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Review Article

Dentistry Section

Artificial Intelligence and Digital Pathology: A Narrative Review on Advancements and Opportunities for Improved Diagnosis and Treatment

MADHURA UMESH DHAMAPURKAR[1], RATANPRABHA DHANRAJ BARBADE[2], SM MEGHANA[3], SANDIP KULKARNI[4], POURNIMA GODGE[5]

ABSTRACT

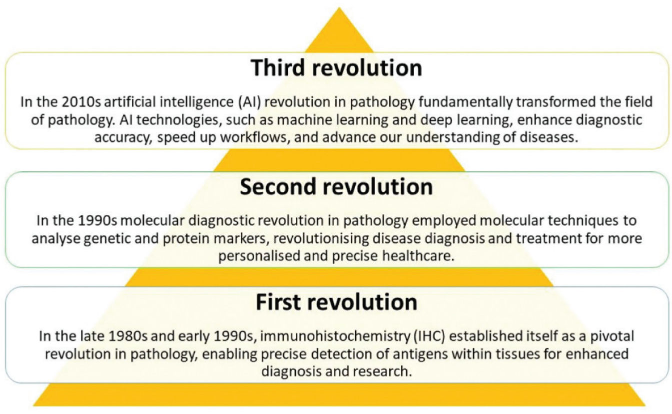
Recent advancements in Digital Pathology (DP) have empowered pathologists to provide more accurate diagnosis through digital means. Whole-slide Imaging (WSI) technology has enabled the digital scanning, representation, and preservation of numerous tissue slides, while Artificial Intelligence (AI), image analysis, and Machine Learning (ML) have enhanced disease diagnosis accuracy. There is a growing acceptance of the transition from traditional glass slide histopathological diagnosis to AI-assisted diagnosis using digital slides, driven by the substantial data accumulation that demands computer-aided analysis. Maximising the potential of AI breakthroughs in DP is critical, offering significant research opportunities across related fields. DP offers significant potential for telepathology, second opinions, and educational purposes. Additionally, it presents substantial research opportunities in image computing due to its vast reservoir of data. Pathologists have discerned characteristics beyond the naked eye's perception by analysing "sub-visual" images using DP. The flexibility of workflow provided by DP will be the main reason for its widespread adaptation and acceptance. DP also has the potential to be an essential tool to maintain operations of the pathology department in case of public health emergencies, which will streamline, fast-track, and improve patient care. Given the expanding accessibility and prevalence of the internet, it is crucial to develop innovations like DP. This technology catalyses enhancing patient care, opening avenues for further advancements in healthcare delivery. The purpose of present review was to bring to light the great potential that DP encompasses to improve diagnosis and treatment planning, which will ultimately lead to better patient care. However, integrating DP systems necessitates collaboration from various stakeholders beyond the Pathology Department. Despite evident advantages, several challenges must be addressed for the successful implementation and mass acceptance. Therefore, this narrative review aimed to illuminate the substantial potential inherent in DP for enhancing both diagnosis and treatment planning processes, consequently fostering improvements in patient care and also understanding DP, highlighting its challenges and opportunities. It also delves into the role of AI, image analysis, and ML in aiding disease diagnosis and reporting. With social distancing measures in place during the Coronavirus Disease -2019 (COVID-19) pandemic, pathologists were able to remotely access and analyse DP images, further cementing the importance of DP in current scenarios.

Keywords: Digitalisation, Slide imaging, Slide preparation, Telemedicine, Virtual microscopy

INTRODUCTION

Over thousands of years, disease concepts, diagnosis, and treatment have evolved significantly. The recent digital healthcare revolution, along with the development of microscopes, has further accelerated progress in disease management. The introduction of the microscope revolutionised scientific inquiry, shifting the focus from entire organs to tissues and eventually to cells [1]. This transformation gave rise to histopathology, a dominant discipline in pathology for the past 150 years [1]. The advancement in pathology can be divided into three revolutions: first, second, and third, as illustrated in [Table/Fig-1]. The combination of AI and DP is undoubtedly the third revolution of pathology [2]. The rapidly growing field of DP has changed the way we approach the diagnosis and treatment of diseases [2]. Pathology images can now be digitally stored, processed, and analysed using potent ML algorithms by leveraging digital imaging technology [3]. As a result, diagnostic accuracy, effectiveness, and speed have significantly increased, empowering medical professionals to make better decisions and treat patients [3].

In recent years, pathology has seen significant changes as a result of digitisation and the development of new computing technologies, similar to other medical specialties. The era of optical microscopy, which has lasted for more than 100 years, is coming to an end.



[Table/Fig-1]: Significant revolutions in pathology. With its associated benefits and challenges, Artificial Intelligence (AI) is a budding "third revolution" [2].

A new era in which pathology diagnosis are made using digitised WSIs is being ushered in by DP [3]. WSI has emerged and evolved immensely over the last 20 years, enabling complete slides to be scanned and permanently saved at high resolution [4]. The invention of WSI in 1999 by Wetzel A and Gilbertson J made it possible to digitally convert the entire tissue on a glass slide into a high-resolution Virtual Slide (VS) [5]. A WSI, also known as a virtual image or digital slide, refers to a digitised representation of an entire histopathology slide or a specific region within it [6]. The technology for acquiring VS and its applications in various pathology subspecialties has grown exponentially over the past two decades [7]. As the adoption and use of WSI increase, a greater volume of digital tissue data becomes accessible for applications involving ML and other methods derived from AI [8]. In recent years, several computer algorithms, such as the one developed by Yuan Y et al., have been developed to assist pathologists in diagnosing and predicting outcomes, particularly in the analysis of pathology images stained with Haematoxylin and Eosin (H&E) [9]. For automated or computer-aided diagnosis, pathologists have heavily researched the development and improvement of AI and ML algorithms. WSI is an effective tool for creating and implementing these algorithms for use in diagnostic pathology [7]. Since the COVID-19 pandemic, there has been a surge in demand for telemedicine, which has increased the need for digitised WSI for virtual diagnosis and treatment. Farris AB et al., in 2017, suggested that when implementing telepathology, it is essential to thoroughly evaluate network connections and file server needs while ensuring strict compliance with Health Insurance Portability and Accountability Act (HIPAA) regulations [10,11]. In terms of security, HIPAA requires that all medical images have backup and disaster management plans in place [12]. This review will elaborate on WSI, the integration of DP in clinical practice, the workflow of DP, image analysis, and ML, the advantages and disadvantages of DP, and DP in times of the COVID-19 pandemic.

REVIEW OF LITERATURE

A comprehensive literature review was carried out, involving a meticulous search of published peer-reviewed journals. Articles spanning from 2006 to 2023 were carefully examined, with the search conducted exclusively on the PubMed and Google Scholar databases. The search criteria encompassed the terms "DP and AI", "WSI", "Challenges and opportunities in DP", and "DP during the COVID-19 pandemic". Ultimately, a total of 34 journal references were selected, all directly pertinent to the topic of "AI and DP: A Narrative Review on Advancements and Opportunities for Improved Diagnosis and Treatment". This narrative review was conducted at TPCT's Terna Dental College, spanning from March 2023 to September 2023.

DISCUSSION

Whole-slide Imaging (WSI)

The WSI is the process of digitising a histopathology slide in its entirety or a chosen focal area [8]. The four sequential steps of WSI are illustrated in [Table/Fig-2].

[Table/Fig-2]: The four sequential steps of WSI [8].

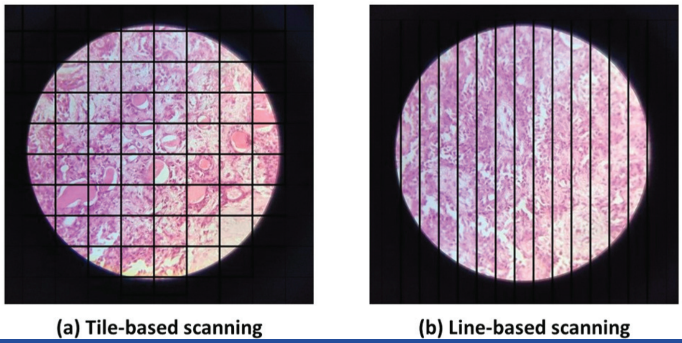
The four Sequential Steps of WSI

Image acquisition: This involves converting glass slides into high-quality digital images using specialised scanners [8].

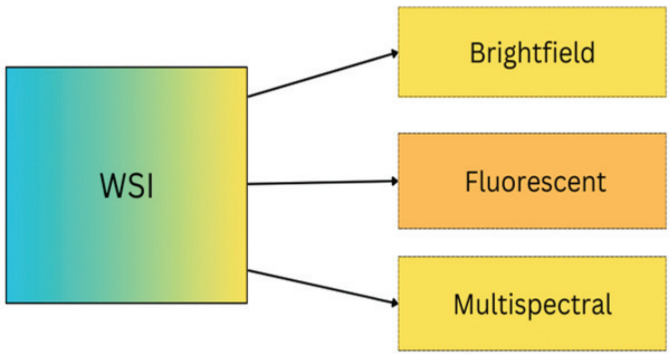
Storage: The high-resolution digital images are subsequently stored in a manner and location that facilitates convenient access and organisation [8].

Processing: Once stored, the images may undergo processing or editing, if required, to improve quality or add annotations to certain features [8].

Visualisation: Ultimately, the images are showcased for examination, evaluation, or sharing with others, typically using specialised software (for example: Image J) that facilitates navigation through the digital image [8]. Image capture and image display are the two systems that make up the hardware parts of the device needed to acquire images. Digital scanners, which are essentially trinocular microscopes with robotic illumination intensity control, mechanical stages, objectives, coarse and fine focusing capabilities, and cameras with high resolution, are used to capture images [7]. WSI scanners capture sequential images in two manners as illustrated in [Table/Fig-3]. To produce a digital image of the entire slide, multiple images (tiles or lines, as appropriate) are taken and digitally assembled (or "stitched") [7]. The WSI can be categorised as bright field, fluorescent, and multispectral when scanners are combined with slide staining methods as illustrated in [Table/Fig-4] [8]. The choice of a WSI system is a crucial first step on the path to comfortable image viewing. It is essential to view digitised slides on monitors with sufficient resolution [8].



[Table/Fig-3]: a) Tile and b) Line scanning manner for capturing sequential images by WSI scanner.



[Table/Fig-4]: WSI can be categorised as brightfield, fluorescent, and multispectral when scanners are combined with slide staining methods [8].

Integration of DP in Clinical Practice

Glass slides are converted into digital images through whole slide scanning, which can be interactively navigated with the right software. Prerequisites for digitally recording the slides: To reproduce the desired magnifications, the slide must be recorded at a sufficiently high resolution and with an adequate colour depth. According to Kumar N et al., a resolution of roughly 0.25 μm per pixel and a 24-bit colour depth, a typical WSI scanned at 40x has these characteristics. As a result, a 1 mm^2 area of the slide contains 384 million bits of information, resulting in a file size of roughly 48 MB in the absence of additional measures to manage the data more effectively [7]. In WSI, there are numerous techniques for image compression file size reduction. The file size is frequently reduced by a factor of seven or more when using Joint Photography Expert Group (JPEG), JPEG 2000, or Lempel-Ziv-Welch (LZW) compression, which is used by many vendors to reduce file size to manageable levels [7]. To facilitate a streamlined method of loading images, WSIs are stored at multiple resolutions [7]. Viewing the digital image is also an important component, and research has suggested that diagnosing scanned glass slides is more effective on computer widescreens compared to iPads [8]. Popular image viewing software that allows finger touch annotations using an onscreen virtual keyboard and allows the export of images in different formats are:

- Path XL;
- Surface Slide;
- Aperio Image Scope [7].

A decision has to be made by organisations regarding the use of a cloud-based or server-based network that fulfills the needs of the users and complies with the information system protocols of the organisation as illustrated in [Table/Fig-5] [8]. WSI provides a chance to increase the number of tools that are available to users, adding digital annotations, quick navigation/magnification, and computer-assisted viewing and analysis [8].

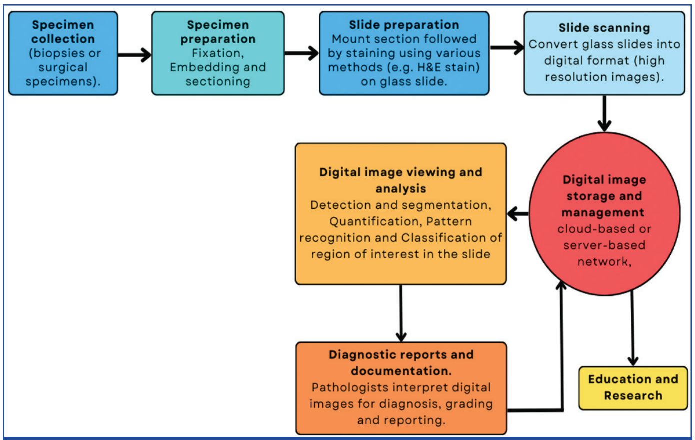
[Table/Fig-5]: Different types of WSI storage: Cloud-based and Local server-based.

The study done by Bauer TW and Slaw RJ supports the safety and effectiveness of WSI for diagnosis in surgical pathology [13]. The data collected by Borowsky AD et al., indicates that pathologists who regularly engage in manual slide review can achieve primary histologic diagnosis from WSI review with an accuracy level that matches or exceeds the current standard of practice, which involves viewing glass slides through light microscopy [14]. Several other studies indicate that interpreting pathology images as single-plane WSI offers diagnostic quality on par with the traditional centuries-old practice of viewing tissue sections mounted on glass slides through a light microscope [13,15,16]. There are innumerable uses of digital WSI in clinical practice, including primary diagnosis, second opinion, telepathology, quality assurance, archiving, sharing, education, conferencing, image analysis, ML, research/publications, tracking, tissue procurement, marketing, and business [12].

Workflow of DP

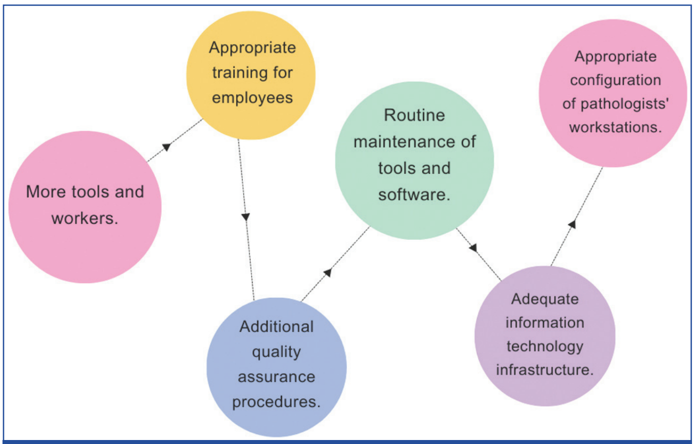
The workflow of DP represents a transformative evolution in the field, where traditional glass slides are digitised to harness the power of cutting-edge technology. It has been previously established that WSIs are non inferior to traditional glass slides for primary diagnosis in anatomic pathology [13,15].

A simplified flowchart for the workflow of DP has been illustrated in [Table/Fig-6] [8,17].



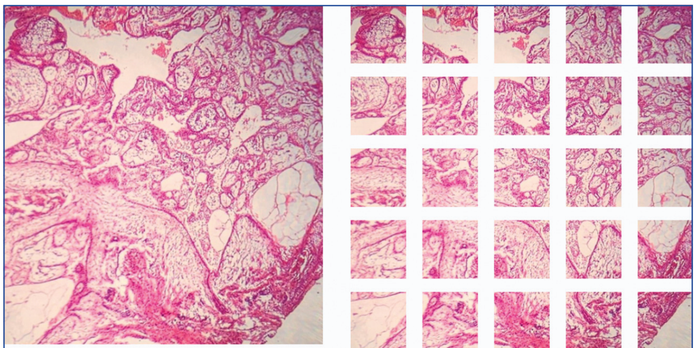
[Table/Fig-6]: Simplified flowchart for the workflow of Digital Pathology (DP) [8,17].

Miscellaneous steps in the workflow: One must be aware that when creating a workflow for DP, additional steps are included when tissue sections are intended for digitisation in addition to the regular histological workflow, these include [Table/Fig-7] [8]. Verifying the scan quality is necessary once slides have been converted to digital format. Due to inappropriate slide preparation before scanning, inadequately focused scans, compensating lines from incorrectly stitched lines or tiles, and other circumstances, scanning artifacts might alter the outcomes [8].

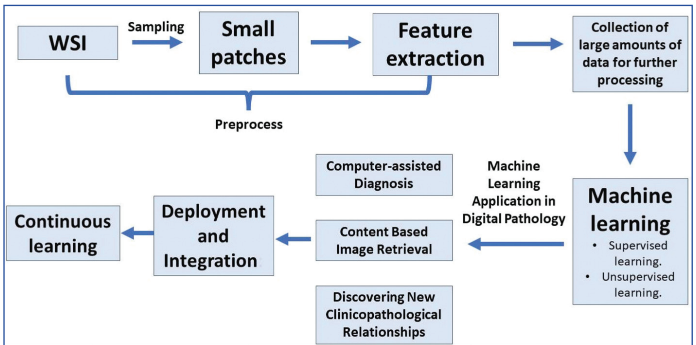


[Table/Fig-7]: Additional steps in the workflow of Digital Pathology (DP) [8].

Image analysis and Machine Learning (ML): The DP generates extensive data, offering significant research potential in image computing. However, it also presents substantial computational and technical obstacles. Existing tools for image analysis and disease detection struggle to handle high-resolution whole-slide images. Image analysis can uncover subtle features in digital slides that may elude pathologists' visual examination [Table/Fig-8]. Computer-based diagnosis, content-based picture retrieval, and finding novel clinicopathological correlations are all examples of machine-learning applications in DP [18]. By automating processes like identifying cancer cells, AI and DP may be able to enhance the level of quality, precision, and effectiveness [19]. Despite challenges such as tissue colour variations and the absence of z-axis data, image analysis and ML offer significant potential to assist pathologists in disease diagnosis and early detection [Table/Fig-9] [18,20]. Image analysis and deep learning will drive the shift from qualitative to quantitative pathology soon. By formalising computer-aided pathology development and validation procedures, increasing the volume of validation data, and improving knowledge of computer-aided pathology diagnosis, confidence in diagnostic outcomes will be enhanced [21].

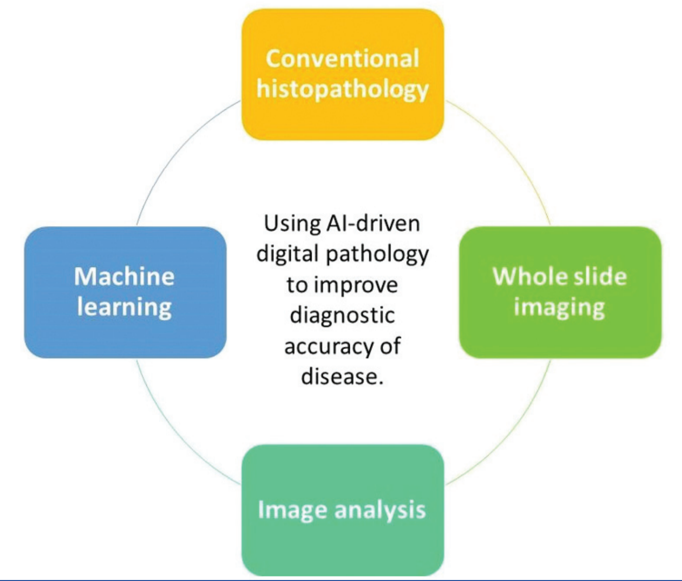


[Table/Fig-8]: The Whole Slide Image (WSI) is divided into distinct segments, facilitating a focused examination of individual areas. This segmentation enhances the efficiency and precision of analysis, allowing pathologists to scrutinise specific regions with detailed attention.

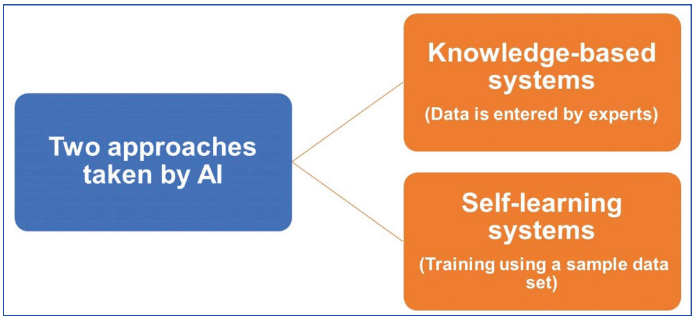


[Table/Fig-9]: Common procedures involved in Machine Learning (ML) for analysing DP images [18].

Advanced multiplex tissue imaging techniques along with AI and DP technologies designed for use with normal clinical samples can produce precise depictions of the intricate spatial structure of the cancer ecosystem [22]. It is anticipated that the use of AI in pathological diagnosis would not only lighten the labour of pathologists but additionally help standardise the diagnosis, which is otherwise subjective and may result in subpar treatment [19]. DP and image analysis also provide a vast array of applications in the field of clinical trials [23]. Utilising DP image systems and solutions offers numerous practical advantages that can significantly benefit translational medicine and clinical practice [24]. Different components that contribute to AI-driven DP are illustrated in [Table/Fig-10]. Two approaches to AI are illustrated in [Table/Fig-11] [25].



[Table/Fig-10]: Using AI-driven Digital Pathology (DP) to improve diagnostic accuracy of disease.



[Table/Fig-11]: Two approaches taken by AI include knowledge-based systems and self-learning systems [25].

Advantages and Disadvantages

The DP, the conversion of conventional glass slides into digital tissue sample images, presents both advantages and disadvantages [26,27].

Advantages:

- Improved consultation and collaboration between experts, regardless of distance obstacles.
- Quantitative analysis increases the ease of understanding treatment efficiency and other issues that are difficult with traditional pathology.
- Effective workflow.
- Education, training, and teaching enable interactive sessions.
- Telepathology facilitates expert opinions from all over the world with ease, especially on rare and complex diseases.
- Ease of telemedicine and teleconsultation.

Disadvantages:

- Lack of cost-effectiveness due to a significant amount of initial investment.
- Acquiring the learning curve by pathologists and staff.
- Data safety concerns when dealing with sensitive patient data.
- Limited accessibility in semi-urban and rural areas.

DP in Times of COVID-19 Pandemic

The 2020 COVID-19 pandemic is a recent crisis that confined everyone to their homes and saw the implementation of social distancing. DP came to the rescue of many institutions to assist with treatment and diagnosis while adhering to COVID-19 norms [28-31]. The COVID-19 crisis led to the normalisation of working from home and digital transmission of data [29]. The availability of faster internet networks and cheaper storage helped with working remotely. For example, Universitair Medisch Centrum Utrecht in the Netherlands started to build-up DP infrastructure in 2008 and was able to adapt to this unique situation of the COVID-19 pandemic [30]. A crisis like this amplifies the importance of having a DP system in place to be prepared in advance for any unforeseen incidences in the future. A UK guidance study done by Williams BJ et al., from the RCPath offers recommendations for using DP during the COVID-19 pandemic [31]. A recent US study done by Hanna MG et al., examined the "emergency" adoption of DP in home offices during the pandemic, made possible by temporary regulatory waivers [32]. This study found that there was close agreement between glass slides and digital images for diagnosis and clinically relevant parameters [32]. Participants managed to work on non-DP dedicated hardware, despite some using small screens. Internet speeds were generally sufficient, with 13% having connections below 20 Mbit/s. WSI latency was affected by internet speed but not computer performance. Most pathologists (90%) expressed high comfort levels with DP and the option to request glass slides [32]. Certainly, the COVID-19 pandemic has accelerated the transition to a digital age, where DP, along with advancements in AI, image analysis, and ML, has become indispensable, especially in the fields of cancer diagnosis, monitoring, and treatment, thanks to their clear advantages [33,34].

CONCLUSION(S)

Digital pathology epitomises a transformative era in pathology, integrating cutting-edge imaging and AI technologies to significantly elevate diagnostic precision and therapeutic efficacy. Its seamless assimilation into clinical workflows underscores its potential to furnish tailored treatment modalities in alignment with precision medicine's objectives. Despite facing implementation challenges, the empirical advantages of digital pathology in research, education, and clinical realms signal a trajectory of expansion. This convergence of traditional expertise with contemporary methodologies heralds a pivotal juncture in pathology, promising expedited and accurate diagnoses, thereby fostering enhanced patient outcomes. As AI continues to permeate society, prioritising the professional development of healthcare practitioners in digital pathology is paramount to fully capitalise on its transformative potential in advancing medical practice.

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PARTICULARS OF CONTRIBUTORS:
1. Intern, Department of Oral Pathology and Microbiology, Terna Dental College, Nerul, Navi Mumbai, Maharashtra, India.
2. Intern, Department of Oral Pathology and Microbiology, Terna Dental College, Nerul, Navi Mumbai, Maharashtra, India.
3. Associate Professor, Department of Oral Pathology and Microbiology, Terna Dental College, Nerul, Navi Mumbai, Maharashtra, India.
4. Associate Professor, Department of Oral Pathology and Microbiology, Terna Dental College, Nerul, Navi Mumbai, Maharashtra, India.
5. Professor and Head, Department of Oral Pathology and Microbiology, Terna Dental College, Nerul, Navi Mumbai, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Madhura Umesh Dhamapurkar,
Department of Oral Pathology and Microbiology, Terna Dental College,
Plot No. 12, Sector-22, Nerul, Navi Mumbai-400706, Maharashtra, India.
E-mail: madhurabds@gmail.com

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