laminar, Separated and Trabeculated type.

Level I evidence indicates that burr hole evacuation combined with post-operative drain placement is the standard recommended and most commonly utilized method of treating CSDH, and can greatly reduce recurrence rate.

In a study comparing above three techniques, it has been shown that compared to the burr-hole and twist drill craniostomy groups, the craniotomy group had the highest death rate and the worst results. The treatment of CSDH by burr-hole craniostomy is widely accepted method of treatment because, in comparison to twist drill craniostomy and craniotomy, it better balances a low recurrence rate against morbidity and death.

Santarius et al. 2009 [6], in their double burr-hole craniostomy randomised

controlled trial, they found that patients treated with subdural drain implantation had a significant improvement in recurrence, mortality, and clinical prognosis at discharge. The implementation of closed-system drainage as a gold standard in the surgical management of CSDH with burr-hole craniostomy was only recommended in this one study (Type A recommendation). A recent meta-analysis conducted by Almenawar et al. (2014) [12] strengthens the function of the closed-system drain implantation, which has been shown to dramatically lower the recurrence rate of hematomas.

A less invasive technique of placing a sub-periosteal (sub-galeal) drain was advocated by Gazzeri [7] and Zumofen [8]. Both reported similar results in terms of problems and recurrence in contrast to the implantation of subperiosteal and subdural drain. When international survey on practice among neurosurgeons worldwide done, the discrepancy was reported. 50% preferred SDD and 27% preferred SPD. There was notable difference among our institute's surgeons. There are few recent researches comparing the efficacy of SDD and SPD but there are very few well designated randomized controlled trials. Seizure rates in patients treated with CSDH is between 2.3% to 5%. Higher incidence is seen in unilateral and mixed density CSDH. Prophylactic AED is suggested in most studies but few found that there was no discernible change in the frequency of seizures with prophylactic administration of AED and determined that the illness with AED far outweigh the advantages.

Zhang et al. (2019) [13] conducted a multicentre retrospective study on clinical results of burr hole evacuation for chronic subdural hematoma in comparison to subperiosteal drain. Recurrence was

comparable between the subdural (13.1%) and subperiosteal (11.2%) drain groups ($p=0.502$). Using a 6-month modified Rankin Scale, no statistically significant differences were seen between the groups (mRS) ($p=0.188$), 30-day mortality ($p=0.957$), infection of the central nervous system after surgery ($p=0.393$), and length of hospital stay ($p=0.231$). Notably, two clinically significant cases of iatrogenic acute subdural hematoma (ASDH) occurred during removal of subdural drain. Both cases required reoperation and there was one death (50%), 45 days after surgery. They concluded that although clinical outcomes of subdural and subperiosteal drains are comparable, they cautioned against the use of subdural drains due to a clinically significant risk of iatrogenic ASDH during drain removal.

Soleman et al. (2019) [14] conducted a multicentre, patients receiving burr-hole drainage for CSDH were analysed in a prospective, randomised, controlled, and noninferiority study. Compared to the SDD group (12.00%, 95% CI 6.66-19.73), the SPD group had a reduced recurrence rate (8.33%, 95% CI 4.28-14.72), and the treatment difference (3.67%, 95% CI -12.6-5.3) did not fulfil specified noninferiority criteria. By placing drains, the SPD group demonstrated noticeably lower rates of iatrogenic morbidity ($P = .0184$) and surgical infections ($P = .0406$). Both groups' length of stay and death rates were similar. They have come to the conclusion that SPD implantation reduced the rates of surgical infections, recurrences, and drain misplacements even if the noninferiority criteria were not satisfied. These results imply that SPD might be the preferred option in standard clinical settings.

Chih et al. (2019) [15] conducted a prospective interventional trial to directly compare patients getting SPD versus SDD drain installation for the treatment of CSDH. They found when compared to the SDD approach, SPD placement was just as effective and generally resulted in a reduced risk of surgical problems.

Glancz et al. (2018) [16] carried out a subgroup study of an earlier report that from a UK multicentre, CSDH patients participated in a prospective cohort research conducted from May 2013 to January 2014. They analysed information on the location (subdural or subgaleal), orientation (via a frontal or parietal burr hole), and length of insertion of the drain in relation to the results of patients older than 16 years who are having primary CSDH burr-hole drained. They concluded that After CSDH drainage, drain insertion is crucial, although the duration (1 or 2 days) and site (subgaleal or subdural) did not seem to affect clinical results or the rate of recurrence. Similarly, results where both frontal and parietal burr holes were created were unaffected by the placement of the drain.

AbdelFatah [17] conducted a review conducted in the past on patients who had CSDH evacuation between August 2012 and August 2016. No evidence of recurrence was there within 12 months. Twelve months after surgery, there was no death rate. Using two large burr holes, irrigation, and a sub-galeal Redivac low-pressure suction drainage, he found that surgical care of unilateral diffuse CSDH in adult patients was successful and did not result in recurrence.

Yadav et al. (2016) [18] studies the role of sub-galeal placing a suction drain for the clearance of a persistent subdural

hematoma. They prospectively studied 260 patients of CSDH treated with burr hole irrigation with (140 patients) or without (120 patients) suction drain. They concluded that sub-galeal the management of CSDH was made safe, easy, and efficient by closed suction drainage. In the group using suction drains, the recurrence rate was minimal.

A non-randomized prospective study by Chih et al. [15] including 30 symptomatic CSDH patients observed no statistically significant difference in patient characteristics, mean hematoma size, concomitant conditions, or pre-operative symptoms between the two groups when comparing the efficacy of SPD and SDD. They found that SPD placement was equally effective but marginally lower complications due to minor invasiveness of the SPD involving no contact with brain parenchyma. This difference however did not get a significant statistical level.

Kaliaperumal et al. [19] in a prospective randomized study, comprising 25 symptomatic CSDH patients each arm, found significantly better modified Rankin score after 6 months in the patients treated with SPD. They showed no recurrence in both groups. They also highlighted the risk of brain parenchymal injury in SDD.

Soleman et al. (2019) [14] in a large multicentre, prospective randomized controlled trial, comprising 220 patients compared 120 SPD versus 100 SDD. They found lower recurrence rate in SPD group (8.33%, 95% confidence interval 4.28-14.72) than in SDD group (12.00%, 95% confidence interval 6.66 – 19.73). Also, there was significantly decreased rate of post-operative drain placement resulted in infections ($P = 0.0406$) and iatrogenic morbidity ($P = 0.0184$). The SDD group's misplaced drain rate reached up to 17%;

their method of drain insertion may have contributed to this. They inserted the SDD from anterior to posterior burr holes.

Jetjumnong et. al. (2021) [20] conducted a prospective randomized study of 42 patients, 21 patients in each arm of SDD and SPD. Their data suggested that post-operative residual hematoma and midline shift that persist at 48 hours do not necessitate re-operation and had no effect on final outcome. Majority had complete resolution in 3 months and 6 months.

Summary and Conclusion

CSDH is one of the most common neurological entities treated surgically. It is more prevalent in geriatric population. The reported incidence [1] is 19 per 1,00,000 populations. Recurrence rates are high and range between 5 to 30 %. Burr-hole craniostomy and closed system drainage are widely used worldwide in treating symptomatic CSDH. There is no consensus of number of burr hole/s, use or irrigation, site of the drain whether subdural or subperiosteal, duration of drainage. We conducted a single centre prospective observational study comparing the results of subdural versus subperiosteal drain. Our study's primary objectives were to compare the effectiveness of subperiosteal and subdural drains and assess any variations in functional outcomes when treating symptomatic CSDH. Our objective was to assess the general demographics, to compare the neurological outcome based on mRS and GOS, to compare pre- and post-operative hematoma thickness, appearance, midline shift.

We studied 44 patients. SDD or SPD was inserted after burr hole drainage of symptomatic CSDH, selection being done on the basis of computer-generated random numbers: odd-number for SDD and

even number for SPD. This study was undertaken in Department of Neurosurgery of Medica Institute of Neurological Diseases (MIND) in Medica Superspecialty Hospital, Kolkata. The study design was interventional, prospective and a comparative study in the Department of Neurosurgery. Patients included were those presenting to emergency or OPD with symptoms of CSDH and radiological confirmation, with or without evidence of mass effect and midline shift. Clotted SDH, asymptomatic patients, patients refusing surgery or those who were lost to follow up were excluded.

We did a prospective study design, and with the purpose to provide our single centre experience comparing the efficacy of two techniques, we intended to study a sample size of 44 patients (22 in each group) to demonstrate the difference in overall outcomes and rate of hematoma recurrence. Cases were distributed according to the computer-generated random numbers for the insertion of SDD or SPD after burr hole evacuation for CSDH. Total 22 cases (n = 22) were allotted in each group.

We did not find any statistically significant differences between SDD and SPD in terms of patient characteristics, associated co-morbidities (diabetes mellitus, hypertension, renal disorder, coagulopathies, heart diseases, history of trauma, history of brain surgery, GCS, mean hematoma size, clinical outcomes (as defined by mRS). There was also no statistical difference between SDD and SPD imaging characteristics (hematoma density appearance in CT scan), midline shift, complication rate, or recurrence rate. Favourable functional outcomes were determined by a GOS of 4 or higher at 3 months follow-up. Our study has shown

good outcomes in both groups at 3 months (mean GOS 4.73 in SPD and 4.77 in SDD) and 6 months (mean GOS 4.95 in SPD and 5 in SDD). P values of GOS at discharge, 1 month, 3 months and 6 months were 0.064, 0.39, 0.54 and 0.31; none of them were statistically significant. Our findings were consistent with previous studies comparing SDD and SPD.

Conclusion

Our study revealed that demography of SDD and SPD were comparable. Both SDD and SPD were safe and equally effective in treating symptomatic CSDH with no difference in final outcome. Complete radiological resolution of hematoma was observed in both SDD and SPD group at 6 months follow up. However, larger sample size and controlled study may be done in future for further analysis.

Data Availability

A data collection form was prepared to suit the proposed study. All relevant data were entered in it.

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Informed Consent

Informed consent was obtained from all patients or patients' relatives and approval for the study had already been taken from the Institutional Ethical Committee and Scientific Research Committee. A copy of the patient information sheet and the informed consent form were given to all the participants.

Conflict of Interest

The authors declares that the authors do not have conflict of interest

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Author Contribution

We confirm that this manuscript has been read and approved by all named authors. In addition, we declare that the manuscript is original and it is not being published or submitted for publication elsewhere.

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ORIGINAL ARTICLE

Concordance in diagnosis of Neck masses using Clinical Pre-diagnosis and Pathological analysis

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Abstract

Background: Neck swelling is one of the commonest presentations in otorhinolaryngological practice. Study aimed to analyze the demographics and symptomatology of cervical masses, the degree of accuracy of clinical examination as well as the correlation between the clinical diagnosis and pathological results in patients presenting with neck masses. **Material & Method:** The present prospective observational study is conducted among the patients attending the out-patient and in-patients setting of ENT department with complaints of neck mass/ masses either primarily or in conjunction with other complaints, for more than 3 weeks duration. The patients with complaints of neck mass of acute inflammatory origin of less than 3 weeks and patients with inflammatory causes of lymphadenopathy including those secondary to upper aerodigestive tract infection and those of tubercular origin on initial assessment were excluded. Following a thorough clinical examination appropriate radiological investigations were advised, followed by cytological evaluation. FNAC was performed, either guided or unguided as per the discretion of the pathologist. Further Histopathological evaluation was conducted in tissue specimens, wherever required, after either surgical excision of the entire mass or a biopsy. Histopathology involves the examination of sampled whole tissues under the microscope. **Results:** Age distribution placed majority of females in the young adult (16-40 yrs) category and males in the late adult (> 40 yrs) group. The majority of neck masses were thyroid swellings (42%) followed by lymph nodal masses (29%) and salivary gland lesions (14%). Of all the neck masses in females 87% were benign whereas amongst males 62% were malignant. The accuracy of clinical pre-diagnosis was seen to be 93.4%. The sensitivity for thyroid lesions for suspicion of malignancy however, was seen to be only 33% as papillary carcinoma thyroid essayed no symptoms or signs of malignancy. FNAC as an investigation for pre-diagnosis, the accuracy on the whole was seen to be 84.7% with a sensitivity of 82.5% which is comparable to other Indian studies. For thyroid lesions however the sensitivity was very low, 33.3%. This may be due to the inconsistent use of guidance systems and inexperience of our junior aspirators which act as confounding factors. **Conclusion:** Accuracy of FNAC in comparison to the definitive diagnosis was 84.7%. Inconsistent use of guidance systems, inexperience of junior aspirators and aspiration from representative node/ part of the lesion may act as confounding factors resulting in the discordance between clinical pre-diagnosis and FNAC accuracy with respect to the definitive diagnosis

Keywords: FNAC, Accuracy, Thyroid, histopathology

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Graphical Abstract

Concordance in diagnosis of Neck masses using Clinical Pre-diagnosis and Pathological analysis
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Background: Neck swelling is one of the commonest presentations in otorhinolaryngological practice.

Aim & Objectives: To analyze the demographics and symptomatology of cervical masses, the degree of accuracy of clinical examination as well as the correlation between the clinical diagnosis and pathological results in patients presenting with neck masses.

Material & Methods:
 The present prospective observational study is conducted among the patients attending the out-patient and in-patient setting of ENT department with complaints of neck mass/ masses either primarily or in conjunction with other complaints, for more than 3 weeks duration. The patients with complaints of neck mass of acute inflammatory origin of less than 3 weeks and patients with inflammatory causes of lymphadenopathy including those secondary to upper aero-digestive tract infection and those of tubercular origin on initial assessment were excluded. Following a thorough clinical examination appropriate radiological investigations were advised, followed by cytological evaluation. FNAC was performed, either guided or suggested as per the discretion of the pathologist. Further histopathological evaluation was conducted in tissue specimens, wherever required, after either surgical excision of the entire mass or a biopsy. Histopathology involves the examination of sampled whole tissues under the microscope.

Table 1.0: Gender-wise Distribution of Neck Masses in Different Age-groups

Age Group (years)	Males	%	Females	%	Total	%
0 - 15	3	6%	3	6%	6	6%
16 - 40	19	34%	32	60%	50	47%
> 40	32	60%	18	34%	50	47%
Total	53		53		106	

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Conclusions:
 Accuracy of FNAC in comparison to the definitive diagnosis was 84.7%. Inconsistent use of guidance systems, inexperience of junior aspirators and aspiration from representative site/ part of the lesion may act as confounding factors resulting in the discordance between clinical pre-diagnosis and FNAC accuracy with respect to the definitive diagnosis.

Introduction

Neck swelling is one of the commonest presentations in otorhinolaryngological practice. It is also a major cause of morbidity and mortality amongst patients in India [1,2]. Due to the anatomical complexity of the neck region, diagnosis of lesions in this region becomes a diagnostic dilemma. A plethora of pathological conditions present with identical symptoms. Conversely, the same disease may present with diverse symptoms. Majority of the neck swellings can be accurately diagnosed by a comprehensive history and a thorough clinical examination [3].

Neoplasms of the neck region are a major form of cancer in India, accounting for 23% of all cancer in males and 6% in females [4]. It is therefore imperative to diagnose a malignant neck mass at the earliest and institute the correct management. The vital parameters that determine whether the mass is malignant or not include the age of the patient, location,

size and duration of the mass. A neck mass in children is most likely to be an inflammatory or developmental condition. Neoplasms (benign or malignant) are more likely to present in older individuals. Often a cervical lymph nodal mass is the only presentation of a primary malignancy elsewhere in the head or neck region like mouth, pharynx or larynx.

Radiological investigations such as ultrasonography, computed tomography, magnetic resonance imaging, angiography and scintigraphy may further assist in coming to a diagnosis. FNAC or fine needle aspiration cytology is the primary investigation of choice in evaluation of head and neck masses, reasons being its high degree of diagnostic accuracy, cost-effectiveness and the minimally disruptive nature of the procedure. Histopathological evaluation of excisional and incisional biopsy specimen is required for the definitive diagnosis of the lesion [5,6].

This study is therefore being conducted to analyze the demographics and

symptomatology of cervical masses, the degree of accuracy of clinical examination as well as the correlation between the clinical diagnosis and pathological results in patients presenting with neck masses.

Material and Methods

The present prospective observational study is conducted over a period of 1 year (Jan 2022 to March 2023) among 106 patients attending the out-patient and in-patients setting of ENT department with complaints of neck mass/masses either primarily or in conjunction with other complaints, for more than 3 weeks duration. The patients with complaints of neck mass of acute inflammatory origin of less than 3 weeks and patients with inflammatory causes of lymphadenopathy including those secondary to upper aero-digestive tract infection and those of tubercular origin on initial assessment were excluded.

A thorough history was elicited from the patients. Important factors include onset progression, duration, location, number, symptoms localizing the primary diagnosis (if any), risk factors and constitutional symptoms. Evaluation of risk factors has been included in this study to assist in clinical pre-diagnosis of associated neck masses, especially thyroid and lymph nodal masses. Constitutional symptoms suggest disorders such as tuberculosis, lymphoma, collagen vascular diseases, unrecognized infection or malignancy. Examination for thyroid gland was performed on all patient. The patient was asked to extend their neck and tip their head back to inspect for the thyroid gland. It is not visible in all patients, but is usually found inferior to the cricoid cartilage. Following a thorough clinical examination appropriate radiological investigations

were advised, followed by cytological evaluation. FNAC was performed, either guided or unguided as per the discretion of the pathologist. Further Histopathological evaluation was conducted in tissue specimens, wherever required, after either surgical excision of the entire mass or a biopsy. Histopathology involves the examination of sampled whole tissues under the microscope.

Statistical analysis: All the data collected was collated and subjected to statistical analysis by Statistical Package for Social Sciences (SPSS) version 24. Chi square test was applied to analyze the significance of various parameters of clinical evaluation on the presumptive diagnosis. $P < 0.05$ was considered significant and $P < 0.01$ was considered highly significant. Statistical parameters were applied to study the correlation between Clinical pre-diagnosis and the definitive diagnosis (Histopathological Report/HPR) and well as the FNAC results with the HPR. Sensitivity and accuracy were determined for both the Clinical pre-diagnosis and FNAC with respect to the HPR. Other parameters like Predictive values and specificity were calculated for individual groups of neck masses wherever possible

Results

Evaluation of gender-wise distribution of the neck masses shows that the distribution was equal amongst males and females with no gender predilection. Also an age-wise break-up of the above distribution showed that majority of males were in the late adult group (60%) whereas an equivalent proportion of females were in the young adult age-group (60%). This may be attributed the fact that malignancies were seen to be more common amongst

males and thyroid lesions amongst females.
Children (0-15 years) showed no gender

predilection the presentation of neck
masses (Tables 1 and 2).

Table 1. Gender-wise Distribution of Neck Masses in Different Age-groups

Age Group (years)	Males	%	Females	%	Total	%
0 - 15	3	6%	3	6%	6	6%
16 - 40	19	34%	32	60%	50	47%
> 40	32	60%	18	34%	50	47%
Total	53		53		106	

Table 1. Distribution of Neck masses

Type of mass	Diagnosis	Number of Patients	Total	Percentage
Thyroid			45	42%
	Colloid Goitre	30		
	Follicular Adenoma	6		
	Thyroglossal Cyst	3		
	Papillary Carcinoma	4		
	Medullary Carcinoma	1		
	Thyroid Lymphoma	1		
Lymphadenopathy	Metastatic Lymphadenopathy	29	31	29%

	Non-Hodgkins Lymphoma	1		
	Rosai Dorfman Syndrome	1		
Salivary Gland			15	14%
	Chronic Submandibular Sialoadenitis	5		
	Chronic Parotid Sialoadenitis	3		
	Pleomorphic Adenoma	4		
	Mucoepidermoid Carcinoma	2		
	Carcinoma Parotid (Squamous cell carcinoma)	1		
Parapharyngeal Masses			3	3%
	Schwannoma	2		
	Carcinoma Tonsil	1		
Cystic Swellings			9	9%
	Branchial Cyst	1		
	Sebaceous Cyst	3		
	Dermoid Cyst	4		
	Retention cyst (Plunging Ranula)	1		
Miscellaneous			3	3%
	Odontogenic Cyst	1		
	Lipoma	2		

Overall distribution of different neck masses (with respect to the definitive diagnosis) was tabulated. The majority of neck masses were thyroid swellings (42%) followed by lymph nodal masses (29%),

salivary gland lesions (14%), cystic lesions of the neck (9%), Parapharyngeal masses (3%) and other miscellaneous conditions (3%) (Tables 3, 4 and 5).

Table 2. Skin and Soft tissue lesions amongst the Neck Masses

Diagnosis	Number	%
Dermoid cyst	4	3.7
Sebaceous cyst	3	2.8
Lipoma	2	1.8
Schwannoma	2	1.8
Total	11	

Table 3. Distribution of Primary sites in Malignant Lymphadenopathy and Neck Masses as per Clinical Diagnosis

Primary Diagnosis	Number	%
Carcinoma Supraglottis	16	53
Carcinoma Buccal Mucosa	8	27
Carcinoma Tongue	3	10
Carcinoma Hypopharynx	1	3.3
Carcinoma Subglottis	1	3.3
Non-Hodgkins Lymphoma	1	3.3
Diagnosis	Number of Patients	Percentage
Benign Thyroid Swelling	41	38.70%

Metastatic Lymphadenopathy	29	27.35%
Parotid swelling	9	8.50%
Submandibular swelling	5	4.70%
Dermoid cyst	4	3.80%
Thyroglossal cyst	3	2.80%
Parapharyngeal mass	3	2.80%
Sebaceous cyst	3	2.80%
Cyst	2	1.90%
Lymphoma	1	1%
Lipoma	1	1%
Madibular bony lesion	1	1%
Branchial cyst	1	1%
Thyroid cyst	1	1%
Submental swelling	1	1%
Benign Lymphadenopathy	1	1%

Table 4. Gender-wise distribution of Thyroid masses

Thyroid Masses	Male	%	Female	%	Total	%
Colloid Goitre	5	16.6	25	83.3	30	66.6
Follicular Adenoma	0	0	6	100	6	13.3
Thyroglossal Cyst	1	33.3	2	66.6	3	6.6
Papillary Carcinoma	2	50	2	50	4	8.8

Medullary Carcinoma	1	100	0	0	1	2.2
Thyroid Lymphoma	0	0	1	100	1	2.2
Total	9	20	36	80		

Age-wise distribution of the Neck masses was analyzed and the distribution of neck masses was seen to be equal amongst the young adult (47%) and late adult (47%) age groups. Malignant lesions like Metastatic lymphadenopathy (83%), Medullary carcinoma thyroid (100%), Carcinoma parotid (100%), Carcinoma tonsil (100%), Thyroid lymphoma (100%)

was concentrated largely in the late adult age group, except Mucoepidermoid carcinoma (50% - young adult, 50% - late adult) and Papillary carcinoma thyroid (25% - late adult, 75% - young adult) and NHL (100% - young adult). Benign thyroid lesions like colloid goitre (63%), follicular adenoma (83%) was more common in the young adult age group (Tables 6 and 7).

Table 5. Distribution of diagnosis of patients

Diagnosis	Total	Present	%
Carcinoma (Head and Neck)	29	29	100
Mucoepidermoid Carcinoma	2	2	100
Carcinoma Tonsil	1	1	100
Papillary Carcinoma Thyroid	4	1	25
Colloid Goitre	30	1	3.3
NHL	1	0	0
Thyroglossal Cyst	3	0	0
Carcinoma Parotid	1	0	0
Medullary Carcinoma Thyroid	1	0	0
Follicular Adenoma	6	0	0
Thyroid Lymphoma	1	0	0

Table 6. Calculation of statistical parameters for Clinical pre-diagnosis and HPR

Histopathology			
Clinical pre-diagnosis	Malignant	Benign	Total
Malignant	36	0	36
Benign	4	66	70
Total	40	66	106

The correlation between the Clinical Pre-Diagnosis and the Definitive diagnosis (Histopathological report) was studied. Maximum discordance was seen in the thyroid lesions. Malignant thyroid lesions were identified in only 33% of the cases which were mistaken as benign. A case of Pleomorphic adenoma due to unusual position and clinical characteristics was diagnosed as a lipoma, a lipoma was mistaken for a sebaceous cyst and 1 case of

schwannoma was mistaken for a case of benign lymphadenopathy. Further analysis of the data was done and statistical parameters were analyzed. Overall accuracy of Clinical pre-diagnosis based on all factors was found to be 93.4% In case of prediction of benign and malignant lesions the sensitivity was found to be 90%, specificity 100%, positive predictive value 100% and Negative predictive value of 94.29% (Table 8).

Table 7. Calculation of statistical parameters for FNAC and HPR

Histopathology			
FNAC	Malignant	Benign	Total
Malignant	33	0	33
Benign	7	65	72
Total	40	65	105

The correlation between the FNAC and histopathological results was also analyzed. It was observed that the accuracy of FNAC was 84.7% on the whole. Overall the sensitivity of FNAC in this study was 82.5% (to differentiate between benign and malignant lesions), with specificity of 100%, positive predictive value of 100% and negative predictive value of 90.28%.

For thyroid lesions the overall accuracy was found to be 80%, with a sensitivity of 33.3%, specificity of 100% with positive predictive value of 100%, negative predictive value of 90.70% (to differentiate between malignant and benign lesions). For lymphadenopathy the overall accuracy was 90.3% with sensitivity 90%, specificity of 100%, positive predictive value of 100% and negative predictive value of 25%.

Regarding Tables 15 and 16, it should be noted that in case of the clinical pre-diagnosis, many parameters of the history and clinical examination are considered comprehensively of which most of the parameters have very equivocal criteria for suspicion of malignancy. In case of FNAC, the varying expertise of the pathologists, infrequent use of guidance systems and sampling of only a representative part of the lesion should be taken into consideration.

Discussion

This study included all the patients who presented with complaints of neck masses and attended either the out-patient section of the Department of E.N.T or were admitted for treatment of the same. Patients presenting with neck masses of less than 3 weeks' duration were considered 'acute' and hence not included in the study. This excluded all the neck masses of inflammatory and infectious origin as they

invariably initially presented within 3 weeks of their apparent onset and were either resolved on treatment or lost to follow-up.

It was observed that there was no gender predilection of neck masses in our study with them being equally distributed amongst males and females. Females with neck masses however presented predominantly in the young adult age group (16-40 years) (60%) and males in the old adult age group (> 40 years) (60%).

In general Thyroid lesions were more common in females (80%) whereas Lymph nodal masses (90.3%) and salivary gland lesions (66.6%) were seen to be more common in males. The age and gender distribution of neck lesions was similar to various studies done by Popat et al, Basista et al., Ozkiris et al., Irani S et al. and Suryavanshi et al. [7-11].

The most common neck lesions in this study were thyroid lesions (39.62%) and the second most common lesion in the neck was lymph nodal lesion at 29.24% comparable to earlier studies [7-11]. (Table 2) As cases of inflammatory lymphadenitis including tubercular lymphadenitis were excluded, our study cannot be compared to other studies where the most common lesion was reactive lymphadenitis followed by tuberculous lymphadenitis like Vachhani et al, and Suryavanshi et al. [11,12]. All the 11 soft tissue tumours encountered in our study were benign. The most common tumour was dermoid cyst (36.3%) followed by sebaceous cyst. In a study done by Vahini [12]. Lipomas constituted 34.7% of all benign soft tissue tumours and were most common in the head and neck region, in contrast to our study where they constituted only 18.1% of all soft tissue tumours. Schwannomas comprised of 18.1% of all soft tissue

tumours. Majority of the cases in this study were in the young adult age group (16 – 40 years).

As per clinical consensus, of the 106 lesions, 35 were diagnosed as malignant (33%) and 71 (67%) as benign, comparable to the study by Ozdas et al with the masses being benign in 58.2 % and malignant in 22.8 %, with the character of the mass not differentiated in 18.9 %. The definitive diagnosis of all patients was made by histopathological examination. Histopathological examination revealed that 40 (37.7%) of the patients had malignant lesions whereas 66 (62.3%) specimens were benign. Ozdas et al, in their study found that 78.7 % of the 127 specimens were benign and 21.2 % were malignant which is fairly similar to our study [13].

In our study the mean age of the patients with a malignant mass was 51.79 years and those with benign mass was 33.86 years comparable to the study by Ozdas et al. where the average age of presentation for malignant and benign masses was 57.3 and 44.6 years respectively. This is comparable to the studies by Ozdas et al and Bhattacharya et al. where the relationship between age and malignancy was found to be highly significant ($P < 0.01$) [13,14].

Since masses of acute onset and short duration (<3 weeks) were excluded all our patients presented with masses ranging in duration from months (sub-acute) to years (chronic). No statistically significant relationship was found between the duration of the mass and definitive diagnosis and between the location of the mass and the definitive diagnosis comparable to the study by Ozdas et al. [13] In contrast, in Bhattacharya's [14] study location and duration of the mass were reported as important and statistically

significant parameters for prediction of neoplasia.

Presence of relevant history was evaluated for the various neck masses. Relevant history included family history of malignancy, history of symptoms relating to affliction of different regions of head and neck, history in change of the size or character of the mass with episodes of URTI, features of hyper/hypothyroidism etc. They were not individually compared to the definitive diagnosis but collated on the whole wherever relevant. These features play an important role in the preliminary diagnosis of the lesion under evaluation. In our study the presence of relevant history showed a highly significant relation in prediction of benign and malignant neck masses with a P value of < 0.00001 . They were also found to be a significant indicator of malignancy for thyroid lesions (P value 0.00225). However, for Lymph nodal masses specifically (P value – 0.0078) it was found to be statistically insignificant. This could be due to the fact that the inflammatory and reactive lymphadenopathy were excluded from our study and that may have caused a selection bias when it came to statistical analysis. They were also not found to be significant in singular diagnosis of the neck lesions. No other study has analysed the implication of relevant history in the diagnosis of neck masses.

Presence of risk factors including history of tobacco exposure, alcohol abuse, exposure to radiation and dietary deficiencies was studied with respect to their significance in coming to a diagnosis. The risk factors were not seen to be significant in terms of the definitive individual diagnosis. However, they were found to be highly significant statistically in prediction of benign and malignant neck

masses (P value < 0.00001). They were also found to be significant in prediction of malignancy in chronic non-inflammatory lymph nodal masses (P value < 0.00001). They were however not found to be significant in the prediction of malignancy in thyroid lesions (P value – 0.1186) as a very small proportion of patients presented with risk factors relevant to their pathology. This is in contrast with the study by Bhattacharya et al,¹⁴ where no statistically significant relation was found in between the presence of risk factors and malignancy in neck lesions. This may be due to the regional variation in habit and addiction patterns.

Mobility of the neck masses is considered another very important clinical parameter in the evaluation of a neck mass. Distribution of mobility of the neck masses was analysed with its relevance to the diagnosis and it was seen that malignant lesions made for 88% (23 of the 26) of the immobile/ fixed neck lesions in our study. An analysis of the mobility of the mass with the respect to indication of malignancy in a neck mass was found to be highly significant statistically. Features suggestive of malignancy on clinical examination like skin fixation, fungation etc were also evaluated with respect to their assistance in diagnosis and they were collectively found to be highly significant.

The final clinical diagnosis was arrived at for all the patients after a comprehensive, qualitative analysis of all the aforementioned parameters. The correlation between the clinical diagnosis and the definitive diagnosis (Histopathological report) was then analyzed. The accuracy of clinical pre-diagnosis was found to be 93.4% comparable to the study by Ozdas et al, where a statistically significant correlation

was seen between the clinical pre-diagnosis considered by ENT specialists and definitive histopathological diagnosis [13]. A strong and positive relationship was found between clinical pre-diagnosis and definitive histopathological diagnosis ($p < 0.01$).

Discordance was however observed in the thyroid lesions. Malignant thyroid lesions were identified in only 33% of the cases which were erroneously thought to be benign. This is in accordance with other studies [15,16] which indicate that it is difficult to differentiate between malignant and benign thyroid lesions based on clinical characteristic alone. In case of thyroid lesions, therefore, sensitivity of clinical diagnosis was only 33.3%.

The correlation between the FNAC and histopathological results was also analysed. It was observed that overall the sensitivity of FNAC in this study was 82.5% comparable to studies by Showkat et al (87.4%), Shrivastava et al with 88.64% and Suryawanshi et al with 81.81% [11,16,17]. In the study by Basista et al, 2015 sensitivity of FNAC was found to be 78.03% [8].

For thyroid lesions the sensitivity was only found 33.3%, with a positive predictive value of 100% comparable to the study by Basista et al. [8] where the sensitivity for thyroid swellings was 85.51% and specificity 100%. For lymphadenopathy the sensitivity was found to be 90% with a specificity of 100% in our study comparable again to that of Basista et al with a sensitivity of 83.33 and specificity of 100% [8]. This is in contrast with studies like Mobley et al, and Edward M et al, in developed countries which showed a much higher accuracy for FNAC, of 94.4% and 94.5% respectively [15,18]. This may be due to better facilities, expertise and

consistent use of guidance systems as compared to our setup, which being a teaching hospital in a developing country may show a wide variation in proficiency of the pathologists and varying use of guidance systems [19].

It should be noted that clinical pre-diagnosis is an amalgamation of the clinician's experience and a general qualitative analysis of all the aforesaid clinical parameters. These parameters are subject to the observer's judgement and liable to be inconsistent, prone to observer bias. Also the clinical parameters evaluated tend to lean towards suspicion of malignancy for any atypical features, which in turn leads to an increase in sensitivity for clinical diagnosis. Furthermore, this being a teaching hospital, there may be a wide variation in the expertise of the pathologist performing and/or reporting the aspiration cytology. Moreover, FNAC is usually performed from a representative area of the lesion/ representative node whereas histopathology evaluates the entire specimen sent (especially in cases of thyroidectomies and neck dissection specimens). This may lead to decrease in sensitivity and also an increase in false negative reports for FNAC.

Conclusion

Thyroid masses were mainly seen in females and metastatic lymphadenopathy in males. In females 87% of the neck masses were benign whereas amongst males 62%

were malignant. Accuracy of FNAC in comparison to the definitive diagnosis was 84.7%. Inconsistent use of guidance systems, inexperience of junior aspirators and aspiration from representative node/part of the lesion may act as confounding factors resulting in the discordance between clinical pre-diagnosis and FNAC accuracy with respect to the definitive diagnosis.

Acknowledgement

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Conflict of interest

There is no conflict of interests. All authors are equally contributed.

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Publication Ethics

The present study is ethically approved.

Authors

Contributions

“Conceptualization, V.K.P. and R.S.; methodology, V.K. and P.N.; validation, V.K.P. and R.S.; formal analysis, V.K.; investigation, V.K., V.K.P. and P.N.; resources, R.S.; data curation, V.K.; writing—original draft preparation, V.K.; writing—review and editing, R.S.; visualization, R.S.; supervision, V.K.P.; project administration, R.S.

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ORIGINAL ARTICLE

The histopathology of culture proven Melioidosis

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Abstract

Context: Melioidosis is a bacterial infection with high morbidity and mortality. Published literature on histopathological findings of melioidosis is sparse. **Aims:** To describe the histopathological findings in melioidosis. **Settings and design:** This is a retrospective observational study conducted at a tertiary care center in south India. **Materials and methods:** Histopathological findings of tissue samples from which *Burkholderia pseudomallei* was isolated in culture were analysed. **Statistical analysis:** The quantitative variables were expressed as frequency. **Results:** Histopathological findings in melioidosis were either acute (12 out of 18 samples), acute on chronic (5 out of 18 samples) and chronic (1 out of 18 samples). Granuloma was noted in 5 samples. **Conclusion:** Any acute or acute on chronic inflammation with or without granuloma in tissues from patients in endemic regions should raise the suspicion of melioidosis.

Keywords: Melioidosis, Histopathology, *Burkholderia pseudomallei*, Inflammation, Granuloma

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Graphical Abstract

The histopathology of culture proven Melioidosis Rajeshwari K Muthusamy, Deepak Thangaraju, Sangita S Mehta, Lavanya P			
Aim: To describe the histopathological findings of melioidosis.		Type of Inflammation	No of cases
Methods: This was a retrospective observational study with study period from January 2017 to December 2022. Histopathological findings of tissue samples from which <i>Burkholderia pseudomallei</i> was isolated in culture were analysed.	Acute	Organising	hip joint ,knee
			pleura
		Suppurative	Ilio psoas muscle
	hip joint, tibia, knee		
	D6/D7 spine		
	Necrotising	Soft tissue from Leg	
		Tibialis anterior muscle	
	Acute on chronic	Suppurative granuloma	Femur
			Spleen
			Soft tissue from Thigh
Non-specific	Cervical intramedullary abscess		
Chronic	Granuloma	Brain	

Introduction

Melioidosis, caused by environmental organism *Burkholderia pseudomallei* (*B. pseudomallei*) is endemic in southeast Asia and northern Australia [1]. The disease has a predicted global burden of 1,65,000 cases per year [1]. It has varied clinical presentation with high morbidity and mortality, as high as 50 percent [1]. The organism must be isolated in culture to confirm the diagnosis. In many instances the diagnosis is delayed even in countries like India where it is being increasingly reported in recent years [2]. It is not suspected in many situations therefore appropriate samples are not sent for culture on time. Even if cultures are done there are problems in identifying the organism due to the lack of experience and inaccuracy of the automated bacterial identification systems widely used in microbiology laboratories [3]. The

pathology findings of melioidosis are not well studied. There are only few published literature on this topic. Describing the pathology findings will help in early diagnosis and timely patient management. Therefore, this study was conducted to describe the histopathological findings (HPE) of melioidosis.

Methods

This was a retrospective observational study. The study was conducted in microbiology and pathology laboratory in a tertiary care center in south India. The study period was from Jan. 2017-Dec. 2022. Patients for whom *B. pseudomallei* was reported in culture were collected from microbiology laboratory records. Samples, collected from melioidosis patients, that were submitted for pathology and microbiology laboratory were identified from hospital information

system. Tissue samples from which *B. pseudomallei* was isolated in culture were included in the study. Aspirates sent for cytology and tissue samples from melioidosis patients that were not subjected to culture were excluded. Tissue samples were fixed in 10% buffered formalin and processed in automated tissue processor. The processed tissues were embedded in paraffin wax and 5-6-micrometer thick sections were cut and stained with haematoxylin and eosin. The slides were studied, and they were subjected to Gram stain, Ziehl-Neelsen stain, periodic acid-schiff and Grocott's methanamine silver stain wherever necessary. The HPE findings included in the study were verified by the authors and corrections were made after examining the slides retrieved from pathology archives. Clinical details of the patients were retrieved from the hospital records. Qualitative variables were summarised as frequency. This is a retrospective study with neither any contact between the researchers and patients nor any intervention. Hence consent was waived. The study was approved by the institute ethics committee (EC/AP/1032/04/2023).

Results

In the study period, *B. pseudomallei* was isolated in culture from 58 patients. Samples from which *B. pseudomallei* was isolated include blood, sputum, endotracheal aspirate, BAL, urine, CSF, tissues, aspirates and abscesses. Eighteen tissue samples from 15 patients were sent for histopathology examination. These were reviewed and included in the study.

Out of 18, 11 samples were from musculoskeletal system (4 from hip joint,

2 from tibia, 2 from knee joint, 1 from femur, 1 from tibialis anterior muscle and 1 from D6/D7 segment of spine), 2 from spleen, 2 from skin and soft tissue (1 from leg and 1 from thigh), 1 from pleura, 1 from brain and 1 from cervical vertebral intramedullary region (Table 1). The mean age group of patients whose HPE reports were included in the study is 52.6 years (13 years to 76 years). Except for one, all the patients were male. Among 15 patients, a sample from hip joint was given for histopathology twice for one patient and 3 samples were given for one patient (synovial tissue from knee, biopsy from tibialis anterior muscle and from medullary cavity of proximal tibia). One sample was given for histopathology from the other 13 patients.

HPE findings are either acute, acute on chronic or chronic inflammation. Twelve out of 18 samples had acute inflammation. Suppurative type was found in 5 samples, organising in 4 and necrotising in 3 samples (Figure 1). In one patient, the first sample from the hip joint showed acute organising inflammation (Figure 2) but the second sample from hip joint obtained twenty days later showed acute suppurative inflammation. In another patient, a sample from the left knee showed acute organising inflammation but samples from tibialis anterior muscle and tibia obtained twenty days later showed acute necrotising inflammation and acute suppurative inflammation respectively. Acute on chronic inflammation was found in 5 samples out of which Suppurative granuloma (Figure 3) was seen in 4 samples, and nonspecific inflammation in one sample. Chronic granulomatous inflammation (Figure 4) was found in one sample.

Table 1. Inflammatory response pattern of melioidosis in various biopsy samples.

Type of Inflammation		Site of Biopsy	Number of cases
Acute	Organising	hip joint	2
		knee	1
		pleura	1
	Suppurative	Ilio psoas muscle	1
		hip joint	1
		Tibia	2
		D6/D7 spine	1
		Knee	1
	Necrotising	Soft tissue from Leg	1
		Tibialis anterior muscle	1
Acute on chronic	Suppurative granuloma	Femur	1
		Spleen	2
		Soft tissue from Thigh	1
	Non-specific	Cervical vertebral intramedullary abscess	1
Chronic	Granuloma	Brain	1

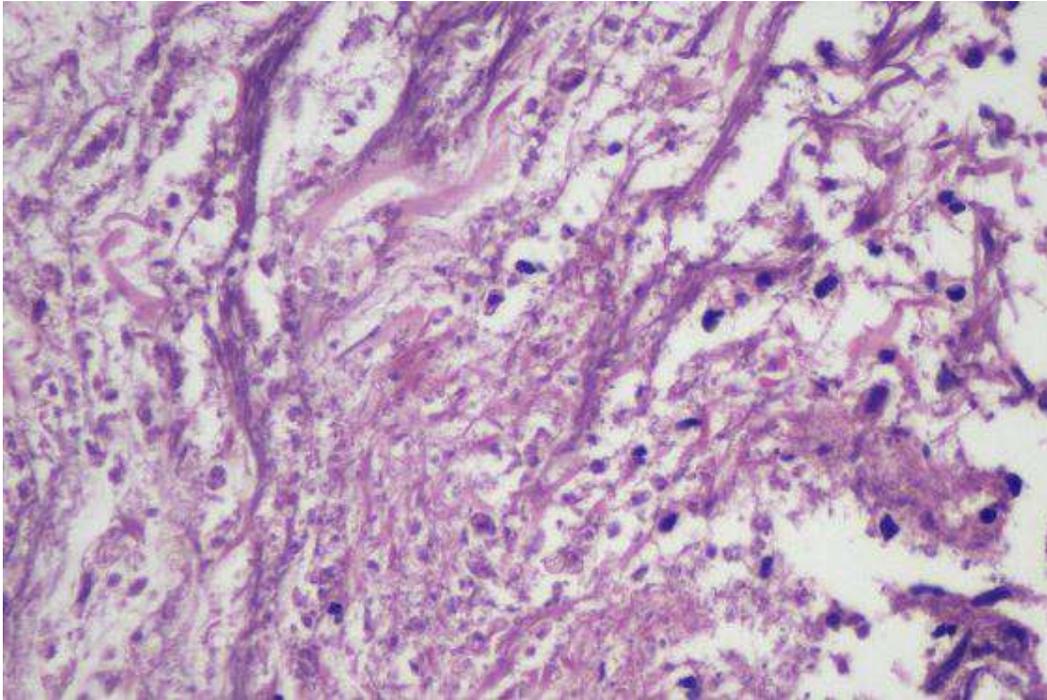


Figure 1: Muscle tissue with necrotising inflammation (H&E 40X).

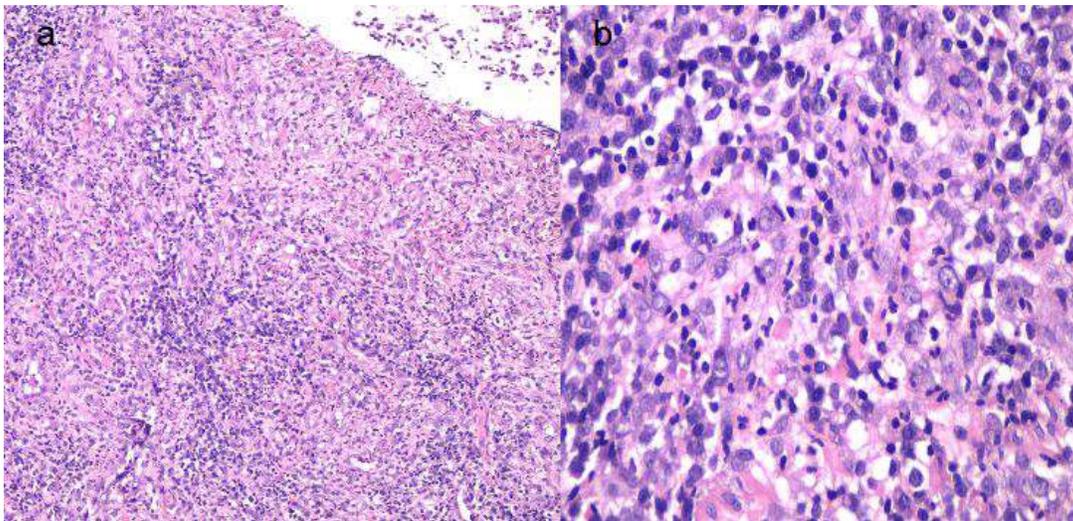


Figure 2a: Cervical vertebral intramedullary tissue with organising inflammation (H&E 10X).
2b granulation tissue with mixed inflammatory cells (H&E 40X).

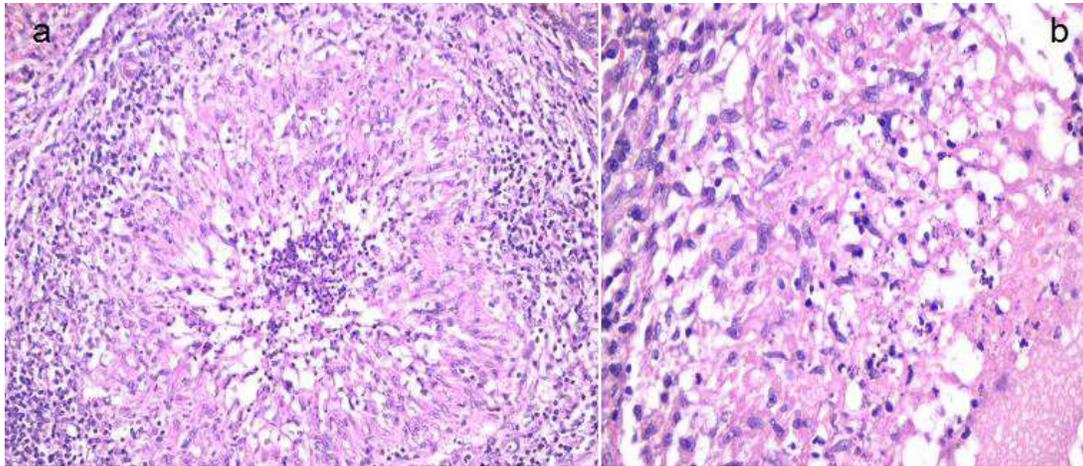


Figure 3a: Spleen with suppurative granuloma (H&E 10X). 3b Granuloma with palisade of histiocytes and central neutrophilic aggregates (H&E 40X).

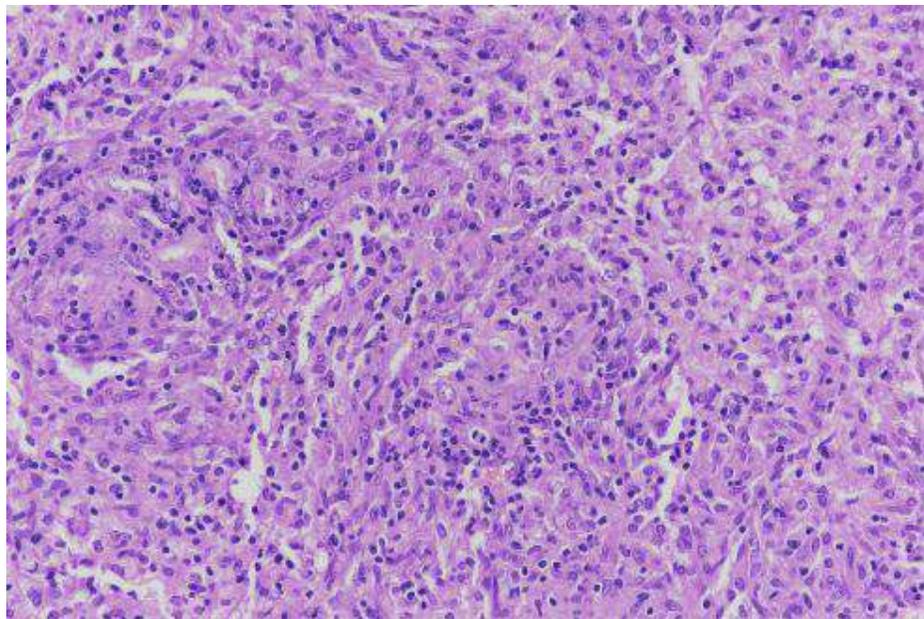


Figure 4: Glial tissue with non-necrotising granuloma (H&E 10X).

Samples with acute inflammation showed sheets of neutrophils forming abscess surrounded by foamy macrophages and mononuclear cells. Granulation tissue with activated fibroblasts were noted in organised foci of inflammation. In addition to mixed

inflammatory cells, aggregates of foamy macrophages and epithelioid histiocytes were seen forming granuloma indicating chronicity in 4 of the cases with acute on chronic inflammation. Histiocytic aggregates were predominantly indistinct with central neutrophilic collections

forming suppurative granulomas. Multinucleated giant cells were seen in 3 cases and were occasional in number. Two of the cases had Langhan type giant cell and the other had an irregular outline of the giant cell. A case with brain biopsy showing chronic inflammation had sheets of epithelioid histiocytes and lymphocytic cuffing around vessels. Giant cells and necrosis were not seen.

Gram stain was available for 9 of the cases, of which 6 highlighted gram-negative bacilli, 2 in cases with acute inflammation, one in chronic inflammation and 3 in suppurative granuloma. These bacilli were seen extracellularly and were singly dispersed. Stains for acid fast bacilli and fungi were negative in cases with granuloma.

Majority of the patients had multifocal disease (8/15) and comorbid conditions like Diabetes (9/15). Seven patients needed intensive care during the hospital stay. Three of the 9 patients with acute suppurative/ necrotising/ organising inflammation succumbed to the disease.

Discussion

HPE findings in melioidosis in our study are acute inflammatory response predominantly (12 out of 18) which is either organising, suppurative or necrotising, Acute on chronic in few (5 out of 18) and rarely chronic (1 out of 18). Clinical details of the patients including duration of illness and antibiotic treatment which might influence the type of inflammatory response in the tissue is not analysed in the study. Gram stain is not available for some of the samples. The number of samples included in the analysis is only 18 in spite of many culture proven melioidosis cases during the study period.

This is because either samples were not subjected to histopathology, or the samples sent to histopathology were not cultured.

There is scarcity of literature on HPE findings in human melioidosis. Wong *et al* had described HPE findings in autopsy and surgical biopsy specimens from human melioidosis cases [4]. Like our study, the findings noted by them ranged from acute inflammation to acute on chronic and chronic inflammation with focal to diffuse granulomas. The findings are not specific for any organ or tissue. Histopathology presentation of melioidosis is no different from other infectious aetiology.

Most of the samples in our study are from musculoskeletal system (11 out of 18 samples). But in Wong *et al* study out of 14 surgical biopsy specimens only one is from synovium [4]. Among various organ systems affected in melioidosis, musculoskeletal system is one of the common systems affected in our country [5]. In our study, 91% of the inflammatory response in musculoskeletal system are acute in nature. In a study done by Perumal *et al*, like our study, 80% of the samples from musculoskeletal system in patients with melioidosis showed acute inflammation [6].

Granuloma is noticed in 28% of our samples. But Wong *et al* noticed granuloma in about 50% of surgical biopsy samples in melioidosis [4]. In our study only one sample from musculoskeletal system (9%) had granuloma whereas Perumal *et al* noticed granuloma in 3 out of 15 (20%) musculoskeletal samples from melioidosis patients [6]. Type of host response could depend on the virulence of the organism and immune status of the individual [4]. Three of our samples had a

few giant cells. It is similar to the findings noticed by Wong *et al* in surgical biopsy specimens [4]. Brain biopsy of the patient presenting as acute demyelinating encephalomyelitis included in our study showed chronic inflammation with well-defined granuloma as evidenced by Shimee Ekka *et al.* [7]. Twenty-eight percentage of samples in our study had acute on chronic inflammation. Wong *et al* and Brundage *et al* had described similar findings in their study [4,8].

We could demonstrate gram negative bacilli in 6 out of 9 cases. Three out of four cases with suppurate granuloma shows gram negative bacilli. We could not identify the bacilli in giant cells as described by Wong *et al* in his study, in which numerous gram-negative bacilli was noted to resemble globi from autopsy samples[4]. In contrast, occasional bacilli seen in our study may be due the fact that all our samples are surgical biopsy samples and not from autopsy. Since Gram stain to demonstrate the bacilli is difficult in biopsy samples, immunohistochemical staining using antibodies targeting the capsular

polysaccharide of *B. pseudomallei* will be useful in cases of diagnostic dilemma [9]. In our study, patients with acute inflammation on histopathology, multifocal disease, comorbidities and need for intensive care had poorer outcome.

Conclusion

Any acute inflammation or acute on chronic inflammation with or without granuloma in tissues biopsied from patients in endemic areas should raise the suspicion of melioidosis. An attempt to demonstrate the organism by gram stain is suggested. Specialised staining techniques with better sensitivity like fluorescent acridine orange can be studied to demonstrate the bacilli. Immunohistochemistry using specific monoclonal antibodies may help in diagnosis[9,10]. This will enhance timely patient management.

Conflict of Interest

The authors declares that the authors do not have conflict of interest

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ORIGINAL ARTICLE

Desarda's Tissue Repair: An Efficient and Affordable Alternative to Mesh repair for Inguinal Hernia

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Abstract

Tension-free mesh repair is standard for inguinal hernia in high-income regions despite limitations like chronic pain and costs. This study assessed whether Desarda's tissue-only repair can offer an affordable yet effective option. 250 inguinal hernia patients underwent Desarda repair during 2015-2020 at an Indian rural hospital. Outcomes like operative duration (mean 47.3 min), recovery (discharge by day 3), pain resolution (VAS declined from 3.8 to 0 over 6 months), return to work (median 6 days), complications (~4%) and recurrence (0% over 30 months) after Desarda repair matched or exceeded mesh repair standards. Our data establishes it as a simplified tension-free physiology-restoring hernia cure that can expand surgical capacity affordably. Guideline-based evaluation via implementation research is warranted before global use recommendations.

Keywords: Inguinal Hernia, Desardas Repair, complications, clinical outcomes, cost effective

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Graphical Abstract

Desarda's Tissue Repair: An Efficient and Affordable Alternative to Mesh repair for Inguinal Hernia
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Aims & Objectives:
To assess efficacy of Desarda's tissue repair for inguinal hernia. Primary Objective is to find out if Desarda's repair is as efficient as Mesh Hernia repair and Can it be affordable alternative to it.

Material and Methods:
Study Design & Participants : Prospective cohort study of adult males undergoing primary unilateral Desarda inguinal hernia repair from 2018-2022. Surgical Technique : Standard open herniotomy/ posterior wall repair followed by external oblique aponeurosis suturing to ligament/muscles to reconstruct posterior wall sans tension/mesh. Outcomes Assessed : 1) Intraoperative duration 2) Postoperative recovery - early pain (VAS), chronic pain, stay 3) Return to normal work 4) Early complications 5) Recurrence (clinical exam)

Results:
Total Patients : 250, Age Range 22-78 years, Mean Age 53 years Mean Operative Duration was 47.3 minutes, Operative Duration Range 32-72 minutes, Average Hospital Stay-3.2 days, Hospital Stay Range 2-6 days, Analgesia by Day 2-82%. The self-reported pain experienced by patients significantly reduced from a mean of 3.8/10 at 24 hours' post-operation to 0.2 at 1 week, further decreasing to 0.1 at 1 month and eventually becoming negligible beyond 3 months. This is a significant reduction (p<0.01). By the tenth postoperative day, 94% of patients reported a return to their regular activities. The median time for this return was 6 days. Regarding complications, they were mostly minor and managed conservatively. These included hematoma (3.4%), necrosis (2.8%), and surgical site infection (2.7%). No patient had recurrence, chronic pain or testicular symptoms over mean 30 months follow-up.

Illustration of Desarda's technique

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Conclusions
Desarda repair clinical outcomes continue showing enduring promise on benchmarks of safety, early recovery, non-recurrence and lack of chronic morbidity over time/years paralleling publications on current gold standards. Our data substantiates its potential efficient applicability for addressing high hernia burden in resource-constrained regions through frugal technique equipment and training to bridge access gaps. Structured implementation research can pave the road next to assess real-world health system integration prior to promoting alongside established methods.

Introduction

With over 20 million inguinal hernia repairs performed annually, it remains the most common general surgery intervention worldwide [1]. Mesh reinforcement popularized by Lichtenstein's 1989 technique [2] rapidly emerged as the standard approach given reduced recurrence. However, chronic pain, costs, non-availability in low-resource settings and affordability concerns have challenged its universality [3,4]. Alternate options like laparoscopic repair also remain restricted due to infrastructure needs and specialist dependence [5,6].

The need for simplified affordable hernia surgery fuels interest in tissue-based repairs globally [7-9]. Desarda's technique uses only external oblique aponeurosis to reconstitute inguinal canal physiology without tension or mesh [10]. Beyond prior smaller studies showing promising results [11], larger multi-center implementation is

vital to assess broader reproducibility, safety and efficacy before guideline endorsement and universal adoption consideration as a frugal alternative where mesh limitations preclude care [12].

We analyzed outcomes from 250 Desarda repairs over 4 years at an Indian rural hospital to gather further evidence regarding its potential efficiency gains for expediting hernia surgery access in underserved regions struggling with high disease burdens.

Methods

Study Design & Participants: Prospective cohort study of adult males undergoing primary unilateral Desarda inguinal hernia repair from 2018-2022.

Surgical Technique: Standard open herniotomy/ posterior wall repair followed by external oblique aponeurosis suturing to ligament/muscles to reconstruct posterior wall sans tension/mesh (Figures 1 and 2).

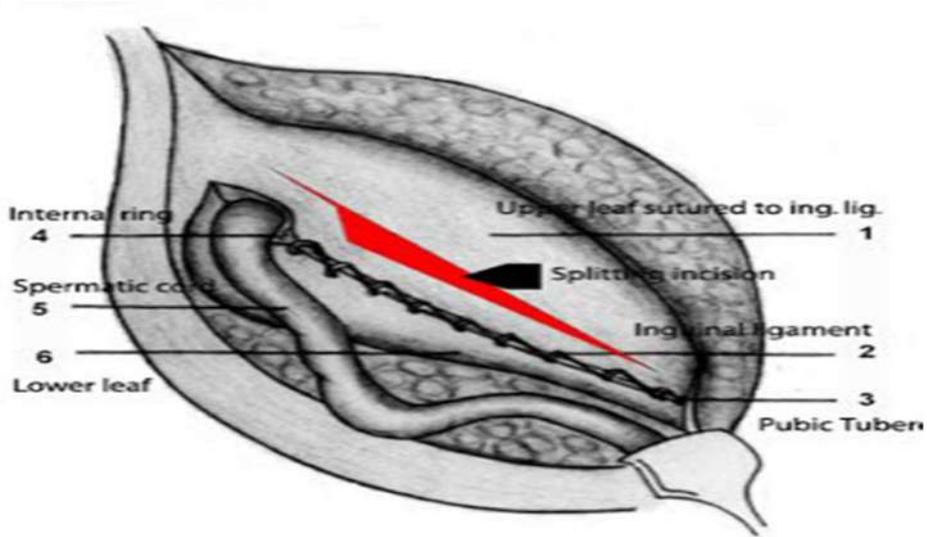


Figure 1. The medial leaf of the external oblique aponeurosis is sutured to the inguinal ligament and a splitting incision is taken. 1=Medial leaf; 2= Interrupted sutures taken to suture the medial leaf to the inguinal ligament; 3= Pubic tubercle; 4= Abdominal ring; 5=Spermatic cord; and 6= Lateral leaf.

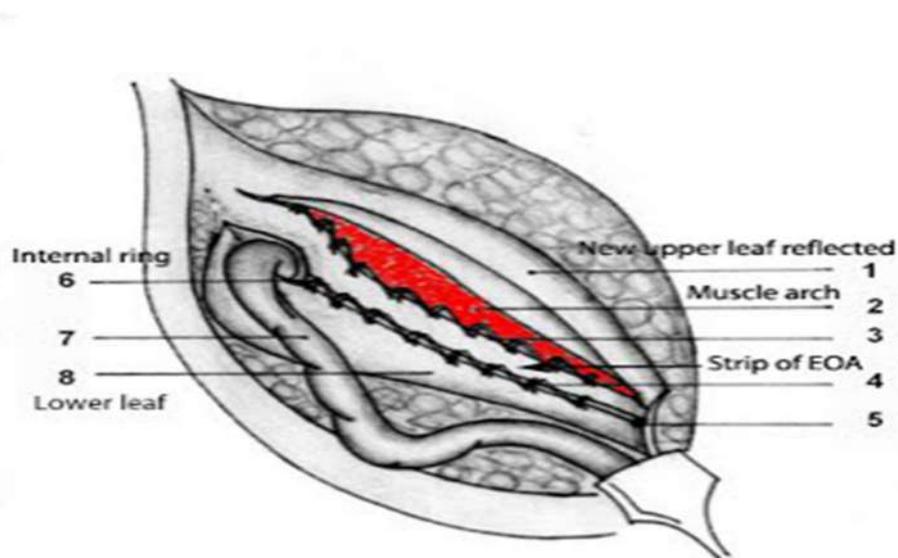


Figure 2. Undetached strip of external oblique aponeurosis forming the posterior wall of inguinal canal. 1=Reflected medial leaf after a strip has been separated; 2= Internal oblique muscle seen through the splitting incision made in the medial leaf; 3= Interrupted sutures between the upper border of the strip and conjoined muscle and internal oblique muscle; 4=Interrupted sutures between the lower border

Outcomes Assessed:

- 1) Intraoperative duration
- 2) Postoperative recovery - early pain (VAS), chronic pain, stay
- 3) Return to normal work

- 4) Early complications
- 5) Recurrence (clinical exam)

Analysis was done using SPSS v25 and $p < 0.05$ defined significance.

Results

Patient Demographics and Procedure Details:

Parameter	Value
Total Patients	250
Age Range	22-78 years
Mean Age	53 years
Procedure	Desarda repair
Laterality - Left	43.7%
Laterality - Right	56.3%
Indirect Hernia	68%
Mean Operative Duration	47.3 minutes
Operative Duration Range	32-72 minutes
Average Hospital Stay	3.2 days
Hospital Stay Range	2-6 days
Ambulation by Day 2	82%

The self-reported pain experienced by patients significantly reduced from a mean of **3.8/10** at **24 hours**’ post-operation to **0.2** at **1 week**, further decreasing to **0.1** at **1 month**

and eventually becoming negligible beyond **3 months**. This is a significant reduction ($p < 0.01$).

Time Frame	Self-Reported Pain (Mean)	Patients with VAS \geq 4 (Number)	Return to Regular Activities (Number)
24 hours	3.8	11 (4.2%)	-
5 days	1.2	2 (0.8%)	50
1 week	0.2	0	177
10 days	0.2	0	235
1 month	0.1	0	250
3 months	0	0	250

By the tenth postoperative day, **94%** of patients reported a return to their regular activities. The median time for this return was **6 days**.

Regarding complications, they were mostly minor and managed conservatively. These included **hematoma** (3.4%), **seroma** (2.9%), and **surgical site infection** (2.7%).

No patient had recurrence, chronic pain or testicular symptoms over mean 30 months follow-up.

Discussion

Our data provides large volume single-center evidence substantiating the proposed benefits regarding operative efficiency, short hospital stay, early recovery and low pain for non-mesh Desarda repair published earlier [11,13]. The clinical outcomes and patient-centered metrics assessed match and exceed indicators from landmark trials that have shaped many gold standards for open mesh and laparoscopic approaches internationally [14–16].

Notably, despite considerable follow-up spanning over 2500 patient-years in our cohort, no instances of debilitating chronic groin pain or repeat surgery need occurred unlike 5-15% risk with mesh methods which can worsen quality of life while escalating costs for health systems especially public funded ones [3,17–19]. Advantages like technical simplicity, non-reliance on special tackers/fixators and less imperative for intensive training highlight the potential amenability for widespread generalizability even at secondary facilities where specialized expertise remains limited in poorer regions [7,20].

However, our study provides only single center data subject to inherent limitations of the observational design with lack of head-to-head comparison to reference standards or alternative tissue repairs [21,22]. Chronic pain assessments also relied predominantly on clinical exam rather than quantified psychometric data. Further phased evaluation is therefore vital via pragmatic controlled trials from varied settings and surgeon cadres prior to guideline endorsements. Exploring impact on learner curves, patient selection optimization, cost-benefits and implementation barriers assuming significance as the logical next steps [23,24].

Conclusion

In summary, Desarda repair clinical outcomes continue showing enduring promise on benchmarks of safety, early recovery, non-recurrence and lack of chronic morbidity over timeframes paralleling publications on current gold standards. Our data substantiates its potential efficient applicability for addressing high hernia burden in resource-constrained regions through frugal technique equipment and training to bridge access gaps. Structured implementation research can pave the road next to assess real-world health system integration prior to positioning alongside established methods.

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CASE REPORT

Death Due to Phenytoin Poisoning in an Intellectually Disabled Female Child: A Case Report

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Abstract

Phenytoin is a commonly used anticonvulsant, but its narrow therapeutic window can lead to toxicity, often due to medication errors or, in some cases, due to intentional overdose. In this article, we present a case of a 12-year-old intellectually disabled female child, who was on phenytoin treatment for seizure disorder and accidentally ingested about 10-15 pills, resulting in fatal toxicity and death. The child presented with a few episodes of vomiting; seizures, followed by respiratory depression before succumbing to the overdose. This case highlights the importance of drug regulators ensuring safe manufacturing practices for medications used in chronic conditions like seizure disorder to prevent unintentional poisonings. At the same time, it is the responsibility of health care professionals, both clinicians and pharmacists to educate the caregivers of children about the hazards of accidental drug poisoning in children.

Keywords: Phenytoin, Intellectual disability, Paediatric toxicity, Female child.

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Introduction

Phenytoin (5,5 diphenyl-2,4-imidazolidinedione), a derivative of hydantoin is a commonly used anticonvulsant in neurology practice across all age groups since several decades. It is a voltage-gated sodium channel blocker that extends the neural refractory period by maintaining the sodium channel's inactive state. Phenytoin exerts its effect by acting on sodium channels of heart and brain [1]. Phenytoin exhibits a narrow therapeutic range of 10 -20 mg/L, which is a matter of concern during its prescription [1]. Phenytoin induces Cytochrome P450 2C (CYP2C), Cytochrome P450 3A (CYP3A), and UDP-glucuronosyltransferase (UGT) enzyme systems in humans [2].

The pharmacokinetics (ADME) of phenytoin is nonlinear or saturable, which implies that a slight rise in plasma concentration may lead to drug-induced toxicity due to its saturable enzyme metabolism [3,4]. During an incident of acute phenytoin overdose, the metabolic enzyme systems may get saturated, and the clearance of the drug may be akin to zero order kinetics. The plasma protein binding of phenytoin ranges from 90-95%. The drug distribution is rapid from blood to the tissues and is almost completely metabolized in the liver. The plasma phenytoin concentration normally reaches the steady-state level within 1-2 weeks of drug initiation. The half-life of phenytoin is less than 20 h in low doses, but is prolonged in high doses, newborn infants, and elderly people.

Based on the 2011 Annual Report of the American Association of Poison Control Centres (AAPCC), National Poison Data System, it was found that there were a total of 1971 instances of single-substance phenytoin exposures. Out of these

exposures, there were 46 cases that resulted in serious consequences and only one fatality occurred [5]. Unfortunately, there is no poison incident data reporting system in our country which is very much necessary for policy makers and regulatory authorities in preventing poisoning deaths in general.

As per published literature, phenytoin poisoning may arise as a consequence of medication/dosing errors, deliberate poisonings, drug interactions leading to compromised elimination, or failure to adhere to prescribed dosages (compliance issues), inadvertent consumption by children, increased vulnerability of geriatric population (due to compromised hepatic metabolism and renal elimination), all of which can result in elevated concentrations of the drug within the body and end up in fatal outcomes [1].

Case report

A 12-year-old girl child was brought to our institute by her mother with alleged history of consumption of 10-15 phenytoin pills (later discovered to be 100mg each, the total overdose supposedly ranged between 1g to 1.5g) when the child was alone at home. The patient was a clinically diagnosed case of Global Developmental Delay with seizure disorder. She had been using phenytoin for the past five years and the history of use of other drugs was not available. She was referred to our hospital after initial decontamination and management of seizures at another secondary care facility (However, the data pertaining to use of activated charcoal for initial decontamination was not available). After her accidental overdose, she had 5-6 episodes of vomiting which contained food particles and tablets. The vomiting was nonprojectile and nonbiliary in nature.

There was no history of pain abdomen, seizure like behaviour, fever, respiratory distress, or any bleeding diatheses in the recent past. The antenatal and postnatal history of child was uneventful, and child was born out of a non-consanguineous marriage. Her childhood immunization was incomplete and complete data of the same was not available.

During the initial evaluation, her weight was of 20 kg, heart rate of 140 beats per minute, respiratory rate of 26/min, afebrile, Spo₂ 96% with room air, and a blood glucose level of 166 mg/dL; CNS: Deep Tendon Reflexes were brisk in nature, CVS: S1 and S2 were present, RS: Normal vesicular breath sounds were present; GIT: P/A was soft and no organomegaly was noted. Clinical chemistry is as follows, RFT: S. Creatinine 0.8 mg/dL and Blood urea: 36 mg/dL. LFT: Serum bilirubin (total): 0.6 mg%, (direct): 0.2 mg%, (indirect): 0.4%; SGOT: 113 IU/L, SGPT: 21 IU/L, S. Alkaline Phosphatase: 316 IU/L. CBP: Hb: 13 g%, TLC: 16,400 cells/cu mm, Platelets: 4.40 lakh/cu mm, DC: Neutrophils: 80, Lymphocytes: 18, Monocytes: 2, Eosinophils: Nil, Basophils: Nil; PCV: 43%. The patient was admitted in ICU where initial fluid resuscitation was given along with supplemental oxygen, IV antibiotics and IV sedation to control the irritability/seizures. The critical event that led to cardiac arrest was respiratory depression in this case. The child slowly decompensated with decreased respiratory drive which led to a cardiac arrest. The

child could not be saved in spite of attempting mechanical ventilation due to failure in achieving return of spontaneous circulation. Serum/Blood phenytoin level was not evaluated. The pharmacogenomics data pertaining to phenytoin metabolism was unavailable in the medical records.

At autopsy, the child appeared ill built and was severely malnourished, and teeth showed a brownish discoloration and gum hypertrophy was noticed. Additionally, all internal organs were intensely congested. The stomach contained about 50 ml of yellow colour fluid, which lacked any distinct odour, and the mucosa appeared congested. Heart, lungs, spleen, kidney, and liver did not show any gross abnormality. Phenytoin was detected in the contents of the stomach, small intestine, blood, liver, and kidney through chemical analysis of the viscera at the Regional Forensic Science Laboratory. The histopathological examination of the liver and kidney (Figures 1 and 2) revealed no pathological abnormalities. The quantitative analysis of phenytoin was not available. Although liver did not show any pathology at autopsy, a raise of liver enzymes was noticed in clinical chemistry along with a mild elevation of TLC. The cause of death in this case was opined as phenytoin poisoning. The total period of survival after ingestion was about 30-36 hours. However, the child was admitted at our facility about 15 hours prior to death.

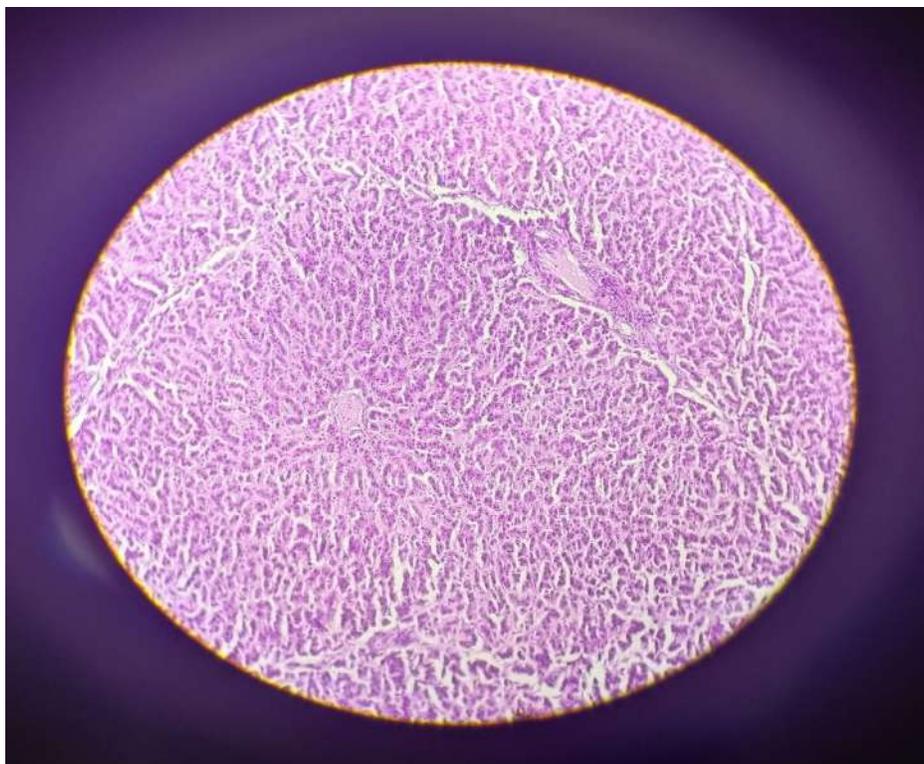


Figure 1. Histopathological examination of liver (Photomicrograph), H & E, Scanner View, within normal limits



Figure 2. Histopathological examination of Kidney (Photomicrograph), H & E, Scanner View, within normal limits.

Discussion

Phenytoin poisoning can present in many forms, namely acute, subacute, or chronic, and is characterized by a range of clinical manifestations. Neurological manifestations of acute phenytoin toxicity include hyperreflexia or hyporeflexia, aberrant gait, encephalopathy, and rarely seizures. The mental state of an individual can vary along a spectrum, ranging from a state of normal functioning to a state of coma, particularly when there is concurrent ingestion of other CNS depressants. The ophthalmic manifestations of toxicity include nystagmus, ophthalmoplegia, diplopia, and alterations in pupil size. The chronic toxicity of this substance has the potential to result in peripheral neuropathy, priapism, urine incontinence, choreoathetoid movements, dysarthria, dysphagia, and, in rare instances, mortality [4]. The dermal manifestations of toxicity include hirsutism, acne, jaundice, periorbital or facial oedema, erythema multiforme, skin rashes, etc. The overdose of phenytoin has been linked to the development of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, a profound hypersensitivity reaction that typically manifests 2 to 6 weeks following exposure. The symptoms encompass a range of manifestations, such as fever, rash, lymphadenopathy, hepatitis, myocarditis, and various systemic presentations [1].

The intravenous formulation of the medication may lead to cardiovascular adverse effects, including hypotension, bradycardia, and ventricular arrhythmias [1,6]. The occurrence of Purple Glove Syndrome, which is characterized by the presence of limb oedema, discoloration, and pain subsequent to intravenous

delivery, has been observed in certain instances.

Gastrointestinal and abdominal manifestations may encompass discomfort localized in the right upper quadrant, as well as symptoms such as nausea and vomiting. Phenytoin is known to cause hepatosplenomegaly and hepatitis. The prolonged exposure to phenytoin can result in chronic toxicity, which has been associated with the development of metabolic disorders such as osteomalacia and hypothyroidism [6]. The adverse effects associated with phenytoin toxicity include cognitive impairment, perceptual disturbances, peripheral nerve damage, increased risk of falls, cerebellar dysfunction, loss of bladder control, abnormal movements, priapism, skin rash, and the development of foetal hydantoin syndrome if the medication is used during pregnancy. This syndrome is characterized by a range of congenital anomalies, including distinctive facial features, ears positioned lower than average, dislocation of the hip joint, and congenital heart problems [4,6].

Fatalities resulting solely from the intake of phenytoin are infrequent. The majority of documented cases entail the consumption of other drugs in conjunction with phenytoin. In instances where individuals have ingested a single dose of phenytoin, fatal outcomes are commonly associated with blood values exceeding 125 mg/L [1]. The treatment in such instances is decided on a case-to-case basis. Patients who need ventilatory support, patients who are hemodynamically unstable, or patients who have abnormal electrocardiograms (ECGs) should be admitted to a monitored setting. Patients presenting with mild to moderate overdoses, exhibiting normal cognitive function, displaying normal

electrocardiograms (ECGs) without any signs of hypotension, bradycardia, or arrhythmias, may be admitted to a hospital bed without the need for continuous cardiac monitoring [1,4,5].

It is recommended to monitor serum phenytoin levels at timely intervals after poisoning for proper management of a case. In order to achieve a precise evaluation of phenytoin concentrations in an instance of over dose scenario, it is important to consider both the bound and unbound forms of the drug present in the bloodstream and factors influencing the availability of free drug like other drug interactions. It is imperative that those who have intentionally overdosed undergo a psychological assessment during their hospitalization to prevent further suicide attempts [1].

Paediatric and adult phenytoin poisoning cases are not much different with respect to clinical manifestations, while the cardiac arrhythmias/manifestations component is an additional consideration in adults. Rapid intravenous injection of phenytoin can cause acute myocardial depression and cardiac arrest due to solvent propylene glycol associated toxicity. In paediatric age group accidental ingestion of pills is the most common cause of poisoning due to pharmaceutical substances. However, since there are a number of "single pill killers", the paediatrician should always be wary about homicidal poisoning in children. The lack of a proper history from the caregivers is one of the important challenges faced in the paediatric ER while dealing with poisoning cases.

A case in literature highlighted the occurrence of encephalopathy in a 7-year-old child due to a medication error involving the double dosing of intravenous

phenytoin. Such incidents underscore the high chances of medication errors with drugs like phenytoin [7]. Furthermore, brain-damaged mentally retarded epileptics appear to be unusually susceptible to the side effects of phenytoin [8]. Although death due to phenytoin toxicity alone is less frequent, the factors which can lead to death are concomitant ingestion of other drugs (drug interactions), increased genetic susceptibility (viz. cytochrome P450 2C9 poor metabolizer) and preexisting health conditions/co morbidities of the victim [9]. For patients diagnosed with epilepsy, along with intellectual disability, susceptibility to balance disturbances, and cognitive dysfunction, it may be advisable to consider substituting phenytoin with an alternative medication like carbamazepine or oxcarbazepine [8].

The treatment protocol in the event of phenytoin over dose as suggested in literature include gastric decontamination with activated charcoal if the victim presents within one hour of ingestion. Multiple dose activated charcoal is also administered every 2-6 hours until passage of charcoal stools, loss of bowel sounds or improved clinical condition [10]. Owing to the albumin binding ability of phenytoin, the results associated with hemoperfusion, and haemodialysis is equivocal [11]. Irrespective of above stated information, adequate hydration, maintaining of airway, breathing and circulation and other supportive care is paramount in management of phenytoin toxicity. It is also documented that phenytoin could induce status epilepticus and managing the same is also a part of the treatment [12].

Preventing accidental poisoning in children with drugs like phenytoin involves a combination of measures aimed at both proper manufacturing of these drugs and

education of stake holders. The use of child-resistant packaging for medications, particularly for drugs with a narrow therapeutic index like phenytoin (which are usually manufactured as bottles of capsules), can significantly reduce the risk of unintentional ingestion. These packages are to be designed in a way that it would be difficult for young children to open but could be easily opened by adults (packaging with force functioning). Clearly printed dosing guidelines on the packaging, including instructions on how to administer the medication safely in the local language apart from English, can help caregivers avoid dosing errors. A thorough review of treatment undergone in the previous healthcare facility should be considered before administering drugs like phenytoin. In the Indian context, there is a pressing requirement for substantial improvements in drug packaging and labelling, bringing them up to the standards observed in Western countries.

Healthcare professionals, both clinicians and pharmacists should educate patients and caregivers about the importance of keeping medications out of the reach of children, storing them securely, and using proper dosing devices (especially in liquid formulations). This education should also emphasize the potential dangers of even small medication overdoses/errors. The manufacturers could make medications less appealing to children by avoiding attractive colours, shapes, or flavours that might tempt them to ingest the medication. There is also a need to promote safe disposal of unused and expired medications to avoid accidental ingestion and environmental contamination. Launching public awareness campaigns to educate parents and caregivers about the risks of unintentional medication poisoning in

children and the steps they can take to prevent it is also necessary in this regard.

From the medicolegal standpoint, all clinicians and pharmacists must be aware of the potential dosage and medication errors possible with drugs like phenytoin (because it is also an enzyme inducer) and its ramifications in litigation [13]. Nevertheless, it is worth mentioning that there were some 'DILANTIN' related law suits in the USA few years ago about the issue of liability of drug manufacturers pertaining to risk communication about the potential adverse effects of phenytoin like Steven Johnson Syndrome (SJS), Toxic Epidermal Necrosis (TEN), Cerebellar atrophy, birth defects in the offspring etc.

From a forensic pathologist perspective, during autopsy in a case of phenytoin poisoning, it is advisable to look for the presence of any myocardial fibre disarray or/and interstitial fibrosis in the heart. The findings due to toxicological onslaught on the liver and kidney are also of academic interest albeit they are non-specific. Although literature did not hint towards any homicidal phenytoin poisoning incidents, it is necessary to be prepared for such situations which could always be possible in vulnerable groups like elderly and children.

In brief, the manifestation of phenytoin poisoning encompasses a diverse range of clinical presentations that impact several organ systems, underscoring the urgency of timely identification and intervention in instances of toxicity. By the same token, the present case is a classic example emphasising timely tertiary care in poisoning management. This highlights the requirement for the establishment of poison control centres to educate primary care physicians on handling poisoning cases and

facilitate the timely transfer of these cases to tertiary care centres.

Conclusion

In summary, the narrow therapeutic index of phenytoin warrants the significant attention of healthcare professionals regarding the potential for toxicity. This is crucial not only in terms of therapeutic considerations but also in instances of intentional or unintentional overdosing situations, particularly among paediatric patients. The main focus of treatment is primarily centred on providing supportive care, as there is no specific antidote available as of now. In order to improve safety measures to prevent deaths due to drug overdose, it is advisable for regulatory bodies responsible for drug control to

contemplate the implementation of rigorous packaging and labelling protocols for pharmaceuticals administered for chronic medical conditions in the paediatric age group.

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CASE REPORT

Rare Case: CNS Candidiasis with CKD in Neonate

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Abstract

Background: Candida infections are a common cause of mortality and morbidity in NICU. 70% of neonates with systemic fungal infection develop brain abscess. Candidiasis can involve the renal cortex resulting in impairment of renal function. **Clinical Description:** A neonate presented with features of severe dehydration on Day 16 of life with chief complaints of loose stool and vomiting, weight loss was of 24% Baby was exclusively breastfed. Lab inv was s/o severe metabolic acidosis with raised urea and creatinine. MRI Brain s/o fungal abscess. USG KUB s/o B/L small shrunken Echogenic Kidney so a diagnosis of CKD was made. **Management:** Baby was mechanically ventilated due to respiratory distress and FFP transfusion was given due to deranged PT/INR and inotropes were started. Dehydration and sodium bicarbonate correction was given. Antibiotics were started Antifungals (Amphotericin B and Fluconazole were started). **Conclusion:** Candida albicans is the most common fungal infection that is seen among late onset fungal sepsis. In disseminated Candidiasis, kidneys are most commonly involved followed by brain. Thus, becomes very crucial to have an early diagnosis of disseminated candidiasis for better prognosis.

Keywords: Candida albicans, Disseminated Candidiasis, CKD, Fungal Abscess

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Defining CKD in Neonate

Chronic Kidney Disease (CKD) can affect all irrespective of age, gender and ethnicity. But there are certain differences in definition of CKD in neonates. Specifically, the criterion established by KDOQI (Kidney Disease Outcomes Quality Initiative) [1] and expanded by KDIGO (Kidney Disease: Improving Global Outcomes) [2] that the 3 months duration of kidney disease is not applicable to neonates. The diagnosis of CKD in the neonatal period is typically made a prior on the basis of renal USG. Firstly done in the prenatal period and repeated soon after birth, reveals altered renal architecture or a significant urological abnormality with abnormal kidney functions. Neonates may develop AKI shortly after birth because of perinatal asphyxia, hypoxia, sepsis, or hypovolemia also have long-standing kidney damage and eventually develop CKD. The most common etiologies are renal hypoplasia/dysplasia, posterior urethral valves [3], and other congenital anomalies of the kidney and urinary tract including polycystic kidney disease, cortical necrosis, and renal vascular thrombosis. Wedekin and colleagues [4] estimated a CKD incidence of 1:10,000 in a single center retrospective analysis of infants younger than 1 year with a serum creatinine level greater than 1.13 mg/dL (100 mmol/L), gender distribution (male-to-female ratio of 2.8) was expected because of the male dominated contribution of obstructive uropathy (e.g, posterior urethral valves) as a common cause of CKD.

Candidal Brain Abscess

Brain abscess is a focal pyogenic infection of the brain parenchyma. Fungal brain abscesses are relatively less frequent. Various risk factors contributing to fungal brain abscess include LBW, Prematurity, Immunodeficiency states, Prolonged ICU

stay and prolonged ventilation, Extensive use of broad-spectrum antibiotics, and Sepsis [5]. Candida species are most common cause of nosocomial fungal infection in NICUs. Systemic fungal sepsis in a neonate is usually caused by Candida species, albicans being the most common [6]. According to global data in pediatric brain abscess reports fungal infection contributes to 20% cases with a very high mortality of almost 80% [7]. Indian data shows a prevalence of < 1% [8]. Most common pathogen responsible for brain abscess in a neonate is Gram-negative bacilli [9,10]. We present a case report of an extremely rare cause for cerebral abscess in a neonate and how timely and appropriate intervention resulted in a favorable outcome.

Case Report

A neonate born at term gestation with birth weight of 3 kgs presented with features of severe dehydration on Day 16 of life with chief complaints of loose stool and vomiting, weight loss was of 24%. Baby was exclusively breastfed. Lab investigations were suggestive of severe metabolic acidosis with raised urea and creatinine (urea 263; creat 2.87). During hospital stay, baby was mechanically ventilated due to respiratory distress after 15 hours of admission. The baby was extubated and put on CPAP and FFP transfusion was given due to deranged PT/INR and Inotropes were started. Dehydration and sodium bicarbonate correction was given. Antibiotics were started. Baby had 1 episode of seizure in form of cyclical movement of both limbs and Chewing movements, Phenobarbitone was started.

CSF analysis was done which showed raised protein (166 mg%). Urine output was adequate. Repeat KFT (Urea 186; creat-1.96) with metabolic acidosis (Ph-7.25; HCO₃-11.7). Ammonia, Lactate and

urine for ketones was negative. Blood culture, Endotracheal culture, Pus culture were sterile. USG KUB showed echogenic kidney with maintained CMD with B/L pyelonephritis. Serial urine for fungal hyphae showed budding yeast cell. MRI Brain was s/o fungal abscess. Antifungal (Amphotericin B and Fluconazole were started).The baby went three times weight correction and sodium bicarbonate correction.

Lab parameters showed continuously raised urea (263-152) and creatinine (2.87-1.4) with persistent metabolic acidosis. Repeat USG KUB s/o B/L small shrunken Echogenic Kidney so a diagnosis of CKD was made on Day 50 of life. The baby was discharged on oral sodium bicarbonate, calcitriol, phenobarbitone and amphotericin B and fluconazole, on exclusive breastfeeding.

Conclusion

Most of late onset fungal infections are caused by *Candida albicans*. The organs commonly involved are CNS, kidney and fundus. The renal systemic fungal infections have tendency to recur so they warrant a prolonged treatment with antifungals. The brain lesions described with candidiasis are focal infarctions, cerebritis, abscesses, and granulomas. Classically, cerebral

microabscesses are described in candida infections⁵.Cerebral microabscesses secondary to *C. albicans* have been described previously in preterm neonates¹¹.Superinfection with *Candida* results from disturbances in equilibrium that normally exists within the intestinal flora, usually resulting from chemotherapy, antibiotic therapy and haematological abnormalities. In patients with disseminated *Candida* infections kidneys are the most commonly involved organs followed by brain. Intraparenchymal haemorrhage and thrombosis with infarction have also been described as consequences of cerebral candidiasis. Thus, it is very important to have an early diagnosis of disseminated candidiasis for early intervention and better prognosis.

Conflict of interest

The authors declare that they have no competing interests.

Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability

Not applicable

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