HIGH FREQUENCY ULTRASONOGRAPHY OF BENIGN AND MALIGNANT SKIN TUMORS AND ITS CORRELATION WITH HISTOPATHOLOGY AND DERMOSCOPY

Thesis

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In partial fulfillment of the requirement for the degree of

DOCTOR OF MEDICINE (MD)

(DERMATOLOGY, VENEREOLOGY AND LEPROLOGY)

JULY, 2020 **DR. PRIYANKA KARADIA**

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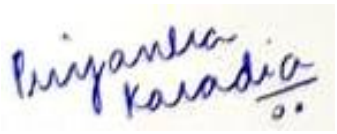
DECLARATION

I hereby declare that the work reported in the thesis entitled **"High frequency ultrasonography of benign and malignant skin tumors and its correlation with histopathology and dermoscopy"** embodies the result of original work carried out by the undersigned in the Department of Dermatology, Venereology and Leprology, All India Institute of Medical Sciences, Jodhpur.

I further state that no part of this thesis has been submitted either in part or in full for any other degree of All India Institute of Medical Sciences, Jodhpur or any other institution.



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CERTIFICATE

This is to certify that the thesis titled **"High frequency ultrasonography of benign and malignant skin tumors and its correlation with histopathology and dermoscopy"** is the bonafide work of **Dr. Priyanka Karadia**, in the Department of Dermatology, Venereology and Leprology, All India Institute of Medical Sciences, Jodhpur.

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CERTIFICATE

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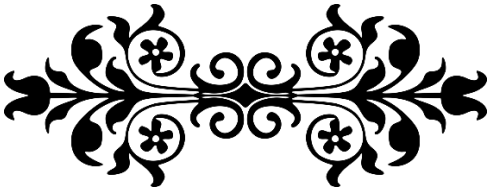

DEDICATED TO
MY FAMILY,
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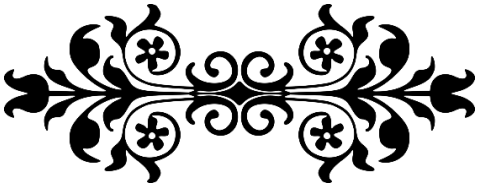
PATIENTS



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-Dr. Priyanka Karadia

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LIST OF ABBREVIATIONS

- BCC:- Basal cell carcinoma
- SCC:- Squamous cell carcinoma
- HFUS:- High-frequency ultrasonography
- USG:- Ultrasonography
- CT :- Computed Tomography
- MRI:- Magnetic Resonance Imaging
- DFSP:- Dermatofibrosarcoma protuberans
- KS:- Kaposi sarcoma
- CD34:- Cluster of differentiation 34
- CD68:- Cluster of differentiation 68
- DEJ:- Dermal-epidermal junction
- HPE:- Histopathological examination
- SD:- Standard Deviation
- NMSC: - Non melanoma skin cancer
- ICC:- Intraclass correlation coefficient

SUMMARY

Background: Skin tumor diagnosis and assessment has focused particularly on visual inspection and skin biopsy. Although in non-invasive diagnostic methods significant technological improvements have been achieved, high frequency ultrasonography is still a novel and understudied technology in connection to all skin cancers. In view of sparse literature on this topic especially on benign and malignant skin tumors, we aimed to study and correlate features of ultrasound, dermoscopy and histopathology of skin tumors.

Objectives: To compare and correlate the ultrasonographic findings of benign and malignant skin tumors with histopathologic findings as a reference standard.

Materials and Methods: It was a cross sectional observational study conducted on patients with benign and malignant skin tumors. A total of 52 patients were recruited in the study as per the selection criteria. We took relevant history, performed clinical examination, dermoscopy with photographic documentation, high frequency ultrasonography and histopathological examinations. Statistical analyses of these parameters were done using SPSS software v.25. $p - value < 0.05$ was considered significant.

Results: The ages of the patients ranged from 18 to 80 years with a mean age of 36.81 ± 18.7 years with female preponderance. 73.08% benign tumors and 26.92% malignant tumors were found. Lesions were most commonly present over the face (46%), scalp (21.15%), and upper extremities (17.31%). 23.08 percent of lesions were found to be BCC followed by appendageal tumors and spindle cell tumors. Dermoscopic findings included a predominantly skin-colored and hyperpigmented background. The most noticeable finding was a homogeneous pattern but clods and pigment network were also present. The majority of skin tumors were described as hypoechoic, homogenous, oval to irregular-shaped solid lesions by HFUS. Statistically significant correlation was noted between clinical size and ultrasonographic size, and between USG depth and HPE depth which highlights the pre-surgical role of ultrasonography. Vascularity was found to have a fair agreement when correlation was analysed between HFUS and HPE.

Conclusion: This study suggests a novel method in diagnosis and assessment of benign and malignant skin tumors with high frequency ultrasonography and its correlation with confirmatory findings seen on histopathology. We also tried to analyse dermoscopic findings along with descriptive correlation with histopathology in which we found good correlation of

individual parameters. This study also demonstrates vascularity and level of invasion through HFUS and its significant correlation with histopathology.

INTRODUCTION

INTRODUCTION

Skin tumors are quite common and present throughout all ages. It represents a higher prevalence worldwide than any other cancer types combined. Although the incidence of skin tumors does not show any signs of plateau, but the mortality rate is stable or decreasing. [1 2]

Skin tumors are classified on the basis of their cell of origin: epidermis, dermis, subcutis and appendages. Basal cell carcinoma (BCC) and Squamous cell carcinoma (SCC) consist of 95% of all non-melanoma skin cancers. Melanoma comprises of only 10% of all skin cancers. [3,4]

Early diagnosis of skin tumors is important for appropriate & prompt management and at the same time, it improves morbidity and survival of the patient. Melanoma and squamous cell carcinoma are high-risk skin cancers with the potential to metastasize whereas basal cell carcinoma is usually localized, with the potential to infiltrate and damage the surrounding tissue.[5]

Although these lesions are diagnosed primarily by clinical examination but multiple modalities have been developed to aid the diagnosis namely- histopathology, digital photography, dermoscopy, optical coherence tomography and high-frequency ultrasound (HFUS).[5]

Ultrasound (USG) has been used in dermatology for nearly 35 to 40 years . In 1979, ultrasound was introduced to measure normal skin thickness by Alexander and Miller and then in 80s and 90s USG was used as in assessment of dermatological tumors and diseases.[6,7]

High frequency ultrasound is a low risk, painless, non-invasive, non-ionizing, and cost-effective method which provides real-time visualization of cutaneous tissue and deeper layers of skin. It is the only imaging modality useful in the diagnosis of very small tumors that are too small to be visualized or detected by MRI (Magnetic Resonance Imaging) or CT (Computed Tomography). Particularly in the head where the subcutaneous layer is very thin, there is greater risk of bony involvement and USG is an effective alternative to CT and MRI in establishing the presence of calvarium infiltration.[6,8]

Appropriate pre-surgical assessment of tumour extent can help reduce the extent of surgical defects. On the other side, infiltration of relevant anatomic structures including fascia, muscles, cartilages and bone can be effectively recognized using USG. [9,10]

Different frequency probes from 7.5 to 100 Hz have been used. It can measure the diameter of tumor in all axes, vascularity of lesion, deeper layer involvement, margin & consistency of lesion, locoregional metastasis, nonpalpable satellite lesion in dermal or subcutaneous locations. By detecting the accurate morphology and extent of the tumor, it aids in pre-surgical workup of patient**.** At the same time ,when there is a concurrent peritumor inflammatory reaction, HFUS falsely gives greater thickness and inaccurate wider excision of lesion.[3,8]

Dermoscopy is a noninvasive, handheld instrument that is equipped with a magnification lens (generally between 10-20X) and a polarized or nonpolarized light source that allows visualization of epidermal and dermal structures which are invisible to the naked eye. Most dermoscopic features have direct histopathological correlation and therefore dermoscopy offers the ideal bridge to improve clinicopathologic communication .[11]

Although newer techniques are evolving in recent times , histopathology still serves as the reference standard in diagnosing skin tumors as well as in providing therapeutic benefit to the patient.[12]

Correlation of all the three modalities i.e. HFUS, dermoscopy & histopathology will play an important role in bridging the gap in the knowledge of diagnosing skin tumors with HFUS or dermoscopy as well as help in earlier detection of skin tumors.

To the best of our knowledge, this is the first study correlating features of USG, histopathology and dermoscopy of benign and malignant skin tumors.

AIM AND OBJECTIVES OF THE STUDY

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To Compare and correlate the ultrasonographic findings of benign and malignant skin tumors with histopathologic findings as a reference standard.

OBJECTIVES

Primary Objective:

1) To assess and compare ultrasonography, histopathology & dermoscopic findings of benign and malignant skin tumors.

Secondary Objectives:

1) To analyze the potential role of pre-biopsy ultrasonography of skin tumors.
2) To assess the vascularity and locoregional spread of skin tumors by USG and dermoscopy
3) To describe and correlate histopathology and dermoscopy findings of skin tumors.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Skin tumors appear as a result of the proliferation of one or more skin components. Benign lesions may just cause cosmetic concerns to the patient but they comprise majority of skin tumors. Khandpur et al summarized some common clinical morphologies of skin tumors. Clinically benign skin tumors present as smooth papules, nodules, cystic lesions whereas malignant tumors present as irregular, solitary, fast growing papules, plaques, and nodules that may ulcerate afterwards.[13]

CLASSIFICATION

The skin is a heterogeneous organ composed of ectodermal and mesodermal-derived components. The majority of these components are able to cause skin cancer. Skin tumors can be classified on the basis of site of their origin - melanocytic tumors, keratinocytic tumors, appendageal tumors and soft tissue tumors.[14] These 4 comprise the majority of skin tumors. Neural tumors and subcutaneous tissue tumors can also be classified as additional separate entities.[13]

Melanocytic tumors comprise of benign tumors such as naevi and malignant tumors such as melanoma. In the recent update of WHO skin melanocytic tumor classification 2018 based on pathway, it has been divided into benign (having single genomic abnormality), intermediate (having two genomic abnormality) and malignant. Malignant melanocytic tumors also known as melanomas are divided on the basis of sun exposed sites and non-sun exposed sites.[15]

Keratinocytic tumors also known as epidermal tumors includes benign acanthomas , premalignant lesions such as actinic keratosis, bowen's disease and Bowenoid papulosis and malignant tumors such as BCC and SCC. [13]

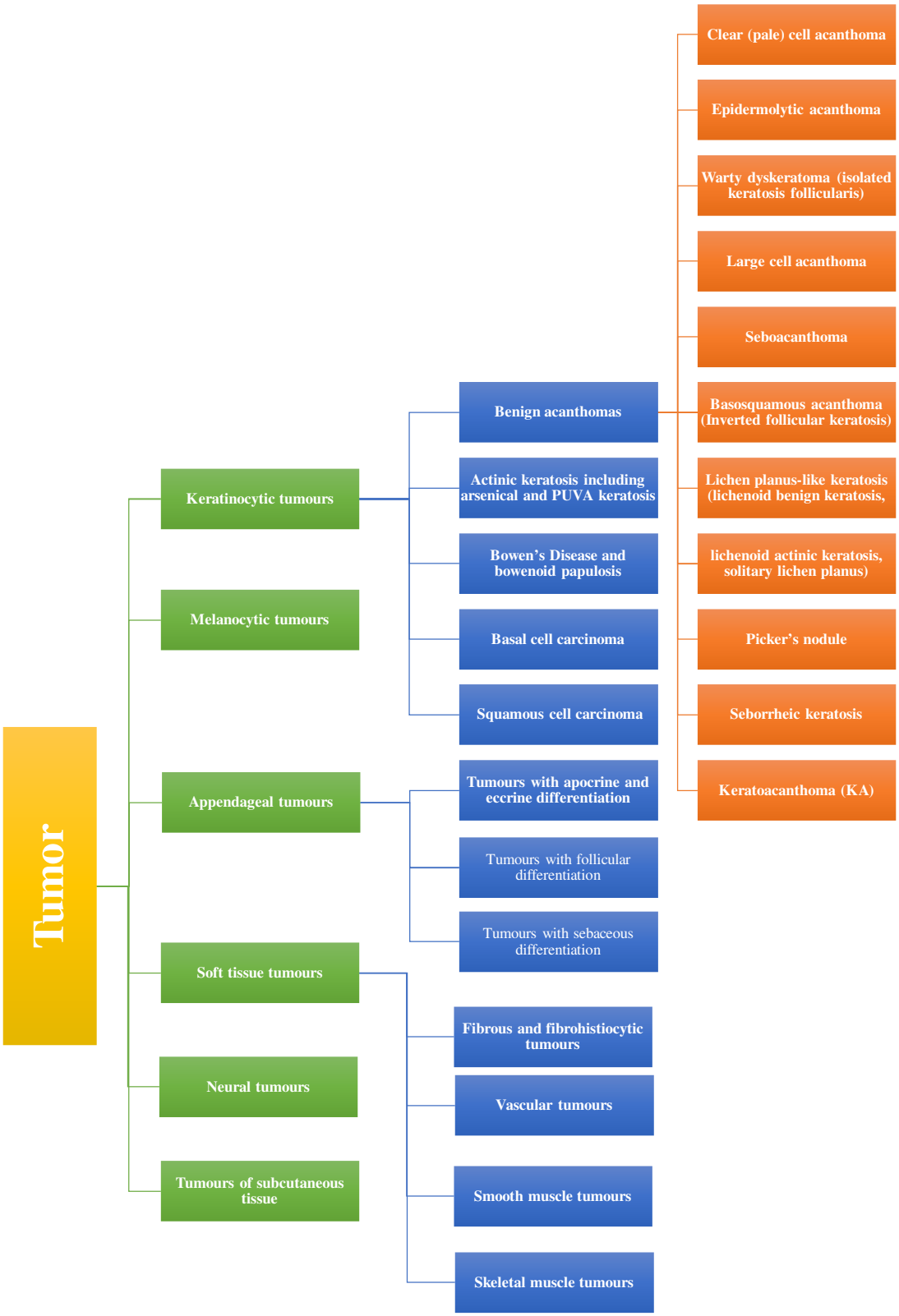


Figure 1 :- Classification of skin tumors[13]

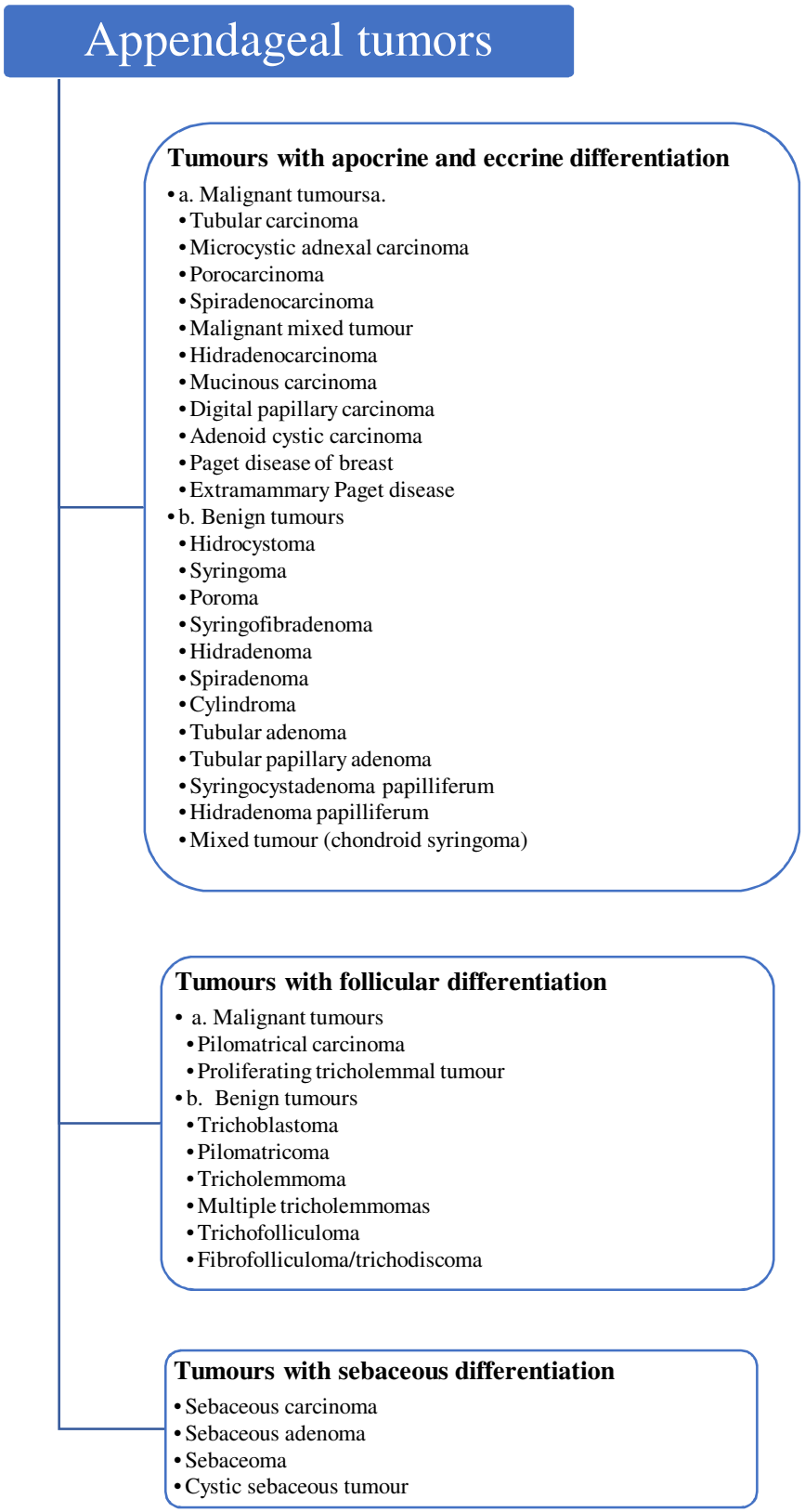


Figure 2:- Classification of Appendageal tumors[13]

EPIDEMIOLOGY

The paucity of epidemiological information on this subject is justifiable given its benign character and lack of reporting. Since melanoma has a dreadful prognosis, the majority of the data concentrate mostly on it with western preponderance.

According to International Agency for Research on Cancer estimates, over 1.5 million new cases of skin cancer was recognized worldwide in year 2020.[16]

Less than 1% of all malignancies diagnosed in India are skin cancers. Despite skin cancer being a less prevalent malignancy in India than in the West, the absolute incidence is still considerable because of the country's greater population.[17]

Keratinocyte carcinoma is a considerable health burden in several nations among melanocytic and non-melanocytic tumors, although its exact occurrence is unclear on a global scale. Approximately 5.4 million cases of keratinocyte carcinoma were identified in the United States in 2012, up from a 2006 estimate of 3.5 million.[18,19] While the mortality for both types of tumors are steady or declining, their global incidence rates continue to rise.[20]

BCC is uncommon in darker-skinned people. Males were impacted more often and at a younger age than females. The facial skin and scalp were the most commonly afflicted sites. [21] Cutaneous spindle cell lesions contain a varied collection of malignancies ranging from benign to borderline to malignant. Dermatofibroma is one of the most prevalent cutaneous mesenchymal tumors. Less than 1 percent of malignant tumors are cutaneous soft tissue sarcomas. The frequent primary cutaneous sarcomas are dermatofibrosarcoma protuberans (DFSP) and leiomyosarcoma. Among vascular neoplasms, Kaposi sarcoma (KS) and angiosarcoma are the most prevalent.[22] Dermatofibromas are more common in women than in men and can appear at any age, though they are most prevalent between the ages of 20 and 40. [23]

Cutaneous appendageal tumors are a vast heterogeneous category of tumors that are often categorized according to their stage of appendageal differentiation - eccrine, apocrine, follicular, and sebaceous. They are rare in the general clinical population. Many appendageal tumors have a non-specific morphological appearance, therefore their identification is mostly reliant on histological criteria, while others (such as syringoma and nevus sebaceous) may be detected clinically with ease. Sweat gland tumors were the most common appendageal

tumors in earlier study (79.8%) followed by follicular tumors (11.6%), sebaceous were 8.3%. The most frequent location of predilection is the face and scalp. [24]

Although it only makes up roughly 1% of skin malignancies, melanoma is responsible for nearly all skin cancer-related fatalities. The lifetime chance of acquiring melanoma is roughly 2.4% in Caucasians, 0.1% in Blacks, and 0.5% in Hispanics.[25] At the time of diagnosis, the usual age is around 60. Males are around 1.5 times more likely than females to get melanoma.[26]

Diagnosis of skin cancer in dark coloured individuals typically occurs at an advanced stage. However, most skin cancers are treatable if detected and treated early on, but these delays imply that diagnoses are sometimes made when the disease has already progressed to a potentially deadly stage. [27]

DERMOSCOPY

Dermoscopy is also referred to as incident light microscopy, epiluminescence microscopy and skin-surface microscopy. It is a low-cost, non-invasive method that allows the detection of morphologic characteristics that are not apparent to the human eye. Different dermatoscopy tools are available which have magnifications ranging from 10x to 100x, however a magnification of 10x is sufficient for evaluating suspicious skin lesions. Both pigmented and non-pigmented skin lesions may be diagnosed using dermatoscopy nowadays.[28] Transillumination of a lesion and analysing it at a high magnification to visualise minor details is the basis of dermoscopy. [29]

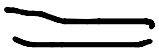
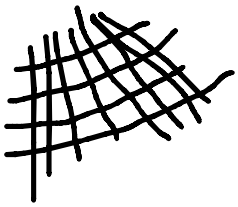
Dermatoscopes can be manufactured with or without the ability to capture images. Both non-contact and contact dermoscopy methods are available. Through the linkage fluid, the instrument's glass plate makes direct contact with the lesion in the contact method. The non-contact method relies on a cross-polarized lens to filter out all scattered light and let in only monochromatic rays. The contact method improves both brightness and resolution. Patient-to-patient transmission of disease is avoided owing to the non-contact method.[30]

Polarized dermoscopy may provide a higher precision for identifying skin cancers due to its capacity to augment the visibility of vascular and crystalline structures, both of which are

frequently observed in skin cancers. It is used to visualize deeper layers of epidermis and papillary dermis till approximately 100um. It can be contact as well as non-contact.[30]

Nonpolarized dermoscopy enhances specificity by facilitating the detection of features of superficial epidermis typically observed in benign lesions, such as milia-like cysts and comedo like areas in seborrheic keratosis.[30]

Table no. 1 : Dermoscopy terminology[30]

TERMINOLOGY	PATTERN	DESCRIPTION
Lines		The length is significantly longer than the breadth
Dots		Miniature, spherical formations that are too little to have any other form.
Circle		Circular. The hair follicles are responsible mostly for this appearance
Clod		Clearly defined solid areas that are bigger than a dot. Typically consisting of a single colour, lesions can take on a variety of shapes and sizes.
Pigment network		Pigmented (brown or black) or non-pigmented (white) reticular (net-like) or branching networks have been seen.
Streaks		Wider than lines and detectable only in isolation
Structureless		Area devoid of any structure

VESSEL TERMINOLOGY	PATTERN	DESCRIPTION
Arborizing vessel		Tree like branching vessels
Linear vessel		A solid linear vessel
Lacunae		Cluster of dilated vessels
Dot		Small caliber vessels that resemble a pinhead.
Comma vessel		Vessels with little branching that are thicker, linear, and may have one end that is thicker than the other.
Loop vessel		Vessels making U shape.
Coiled		Tortuous capillaries coiled up
Polymorphous		Presence of two or more vascular patterns.

Dermoscopy of common skin tumors

BASAL CELL CARCINOMA: Menzies et al proposed dermoscopic criteria to diagnose BCC. Lack of a pigment network and the presence of dermoscopic characteristics such as large blue-gray ovoid nests, arborizing vessels, numerous blue-gray globules, leaf-like areas, spoke wheel areas and ulceration are all consistent with BCC. Diagnostic parameters for pigmented BCC were found to have 97 percent sensitivity. Non pigmented BCC also shows asymmetrical arborizing vessels, focal ulceration and background pink color.[31]

MELANOMA: Holmes et al gave criteria for cutaneous melanoma. Major criteria of 2 points each includes atypical pigment network, blue white veil and atypical vascular pattern. Minor criteria of 1 point each includes irregular streaks, irregular pigmentation, irregular dots and regression structures. A score of 3 or more is consistent with melanoma.[32]

SQUAMOUS CELL CARCINOMA: Scales and clusters of glomerular vessels encircled by a white halo in a non-specific pattern. [28]

DERMATOFIBROMA: Central white scar like homogenous area with peripheral pigment network and absent melanocytic features. [28]

PYOGENIC GRANULOMA: Red homogenous areas with lacunae white lines intersecting the lesion along with scaling, crusting and ulceration.[28]

CYST : The punctum was evident via dermoscopy in nearly 60% of cases while being clinically undetectable.[33] Studies discovered that epidermoid cysts with the pore sign, blue-white veil, and arborizing vessels were more likely to be unruptured, whereas those with red lacunae and peripherally branching linear arteries were more likely to be ruptured.[34]

HIGH FREQUENCY ULTRASONOGRAPHY

In 1979, Alexander and Miller presented ultrasonography (USG) as a noninvasive method for determining normal skin thickness.[7]

Ultrasonography is a diagnostic technology that is commonly utilised in the medical field. This noninvasive skin imaging technique has been utilised in dermatology for the past three decades. For evaluating tumor thickness and skin thickness while treating inflammatory skin illnesses like scleroderma or psoriasis, the utility of high-frequency ultrasonography above

20MHz is well-established.[35] It is used to assess the size, shape, structure and depth of involvement in skin lesions.[6]

The size, location, and topography of the lesions are the primary factors in determining the optimal probe frequency. The field of view is expanded and smooth or regular surfaces are shown clearly at lower frequencies (7.5-13 MHz), whereas superficial features and uneven surfaces may be studied in great detail at higher frequencies (10-20 MHz). [36]

Table no. 2:- Frequency of ultrasound with depth of penetration and structures visible.[6]

Frequency of ultrasound (MHz)	**Approximate depth of penetration (cm)**	**Visualization**
7.5	>4.0	Subcutis and lymph nodes
20	0.6-0.7	Epidermis and dermis
50-100	0.3-0.015	Epidermis

B-scans produce pictures of scanned tissues that mimic anatomical cross sections. High frequency ultrasonography (HRUS) of normal skin reveals a well-defined hyperechoic band known as epidermal "entry echo" at the transducer-skin contact. The dermis is a hyperechoic layer with tiny hypoechoic regions, which correspond to hair follicles, blood vessels, and sebaceous glands. The following layer, subcutaneous tissue, is hypoechoic with connective tissue septa that are hyperechoic separating the adipose lobules. The superficial fascia covering the muscle tissue can be detected as a hyperechoic regular line upon closer inspection. On HRUS, the nail unit structure is represented by parallel hyperechoic lines at the surface, which stand in for the dorsal and ventral plates, and a hypoechoic nail bed below.[6]

Most skin lesions show up as hypoechoic thickening of the skin or the subcutaneous tissue on HRUS. To what degree high-frequency sound waves are transmitted through tumors may depend on their underlying biological characteristics, such as vascularity and density, which in turn reflect differences in collagen and keratin content of tissues. Wortsman conducted a retrospective analysis of 4338 ultrasonography scans of mainly localised skin lesions and 130 healthy controls. In 73% of the lesions, the referring diagnosis was accurate, and the use of ultrasonography raised accuracy to 97% . Overall ultrasound sensitivity was 99 %, and specificity was 100 %.[37]

By utilizing an ultrasound device prior to surgery, we may be able to determine the vascularity of skin lesions, a characteristic crucial for distinguishing benign from malignant tumors. Approximately 44% of malignant tumors had vascularity whereas 75% of benign tumors lacked vascularity. USG for skin malignancies may overestimate or underestimate the extent of the tumor. A 20-MHz ultrasound equipment can only detect depths as much as 8 mm.[38]

BASAL CELL CARCINOMA: Ill defined, hypoechoic mass with uneven borders is seen in the dermis [39]. In high-risk recurrence subtypes such as micronodular or morpheaform variations, a high density of hyperechoic patches representing nests but not calcifications, has been observed to be more prevalent.[3] Low-flow arterial and venous arteries are seen inside or at the base of the lesion. The presence of tortuous arteries is indicative of the presence of further malignancies. [39]

SQUAMOUS CELL CARCINOMA**:** Heterogeneously hypoechoic lesion with irregular boundaries, presence or absence of hyperechoic patches, and a propensity to penetrate deeper layers.[3,39]

EPIDERMOID CYST**:** well-defined oval hypoechoic mass lesion in the subcutaneous plane with a punctum opening in the epidermis[39]

GLOMUS TUMOR**:** mostly presents as well defined hypoechoic mass in the subcutaneous tissue.[39]

MELANOMA: Nodular to irregular hypoechoic mass lesions. A subungual melanoma USG examination reveals a thickened epidermal entry echo with a subepidermal hypoechoic band and an irregular mass lesion entering the dermis and subcutaneous tissue with neovascularization.[39] Nodular melanoma often manifests as a well defined hypoechoic lesion, whereas superficially spreading melanoma manifests as a narrow, lenticular, hypoechoic lesion adjacent to epidermal entrance echo.[40]

DERMATOFIBROMA: irregular borders, spiculation at the edges, and a shift in the echogenicity of the surrounding soft tissues are all features with avascular dermal lesions that extend into the subcutaneous layer.[41]

HISTOPATHOLOGY

An important aspect of the management for proliferative skin disorders is by performing a biopsy for both diagnostic and therapeutic purposes.[12]

When it comes to diagnosing benign and malignant skin diseases, histopathological studies are considered to be the gold standard; furthermore, they are largely viewed as an extremely valuable tool for assisting dermatologists in understanding the overall pattern of skin diseases, the best way to treat them, and the proper correlation of their findings in the clinic.[42]

BCC: appears as an epidermis-based basaloid epithelial malignancy. A palisade is formed by the basaloid epithelium. The formation of a cleft between tumor nests and stroma is known as retraction artefact. Low-risk BCCs are classified as nodular, superficial, pigmented, fibroepithelial, adnexal differentiation/ infundibulocystic, whereas high-risk BCCs are classified as micronodular, infiltrating, sclerosing/morphoeic, basosquamous, and sarcomatoid by the World Health Organization. [43]

SCC: Nests of atypical tumor cells occur in the dermis during the latter phases of invasion. Diagnosis can be aided by the presence of full-thickness epidermal atypia and hair follicle involvement with nuclear atypia and keratinization.[44]

DERMATOFIBROMA: characterized by a storiform fascicular arrangement of small, spindle- and ovoid-shaped cells with slightly unevenly shaped nuclei. Inflammatory cells, foamy macrophages, Touton giant cells, and siderophages are all present in varying proportions. Hyaline collagen is thickened and confined at the lesion's edges. There is also hyperplasia of the epidermis that covers the lesion. Tumor cells are immunohistochemically positive for factor XIIIa, smooth muscle actin, and CD68, and frequently express desmin and CD34. angiosarcoma.[22]

PYOGENIC GRANULOMA: formed by capillaries and veins lined with fat endothelial cells and veins lined with fibromyxoid stroma that divides the structure into discrete lobules. Different stages of development are known as (i)the cellular phase, (ii) the capillary phase or vascular phase, and (iii) the involutionary phase. Untreated lesions show fibromatous regression more slowly over time.[45]

MELANOMA: most frequent histologic subtype is that of superficially spreading melanoma. Nearly three-quarters of all malignant skin tumors (melanomas) are neoplasms. Melanocytes

are poorly circumscribed, solitary melanocytes predominate over melanocyte nests, melanocytes are found above the basal layer (Pagetoid spread), and melanocyte nests are not cohesive. diagnosed when cancerous melanocytes in the epidermis have migrated laterally.[46]

STUDIES CORRELATING DERMOSCOPY, HISTOPATHOLOGY AND ULTRASONOGRAPHY

Clinical diagnosis is the preliminary and most important modality to diagnose skin tumors. Linares at al mentioned in their study that clinical examination can be enhanced using a magnifying lens or a dermatoscope. Dermoscopy seems to increase sensitivity in detecting skin cancers and a working knowledge of this modality can be helpful in the primary care setting. [47]

Pilat et al compared the data obtained from high-frequency ultrasonography, histopathology and dermoscopy in 54 nodular skin lesions, out of which 34 were detected as non-melanoma. The most common lesions were dermatofibroma, melanocytic naevi, basal cell carcinoma and pyogenic granuloma. BCC was found clinically as well-demarcated brownish nodules, on dermoscopy of the same lesion as multiple arborizing vessels and grey blue dots and with HFUS as a hypoechoic irregular shaped nodule with central haphazard echogenic areas. They correlated those weakly hyperechoic central areas to the radiant bands between the nodule on histopathology. In cases of dermatofibromas , areas with decreased echogenicity and irregular shape present intradermally directly correlated with poorly separated areas of connective tissue hyperproliferation. In vascular lesions like pyogenic granuloma, blood clots are visible in the HFUS as minor hyperechoic foci inside the nodule. The study concluded that ultrasound combined with dermoscopy may be a helpful tool in differential diagnostics of non-melanoma skin lesions stating that it allows better preparation for dermatological procedures and allows the selection of a suitable cutting margin.[48]

Dermoscopic features have also been correlated with histopathological features in some previous studies. Yelamos et al described histopathologic and dermoscopic features of various skin tumors and stated that dermoscopic features have direct histopathologic correlations making dermoscopy the perfect link between the clinical and pathological realms. Colours in dermoscopy are determined by the specific chromophores in the skin and where they are located. Most of the shades of skin colour result from greater levels of

naturally occurring substances such melanin (brown, black, grey, blue), blood (red), sebum or keratin (yellow), or collagen (white). Blood clots as black lacunae, balloon cells generation as white globules and xanthomization of cells (yellow granules). Increased pigmentation along extended rete ridges is shown histologically as a result of a higher concentration of melanocytes and pigmented keratinocytes per unit area. Melanocytic nests at the dermal-epidermal junction (DEJ) or in the papillary dermis are represented by brown and black globules, respectively, whereas nests in the reticular dermis are represented by blue globules. [11]

Pre-surgical ultrasonography can be useful in planning surgery and helps in determining the extent of tumor, layers of involvement and vascular pattern. Bobadilla et al and Song et al compared the ultrasonographic depth to histopathologic depth in 25 facial basal cell carcinoma lesions and 40 basal cell carcinoma lesions respectively. They concluded that there was an excellent intra class correlation (0.9) between the two modalities in comparing the thickness. [9,38] Bobadilla et al calculated the mean ultrasound thickness which was found to be 3.71+/-1.1mm and 3.91+/- 1mm from histology . Each patient's resistance index and peak systolic arterial flow velocity was determined. The average resistance index was 0.53+/- 0.1 (0.37-0.67) and the average peak systolic velocity was 9.1+/-4.09 cm/s (range, 4-22.2). [9] Preoperative ultrasonography was conducted on 49 lesions suspected of skin cancer. Ultrasound and histology were used for depth examination. The average ultrasonic depth of a skin lesion was 3.97+/-3.15 mm (range 0.8014.00), whereas the histological depth was 4.04 +/- 2.92 mm (range 1.00-14.00). The ultrasonography and histology measurements of skin lesion depth correlated excellently with one another (interclass correlation value = 0.953). Although USG is not intended to replace histologic examination but it may be utilised as a complementary diagnostic technique to help clinicians better prepare for a procedure.[38] Jo Kim et al also conducted a similar study on non-melanocytic skin cancers including BCC, SCC and merkel cell tumor over 30 patients. They also correlated USG depth and width with the histopathology depth and width. They found moderate correlation in width using kendall's tau-b coefficient and strong correlation in width using spearman's rank correlation coefficient. Mean thickness was lower in histopathology as compared to ultrasound.[49]

On the contrary, Kashani et a compared the depth in 56 primary BCC patients with an ultrasound machine with a 50MHz transducer. The average tumor depth assessed by HFUS (1353.68+/- microns) was less than that measured by the dermatopathologist (1560.71 +/- 1044.323 microns). Statistically, the difference was not significant ($P > 0.05$). The mean

greatest tumour diameter in HFUS and pathology was 5996.7+/- 2271.78 microns and 3807.7 +/-1995.452 microns, respectively (P <0.001). Low correlation in diameter and moderate correlation in depth was seen between these two approaches. It was concluded that the mean depth of tumor in USG was lower than that of histopathological depth. But the difference was not statistically significant.[8]

As most of the studies are on BCC, Kucinskiene et al did a comparative study between the relationship of skin tumor thickness on USG and histopathology in 72 skin tumors including melanoma and non-melanoma skin cancers. They concluded that medium frequency USG is not a reliable tool for precise measurement of thin skin tumors.(<1mm).[50] On the other side Bhatt et al in their publication mentioned that small tumors of 50microns can also be detected on USG. The same study also mentioned about one of the limitations of USG, that it sometimes overestimates the size of lesion due inflammatory infiltrate around tumor giving a falsely larger dimension. [39]

Ultrasonography is increasingly used in evaluation of soft tissue tumors that are palpable as it is non-invasive and much safer. Basic ultrasonographic examination is deficient in complexity of these tumors. C. L. Wu et al correlated the characteristics of echotexture with histology in order to get ultrasonography with cellular resolution. It indicated that a collagen matrix with a high concentration of fibroblasts correlates with a hyperechoic pattern on ultrasonic imaging. The study concluded that if there are fewer cell types and more compact groupings then the echotexture is more homogenous. The homogeneity of echotexture increases with the compactness of the arrangement of tumor cells. The difference in tissue acoustic impedance determines echogenicity; the smaller the difference, the lower the echogenicity.[51]

It is crucial to have early and precise identification of all kinds of skin cancer in order to guide efficient treatment as well as increase survival rates. A systematic review assessed the diagnostic accuracy of HFUS in skin cancers including melanoma, SCC and BCC. They reviewed 6 studies and found sensitivities of 83% for melanoma using qualitative characteristics, and 100% in some other studies & specificity of 33% and 73% respectively. [52]

MATERIALS & METHODS

MATERIALS & METHODS

STUDY SETTING:

This study was conducted on patients with clinical suspicion of benign and malignant skin tumors, attending the Dermatology, Venereology and Leprology OPD [telemedicine and physical] at AIIMS Jodhpur.

STUDY DESIGN:

A Cross-sectional observational study

STUDY PARTICIPANTS:

Inclusion criteria:

Patients fulfilling all the following criteria were included in the study, after informed written consent.

1. Clinically suspected benign and malignant skin tumors
2. Age ≥ 18 years
3. Lesions without any previous treatment or biopsy
4. Lesions more than or equal to 0.5 cm and less than or equal to 5 cm.

Exclusion criteria:

Following patient were excluded from the study.

1. Inaccessible sites where USG cannot be performed
2. Bleeding disorders

SAMPLING: We estimated a sample size of **38** at 0.5 correlation coefficient , 95% confidence interval and 90% power

Using formula , $\mathbf{N=[(Z_\alpha+Z_\beta)/C]^2 + 3}$

$(C = 0.5 * \ln[(1+r)/(1-r)])$

(N-sample size, Z_α –standard normal deviate for alpha, Z_β- standard normal deviate for beta , r-correlation coefficient)

We included 52 lesions in our study.

STUDY DURATION: March 2021 to August 2022 (18 months)

ETHICAL CONSIDERATIONS:

Thesis proposal was approved by the Institutional Ethics Committee, All India Institute of Medical Sciences, Jodhpur [Certificate reference no. AIIMS/IEC/2021/3309 dated 12 march, 2021 (Annexure-I)]. At the time of recruitment, detailed explanation of the study protocol was provided to the participants, following which written informed consent was obtained prior to enrolment.

STUDY PROCEDURE:

Evaluation of Patients

Patients fulfilling the selection criteria were recruited in the study after written informed consent. Detailed history and clinical examination of the recruited patients was done at baseline. A structured case sheet/proforma was filled which comprised of patient characteristics and demographic details including name, age, address, education, marital status, duration of disease, addiction, family history with other relevant history of medications and comorbidities. Baseline clinical photographic evaluation of individual lesions was done .

Dermoscopic examination was performed using a manual hand-held dermatoscope DERMLITE® DL4 at 10X magnification and 12 megapixel(MP) mobile camera for photographic documentation. Features such as background color, vessels, clods, dots, pigment network, and other additional findings were noted.

Figure 3 : Dermoscope(Dermlite DL4) and mobile phone used to capture images

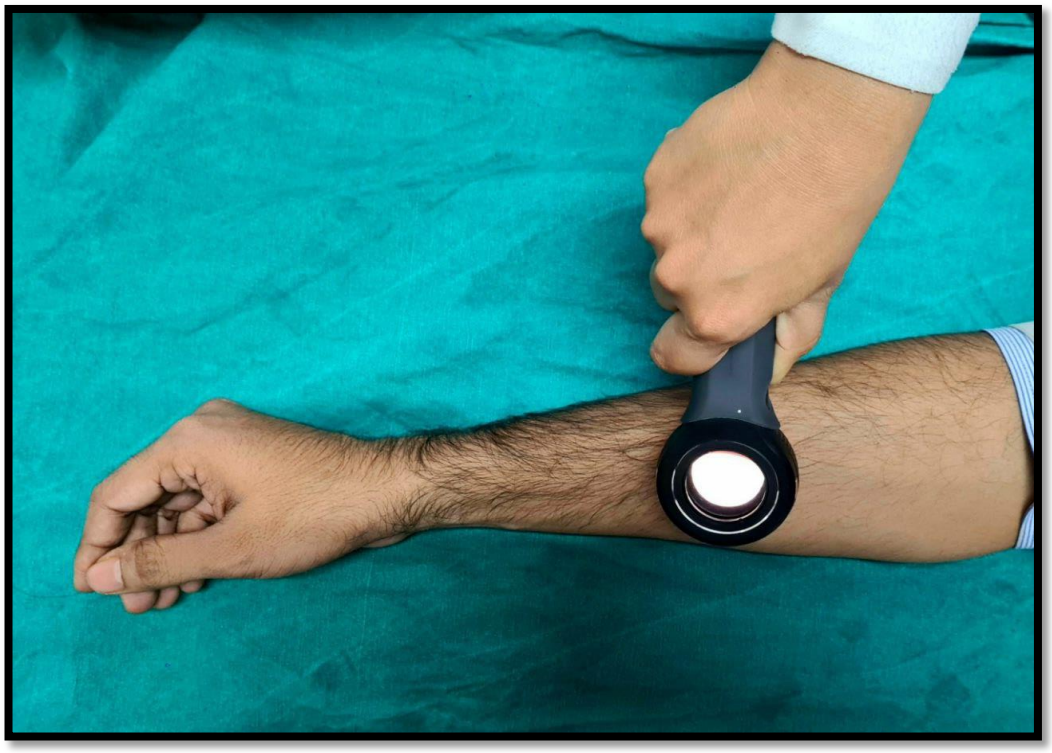


Figure 4 :- Dermoscopic examination of a lesion over forearm

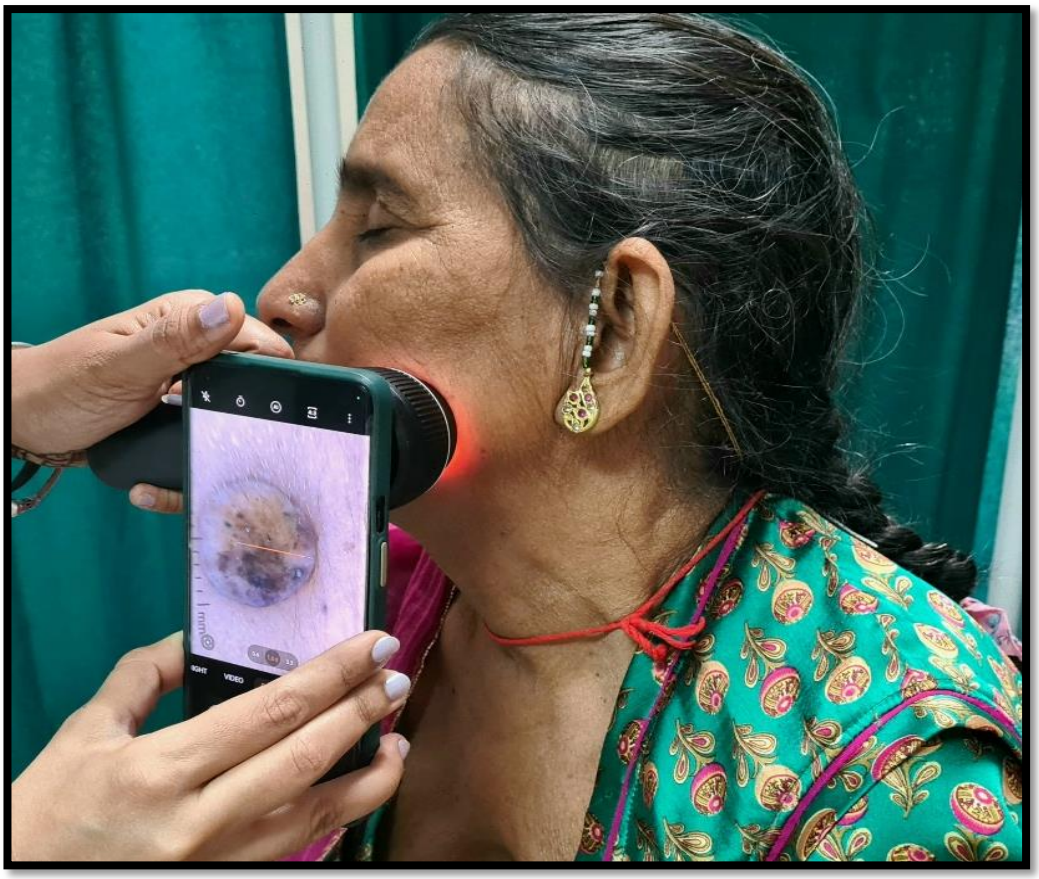


Figure 5 :- Dermoscopic examination and photographic documentation

Ultrasound with color Doppler study of the lesions was performed using an Aixplorer ultrasound machine [Supersonic Imagine, Aix-en-provence, France] with a Super Linear HockeyStick 20-6 transducer with frequency range 6-20 MHz probe . An abundant amount of gel was used over the surface of the lesions. During the whole ultrasonography process, probe was kept perpendicular to the skin without pressure. Compression was avoided in performing ultrasound as it may result in false thinning and movement of nodules on sides of field. HFUS examination of each lesion consisted of (a) morphological analysis of structure, margins, echogenicity, homogenecity of lesion; (b) measurement of transverse diameter and thickness; (c) color doppler USG for vasculature (d) in cases of suspicion of malignancy, locoregional spread of tumor is assessed. Thickness was measured from epidermis till the lowermost involving point of the tumor.

It was followed by tissue sampling (excisional or 4mm punch biopsy) which was sent for histopathological analysis. Sample was fixed in 10% buffered formalin and stained with hematoxylin and eosin and examined under the microscope. The histology report included final histopathological diagnosis, size, depth, level of invasion, inflammatory infiltrate,

vasculature, appendages and collagen. Tumor thickness measurements were made from the epidermal granular layer to the deepest point in the slide with major tumoral infiltration. For most of the lesions, excisional biopsy was preferred as it helped in total removal of the tumor and estimation of tumor depth for further analysis. Excision technique was based on type of tumor i.e. in BCC cases, wide local excision was preferred whereas in other tumors elliptical or punch biopsy was taken. Wound closure was done with sutures.

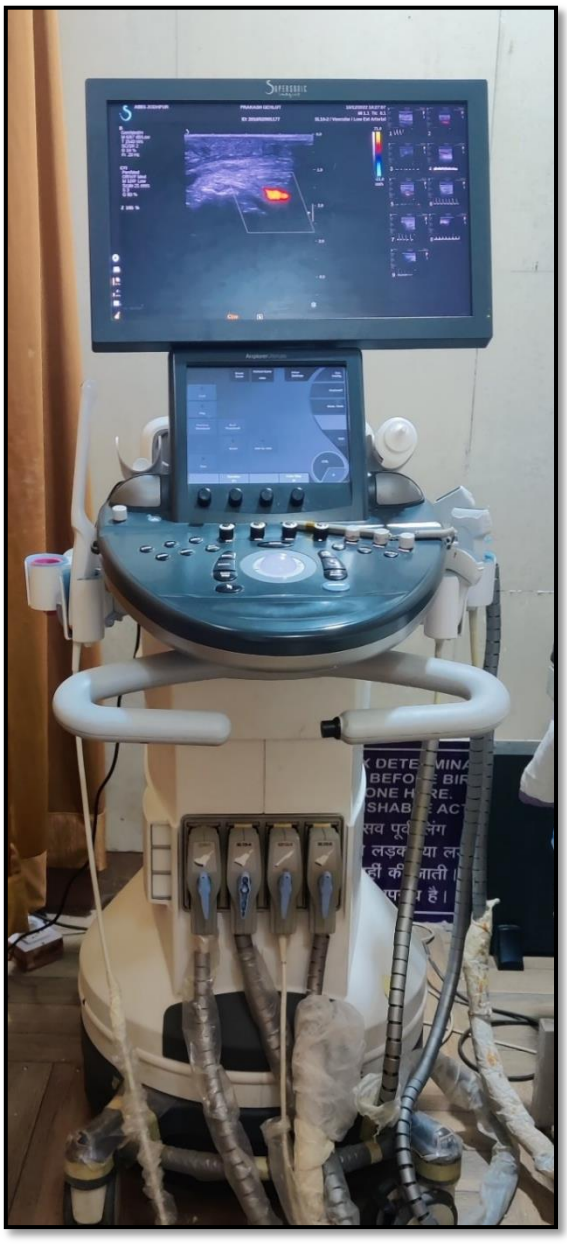


Figure 6 : Supersonic Imagine ,Aix-en-provence, Ultrasound machine

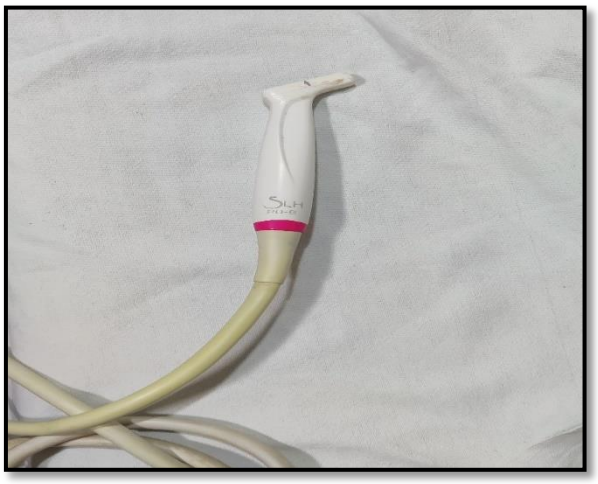


Figure 7 : A SuperLinear HockeyStick 20-6 transducer probe

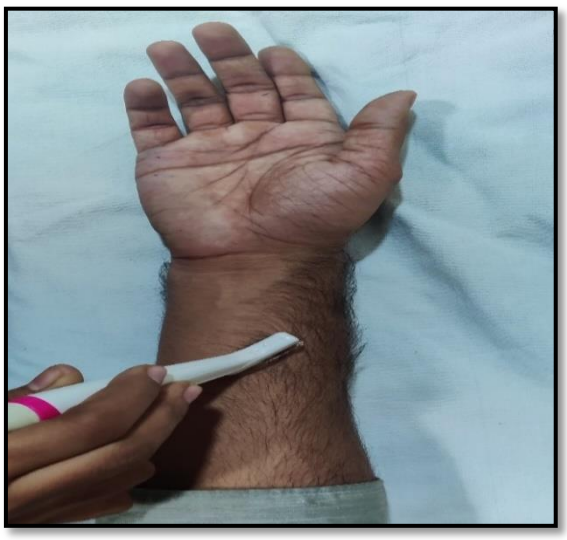


Figure 8 : Ultrasonography of lesion over forearm using 20MHz probe

STATISTICAL ANALYSIS

The presentation of the Categorical variables was done in the form of number and percentage (%). On the other hand, the quantitative data with normal distribution were presented as the means ± SD and the data with non-normal distribution as median with 25th and 75th percentiles (interquartile range). The data normality was checked by using Kolmogorov-Smirnov test. The cases in which the data was not normal, we used non parametric tests. The following statistical tests were applied for the results:

1. The association of the variables which were qualitative in nature were analysed using Fisher's exact test as atleast one cell had an expected value of less than 5.

2. Sensitivity, specificity, positive predictive value and negative predictive value was calculated of USG for predicting vascularity and various diseases after taking histopathology as gold standard.

3. Spearman rank correlation coefficient was used for correlation of clinical width(mm) with USG width(mm) and between USG depth(mm) with HPE depth(mm).

4. Intraclass correlation was used for correlation of USG depth(mm) with HPE depth(mm).

5. Inter-rater kappa agreement was used to assess strength of agreement between USG vascularity and HPE vascularity, between USG level of invasion and HPE level of invasion, between USG diagnosis and final diagnosis. Kappa statistics of 0.21e0.40 indicate fair agreement, 0.41 to 0.60 indicates moderate agreement, 0.61 to 0.80 indicates good agreement and 0.81 to 1.00 indicates very good agreement

The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 25.0.

For statistical significance, p value of less than 0.05 was considered statistically significant.

RESULTS

RESULTS

This study was conducted in Dermatology, Venereology and Leprology OPD [telemedicine and physical] at AIIMS Jodhpur. 52 patients of clinically suspected benign and malignant skin tumors fulfilling the selection criteria were included in the study. Dermatoscopic examination, color doppler ultrasound study and histopathology of the lesions were performed in each patient . In this report we have used HFUS and USG interchangeably .

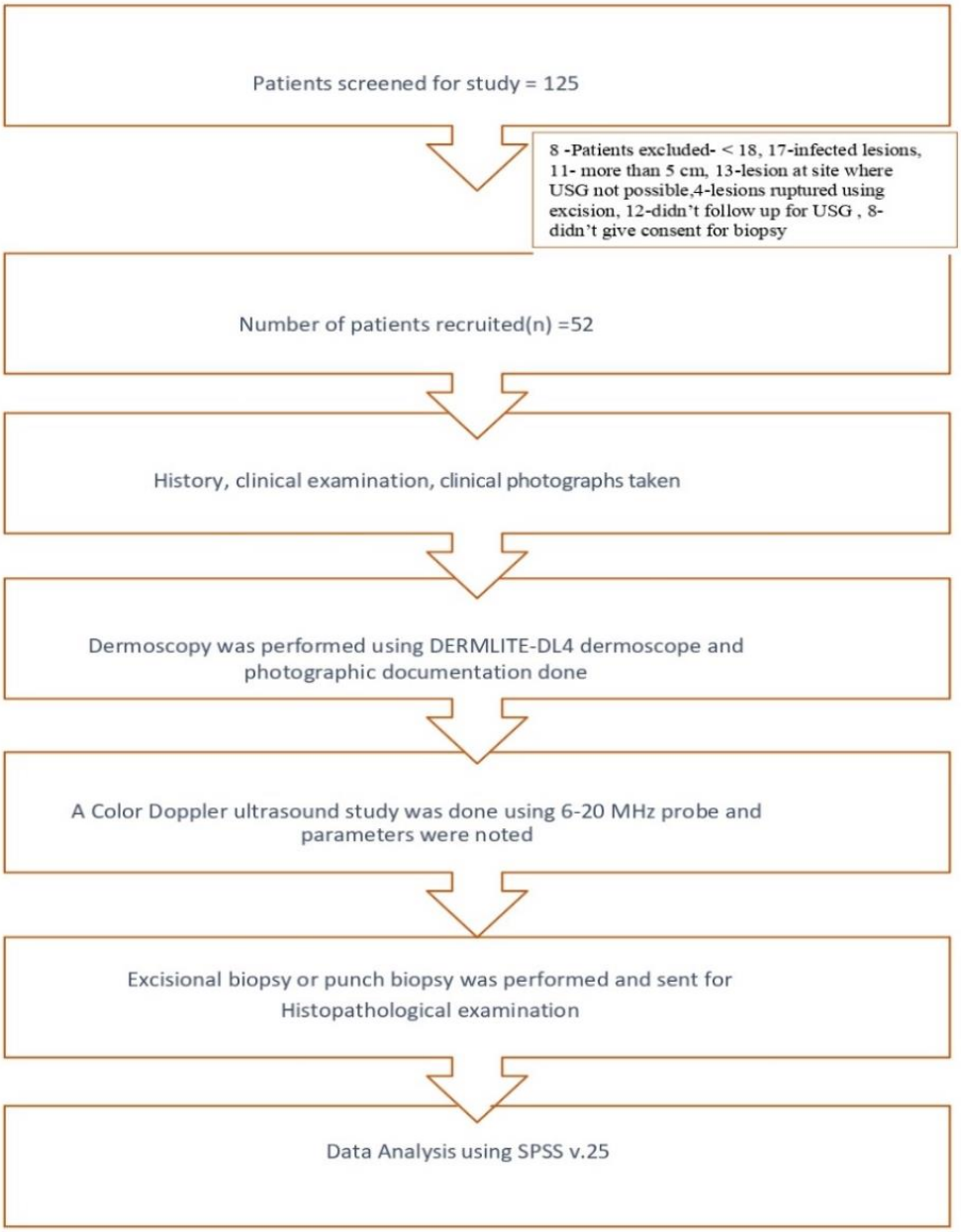


Figure 9 : Consort diagram of the study

Demographic characteristics of patients

Mean age of study subjects was 36.81 ± 18.7(years) . Residence of majority of patients was urban [30(57.69%)]. There was increased female preponderance (61.54%). The common occupations were student (40.38%) followed by housewife [20(38.46%)] and professional [7(13.46%)]. Majority [36(69.23%)] of patients were literate. Mean duration of illness(months) was 38.75 ± 46.5 (mean ± SD) with duration ranging from 2 months to 180 months.

Table no.3: Demographic characteristics of patients (n=52)

Age(years) (Mean ±SD**)**	**Frequency**	**Percentage**
18-20	12	23.08%
21-30	13	25.00%
31-40	9	17.31%
41-50	7	13.46%
51-60	4	7.69%
61-70	2	3.85%
71-80	5	9.62%
Gender		
Female	32	61.54%
Male	20	38.46%
Area of residence		
Rural	22	42.31%
Urban	30	57.69%
Education		
Illiterate	16	30.77%
Literate	36	69.23%
Occupation		
Housewife	20	38.46%
Student	21	40.38%
Semiskilled worker	2	3.85%
Professional	7	13.46%
Unemployed	2	3.85%

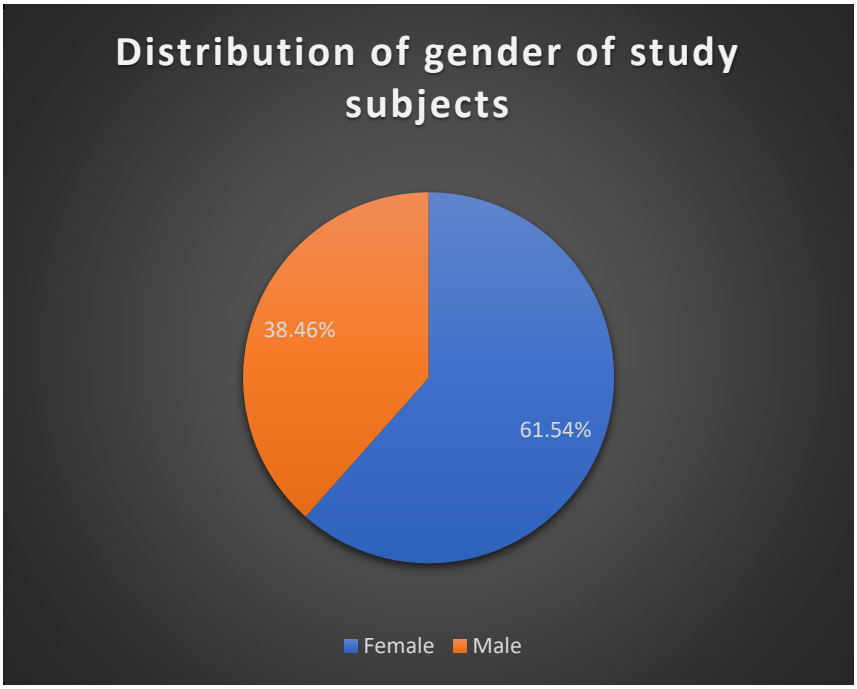


Figure 10 :-Distribution of gender of study subjects

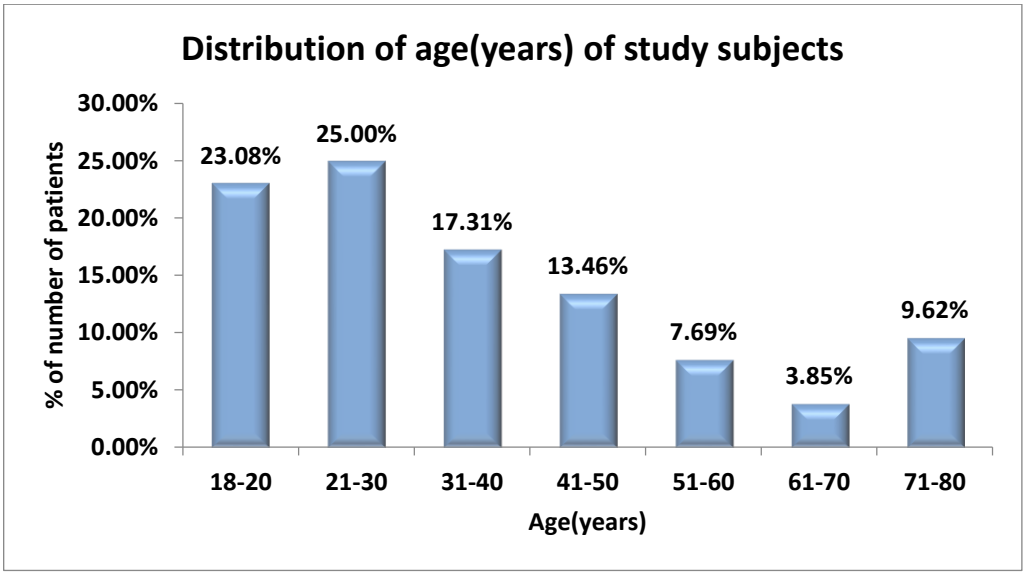


Figure 11 :- Distribution among age groups of the study population

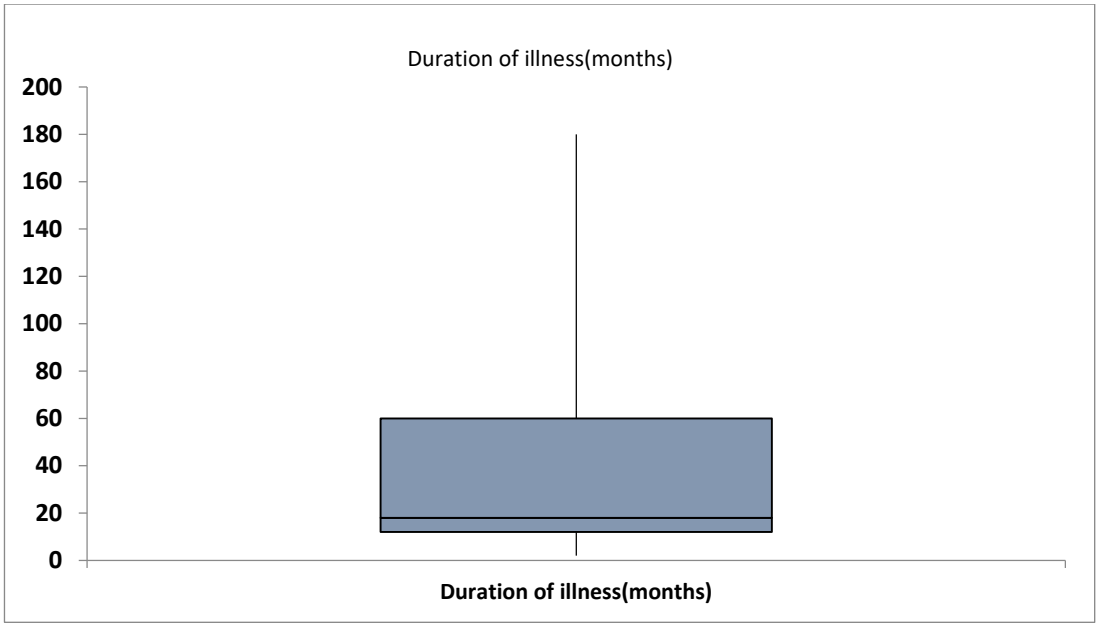


Figure 12 :- Box-plot showing duration of illness(months)

Table no. 4 :-Distribution of clinical findings of study subjects.

Clinical findings	Frequency	Percentage
Site of lesion		
Scalp	11	21.15%
Face	24	46.15%
Upper limb	9	17.31%
Lower limb	4	7.69%
Trunk	4	7.69%
Size of lesion		
<1cm	19	36.54%
1 to 3cm	30	57.69%
>3cm	3	5.77%
Color of lesion		
Erythematous	17	32.69%
Skin colored	21	40.38%
Hyperpigmented	13	25.00%
Violaceous	1	1.92%
Morphology		
Nodule	38	73.08%
Papule	6	11.54%
Plaque	7	13.46%
Noduloplaque	1	1.92%
Specific morphology		
Exophytic	6	11.54%
Raised	29	55.77%
Deep	17	32.69%
Consistency		
Soft	27	51.92%
Firm	23	44.23%
Hard	2	3.85%
Satellite lesion	6	11.54%
Clinical width/size(mm)		
Mean ± SD	13.08 ± 8.27	

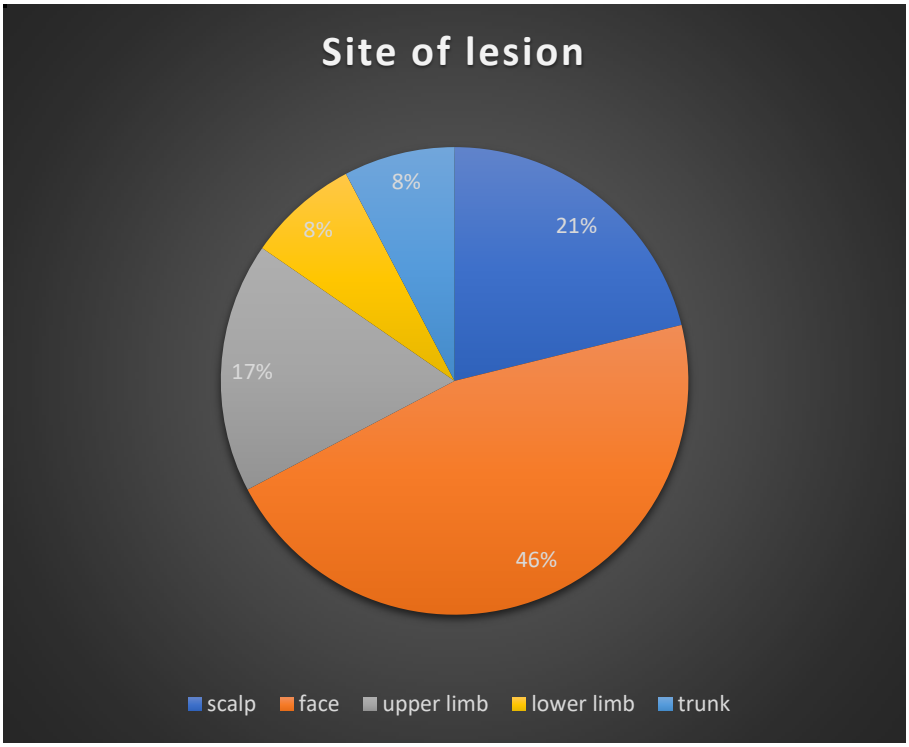


Figure 13 :-Pie chart showing distribution in Site of lesion

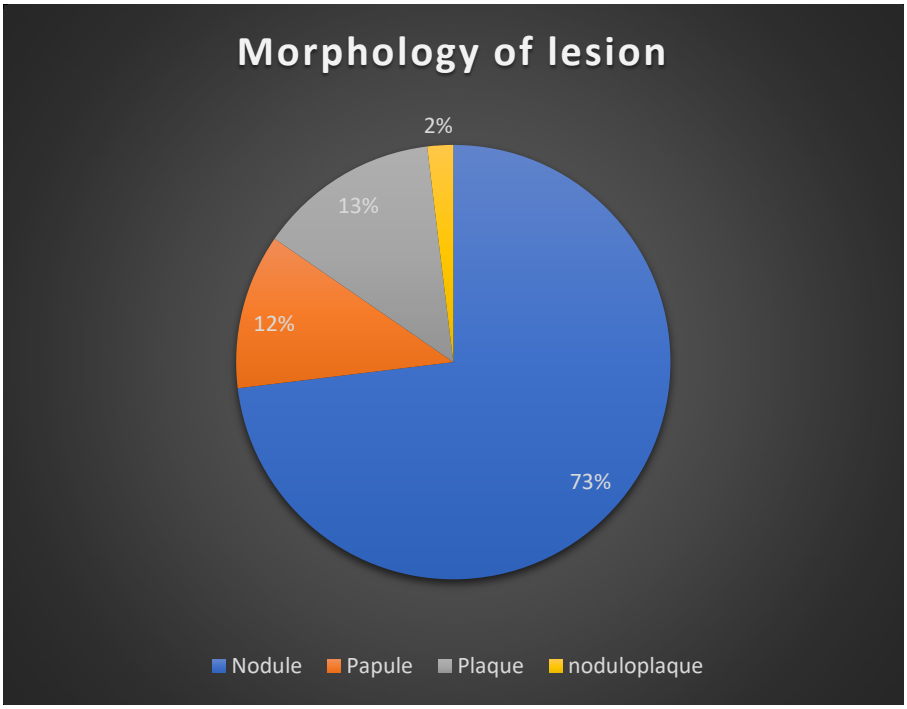


Figure 14:- Pie chart showing distribution in Morphology of lesion

CLINICAL EXAMINATION

The most common site of involvement which was seen in majority [24(46.15%)] of patients, was the face followed by scalp [11(21.15%)] and upper limb [9(17.31%)]. Multiple morphologies of lesion were detected during the study period and predominant morphology was found to be nodule [30(57.69%)] followed by plaque [7(13.46%)]. Most of the lesions were skin colored and erythematous, out of all the lesions larger proportion was soft[27(51.92%)] in consistency followed by firm[23(44.23%)] with only 2 lesions having hard consistency. Clinically, width or diameter of the individual lesions was calculated and the mean value was calculated as 13.08 ± 8.27. Majority [34(65.38%)] of the patients did not have any co-morbidities while hypertension was observed in 9(17.31%) of patients and diabetes mellitus in 5(9.62%) of patients None of the patients had positivity for viral markers or bleeding diathesis.

Table no.5 :-Distribution of dermoscopy features of study subjects.

Dermoscopy features	**Frequency**	**Percentage**
Color		
Skin color	32	61.54%
Erythematous	8	15.38%
Hyperpigmented	12	23.08%
Arborizing vessel	16	30.77%
Linear vessel	20	38.46%
Dotted vessel	8	15.38%
Lacunae vessel	15	28.85%
Polymorphous vessel	9	17.31%
Clods	36	69.23%
Dots	29	55.77%
Pigment network	33	63.46%
Negative pigment network	3	5.77%
Homogeneous pattern	42	80.77%
Streaks	14	26.92%

In majority [32(61.54%)] of the patients, the lesion was skin colored followed by hyperpigmented lesion [12(23.08%)]. Color was erythematous in only 8 out of 52 patients (15.38%). 42(80.77%) patients had homogeneous pattern followed by clods [36(69.23%)], pigment network [33(63.46%)], dots [29(55.77%)], streaks [14(26.92%)]. streaks [14(26.92%)] on dermoscopy.

Table no.6 :-Distribution of USG findings of study subjects.

USG findings	Frequency	Percentage
Shape		
Oval	24	46.15%
Round	9	17.31%
Irregular	19	36.54%
Consistency		
Solid	39	75.00%
Cystic	8	15.38%
Semisolid	5	9.62%
Echogenicity		
Hypoechoic	42	80.77%
Hyperechoic	7	13.46%
Isoechoic	3	5.77%
Homogeneity		
Heterogenous	21	40.38%
Homogenous	31	59.62%
Level of invasion		
Dermis	15	28.85%
Subcutis	7	13.46%
Epidermis+dermis	28	53.85%
Dermis+subcutis	2	3.85%
Location of vessels		
No	17	32.69%
Peripheral	11	21.15%
Base	11	21.15%
Central	8	15.38%
Hypervascular	4	7.69%
Linear	1	1.92%
Locoregional spread	6	11.54%
Vascularity	37	71.15%
Satellite lesion	11	21.15%
Depth(mm)		
Mean ± SD	6.55 ± 5.06	
Width(mm)		
Mean ± SD	13.03 ± 8.24	

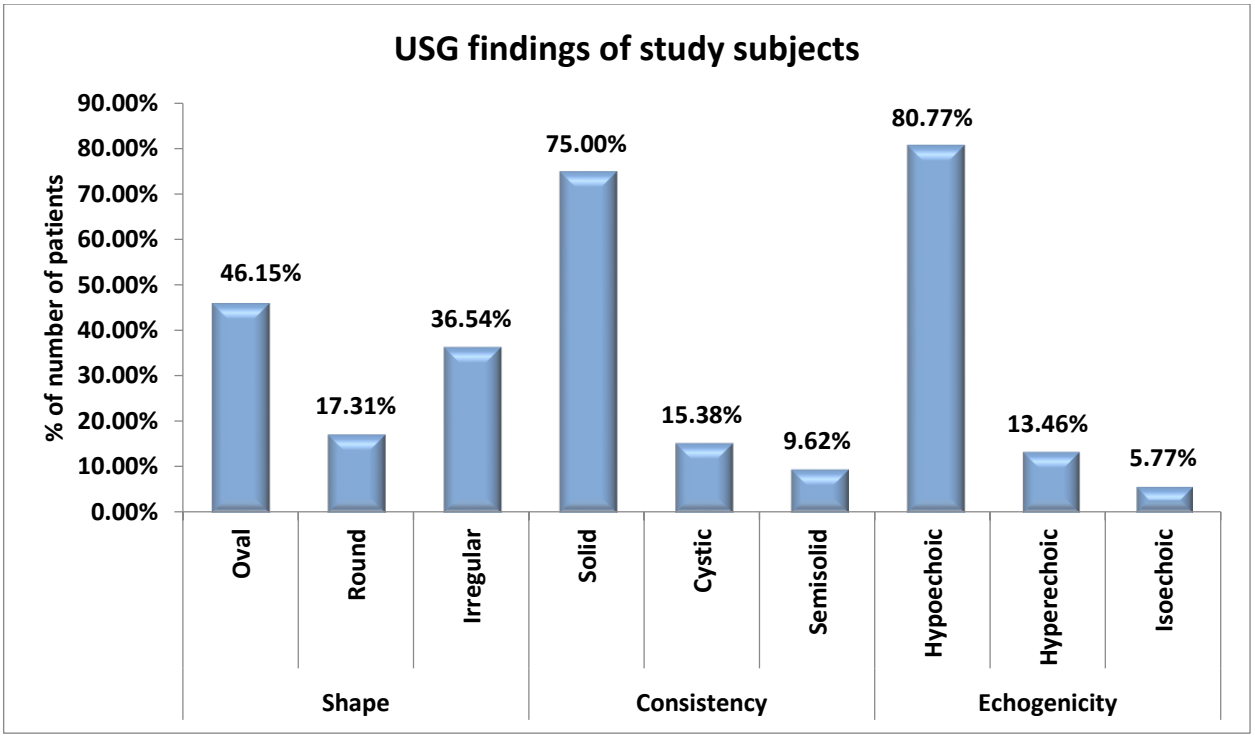


Figure 15: Distribution of USG findings of study subjects

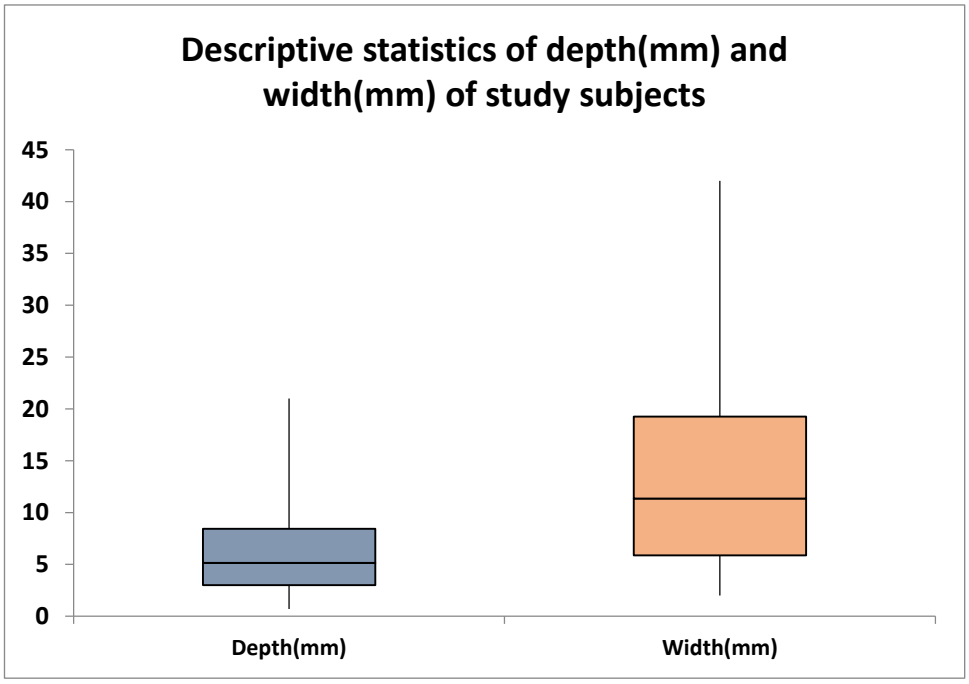


Figure 16 :-Box-plot of depth(mm) and width(mm) of skin tumors.

Table no. 7 :-Distribution of HPE findings of study subjects.

HPE findings	Frequency	Percentage
Level of invasion		
Dermis	20	38.46%
Subcutis	7	13.46%
Epidermis+dermis	23	44.23%
Dermis+subcutis	2	3.85%
Tumor type		
Benign	38	73.08%
Malignant	14	26.92%
Nuclear atypia	6	11.54%
Vascularity	21	40.38%
Depth(mm)		
Mean ± SD	**6.44 ± 4.76**	

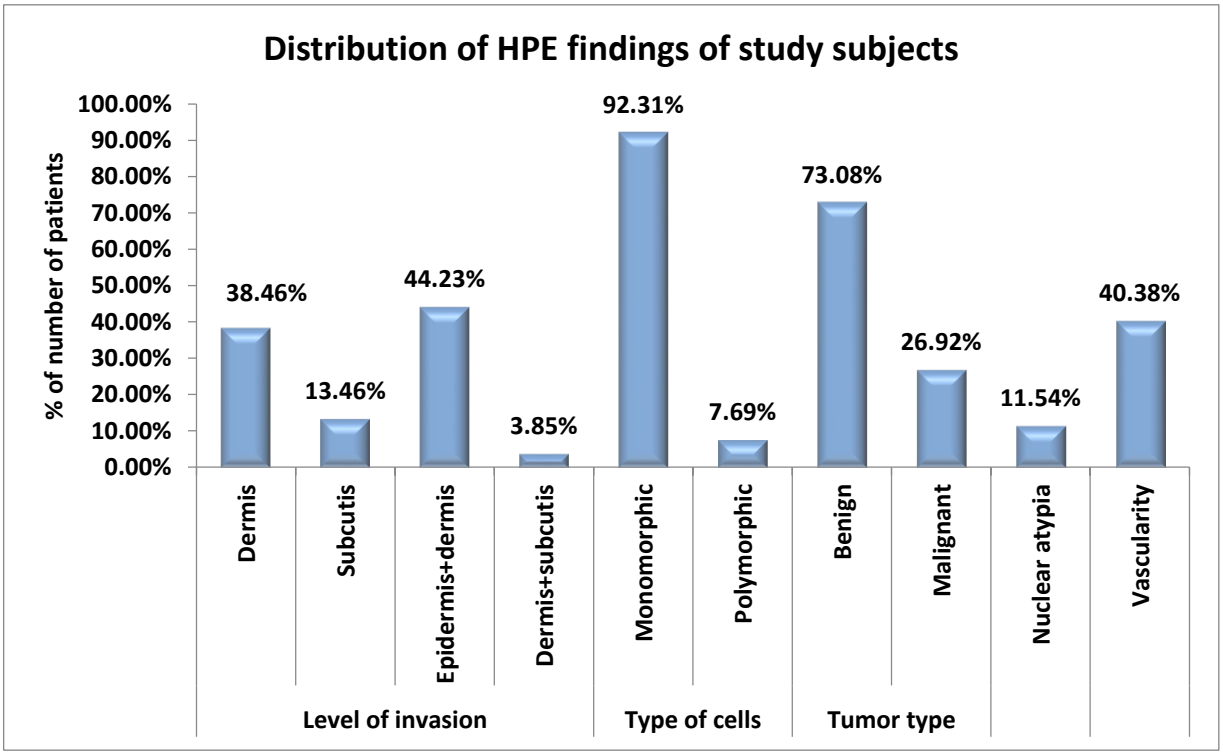


Figure 17 :-Distribution of HPE findings of study subjects.

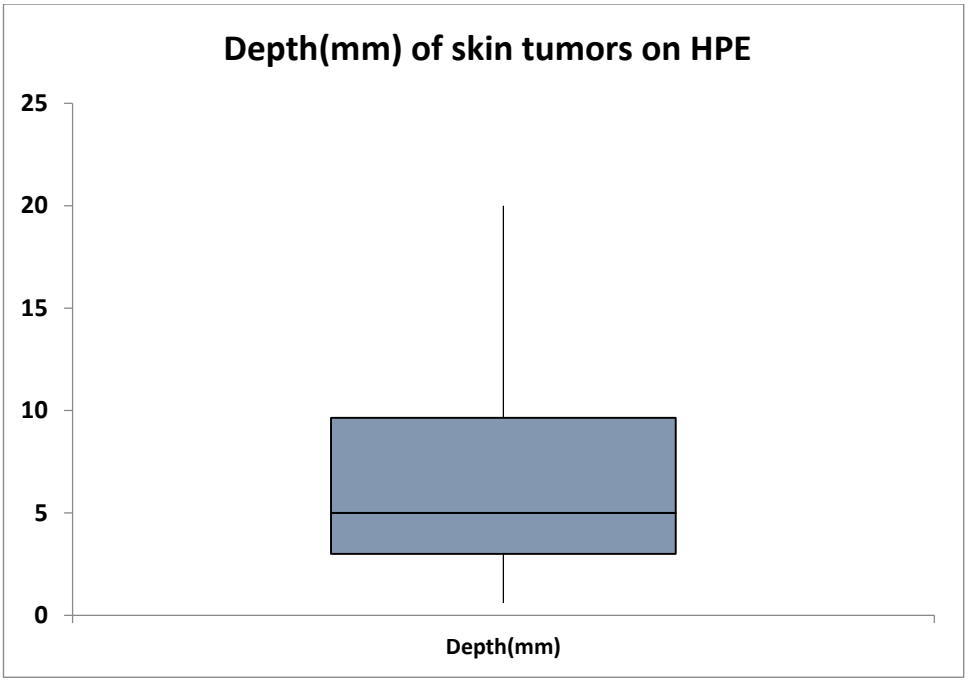


Figure 18 :-Box-plot of depth(mm) of skin tumor on HPE.

DIAGNOSIS :

Tumors in our study were divided into 8 groups for easier analysis and categorization. Appendageal tumors included nodular hidradenoma, trichoepithelioma, trichofolliculoma, syringocystadenoma papilliferum, pilomatricoma and hidrocystoma. Cyst include pilar cyst, epidermal inclusion cyst. Spindle cell tumors include dermatofibroma, neurofibroma and leiomyoma. Adipocytic tumor includes lipoma, pyogenic granuloma is included under heading of vascular tumors. Others includes glomus tumor, keratoacanthoma, cutaneous metastasis and dermal melanocytic nevus.

Table no.8 :-Distribution of diagnosis of study subjects on basis of clinical, ultrasonographic and histopathological examination

Provisional clinical diagnosis	**Frequency**	**Percentage**
Appendageal tumor	9	17.31%
Cyst	5	9.62%
Spindle cell tumor	10	19.23%
Adipocyte tumor	3	5.77%
Vascular tumor	4	7.69%
Basal cell carcinoma	12	23.08%
Others	9	17.31%
HFUS diagnosis		
Appendageal tumor	8	15.38%
Cyst	8	15.38%
Spindle cell tumor	7	13.46%
Adipocyte tumor	4	7.69%
Vascular tumor	5	9.62%
Basal cell carcinoma	12	23.08%
Others	8	15.38%
Final diagnosis{HPE}		
Appendageal tumor	10	19.23%
Cyst	7	13.46%
Spindle cell tumor	8	15.38%
Adipocyte tumor	3	5.77%
Vascular tumor	4	7.69%
Basal cell carcinoma	12	23.08%
Melanoma	1	1.92%
Others	7	13.46%

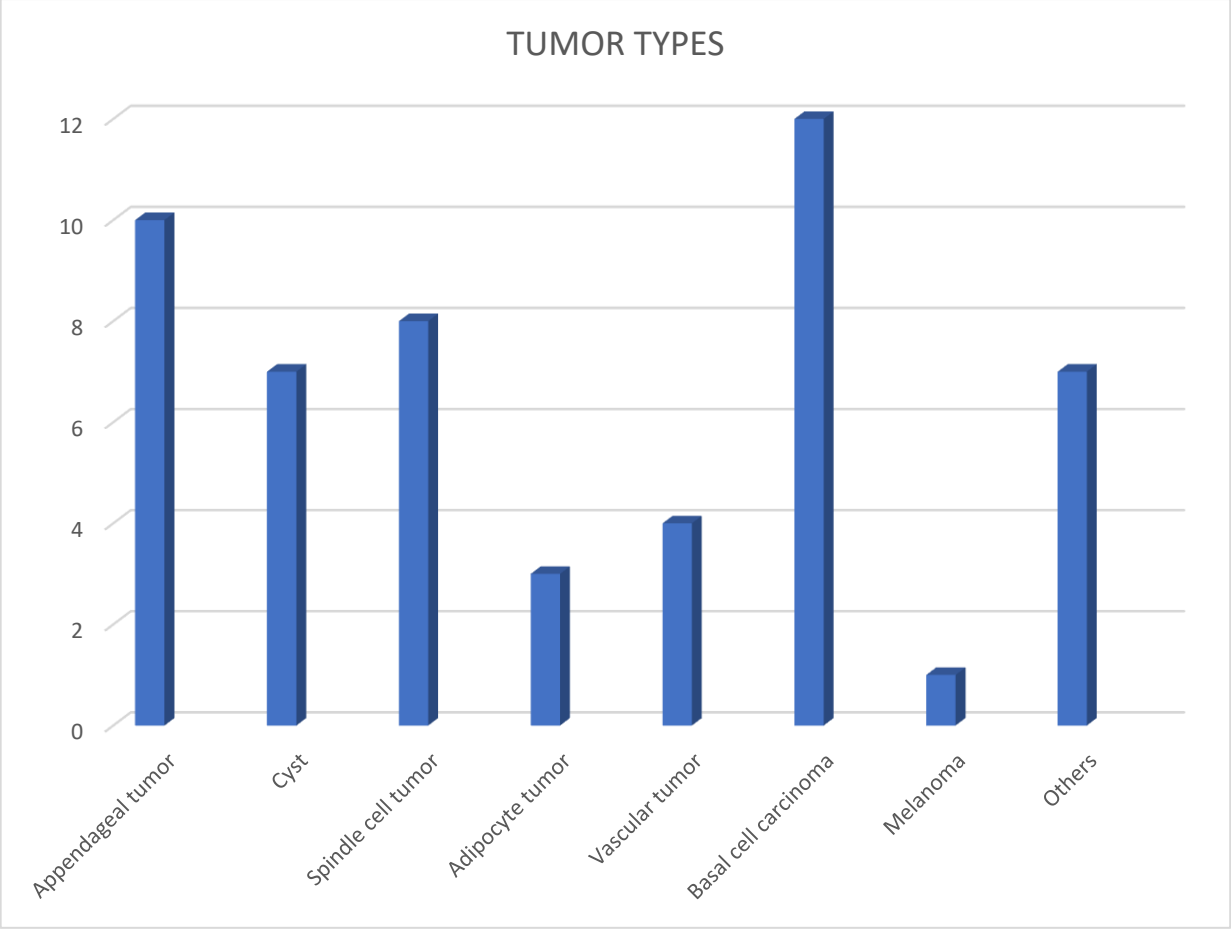


Figure 19 : Distribution of tumors included in the study

INTER RATER RELIABILITY BETWEEN HFUS DIAGNOSIS AND FINAL DIAGNOSIS BASED ON HISTOPATHOLOGY

Table no. 9 :- Inter-rater kappa agreement between HFUS diagnosis and final diagnosis.

HFUS diagnosis	Final diagnosis{HPE}								Total	P value	Kappa
	Appendageal tumor (n=10)	Cyst (n=7)	Spindle cell tumor (n=8)	Adipocyte tumor (n=3)	Vascular tumor (n=4)	Basal cell carcinoma (n=12)	Melanoma (n=1)	Other (n=7)			
Appendageal tumor	**8** (15.38%)	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)	**8** (15.38%)	**<0.0001**	**0.886**
Cyst	**1** (1.92%)	**7** (13.46%)	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)	**8** (15.38%)		
Spindle cell tumor	**0** (0%)	**0** (0%)	**7** (13.46%)	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)	**7** (13.46%)		
Adipocyte tumor	**1** (1.92%)	**0** (0%)	**0** (0%)	**3** (5.77%)	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)	**4** (7.69%)		
Vascular tumor	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)	**4** (7.69%)	**0** (0%)	**0** (0%)	**1** (1.92%)	**5** (9.62%)		
Basal cell carcinoma	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)	**0** (0%)	**12** (23.08%)	**0** (0%)	**0** (0%)	**12** (23.08%)		
Others	**0** (0%)	**0** (0%)	**1** (1.92%)	**0** (0%)	**0** (0%)	**0** (0%)	**1** (1.92%)	**6** (11.54%)	**8** (15.38%)		
Total	**10** (19.23%)	**7** (13.46%)	**8** (15.38%)	**3** (5.77%)	**4** (7.69%)	**12** (23.08%)	**1** (1.92%)	**7** (13.46%)	**52** (100%)		

Among 10 patients diagnosed as appendageal tumor via final diagnosis{HPE}, 8 patients had similar diagnosis in USG . Among 7 patients diagnosed as cyst via final diagnosis{HPE}, 7 patients had similar diagnosis in USG . Among 8 patients diagnosed as spindle cell tumor via final diagnosis{HPE}, 7 patients had similar diagnosis in USG. Among 3 patients diagnosed as adipocyte tumor via final diagnosis{HPE}, 3 patients had similar diagnosis in USG. Among 4 patients diagnosed as vascular tumor via final diagnosis{HPE}, 4 patients had similar diagnosis in USG. Among 12 patients diagnosed as basal cell carcinoma via final diagnosis{HPE}, 12 patients had similar diagnosis in USG. Among 1 patient diagnosed as melanoma via final diagnosis{HPE}, none of the patient had similar diagnosis in USG. Among 7 patients diagnosed as others via final diagnosis{HPE}, 6 patients had similar

findings in USG diagnosis. **Overall concordance rate was 90.38% and overall discordance rate was 9.62% between Final diagnosis{HPE} and USG diagnosis. Very good agreement existed between final diagnosis{HPE} and USG diagnosis with kappa 0.886 and p value <.0001.**

SENSITIVITY, SPECIFICITY, POSITIVE PREDICTIVE VALUE AND NEGATIVE PREDICTIVE VALUE FOR HFUS FOR PREDICTING VARIOUS TUMORS TAKING HISTOPATHOLOGY AS GOLD STANDARD.

USG was 100% sensitive in detecting cyst, Adipocyte tumor, Vascular tumor, Basal cell carcinoma followed by Spindle cell tumor (87.50%), Others (glomus tumor, keratoacanthoma, mets) (85.71%), Appendageal tumor (80%). 1 patient of Melanoma was not detected by USG making sensitivity 0%.USG was 100% specific in detecting Appendageal tumor, Spindle cell tumor, Basal cell carcinoma, Melanoma followed by Adipocyte tumor (97.96%), Vascular tumor (97.92%), Cyst (97.78%)

Table no.10:- Sensitivity, specificity, positive predictive value and negative predictive value of USG for predicting various diseases after taking histopathology as gold standard.

Final diagnosis {HPE}	**Sensitivity (95% CI)**	**Specificity (95% CI)**	**AUC (95% CI)**	**Positive Predictive Value (95% CI)**	**Negative Predictive Value (95% CI)**	**Diagnostic accuracy**
Appendageal tumor (n=10)	**80.00%** (44.39% to 97.48%)	**100.00%** (91.59% to 100.00%)	**0.9** (0.78 to 0.97)	**100.00%** (63.06% to 100.00%)	**95.45%** (84.53% to 99.44%)	**96.15%**
Cyst (n=7)	**100.00%** (59.04% to 100.00%)	**97.78%** (88.23% to 99.94%)	**0.99** (0.91 to 1.00)	**87.50%** (47.35% to 99.68%)	**100.00%** (91.96% to 100.00%)	**98.08%**
Spindle cell tumor (n=8)	**87.50%** (47.35% to 99.68%)	**100.00%** (91.96% to 100.00%)	**0.94** (0.83 to 0.99)	**100.00%** (59.04% to 100.00%)	**97.78%** (88.23% to 99.94%)	**98.08%**
Adipocyte tumor (n=3)	**100.00%** (29.24% to 100.00%)	**97.96%** (89.15% to 99.95%)	**0.99** (0.91 to 1.00)	**75.00%** (19.41% to 99.37%)	**100.00%** (92.60% to 100.00%)	**98.08%**
Vascular tumor (n=4)	**100.00%** (39.76% to 100.00%)	**97.92%** (88.93% to 99.95%)	**0.99** (0.91 to 1.00)	**80.00%** (28.36% to 99.49%)	**100.00%** (92.45% to 100.00%)	**98.08%**
Basal cell carcinoma (n=12)	**100.00%** (73.54% to 100.00%)	**100.00%** (91.19% to 100.00%)	**1** (0.93 to 1.00)	**100.00%** (73.54% to 100.00%)	**100.00%** (91.19% to 100.00%)	**100.00%**

Melanoma (n=1)	**0.00%** (0.00% to 97.50%)	**100.00%** (93.02% to 100.00%)	**0.5** (0.36 to 0.64)	0.00% ()	**98.08%** (89.74% to 99.95%)	**98.08%**
Others	**85.71%** (42.13% to 99.64%)	**95.56%** (84.85% to 99.46%)	**0.91** (0.79 to 0.97)	**75.00%** (34.91% to 96.81%)	**97.73%** (87.98% to 99.94%)	**94.23%**

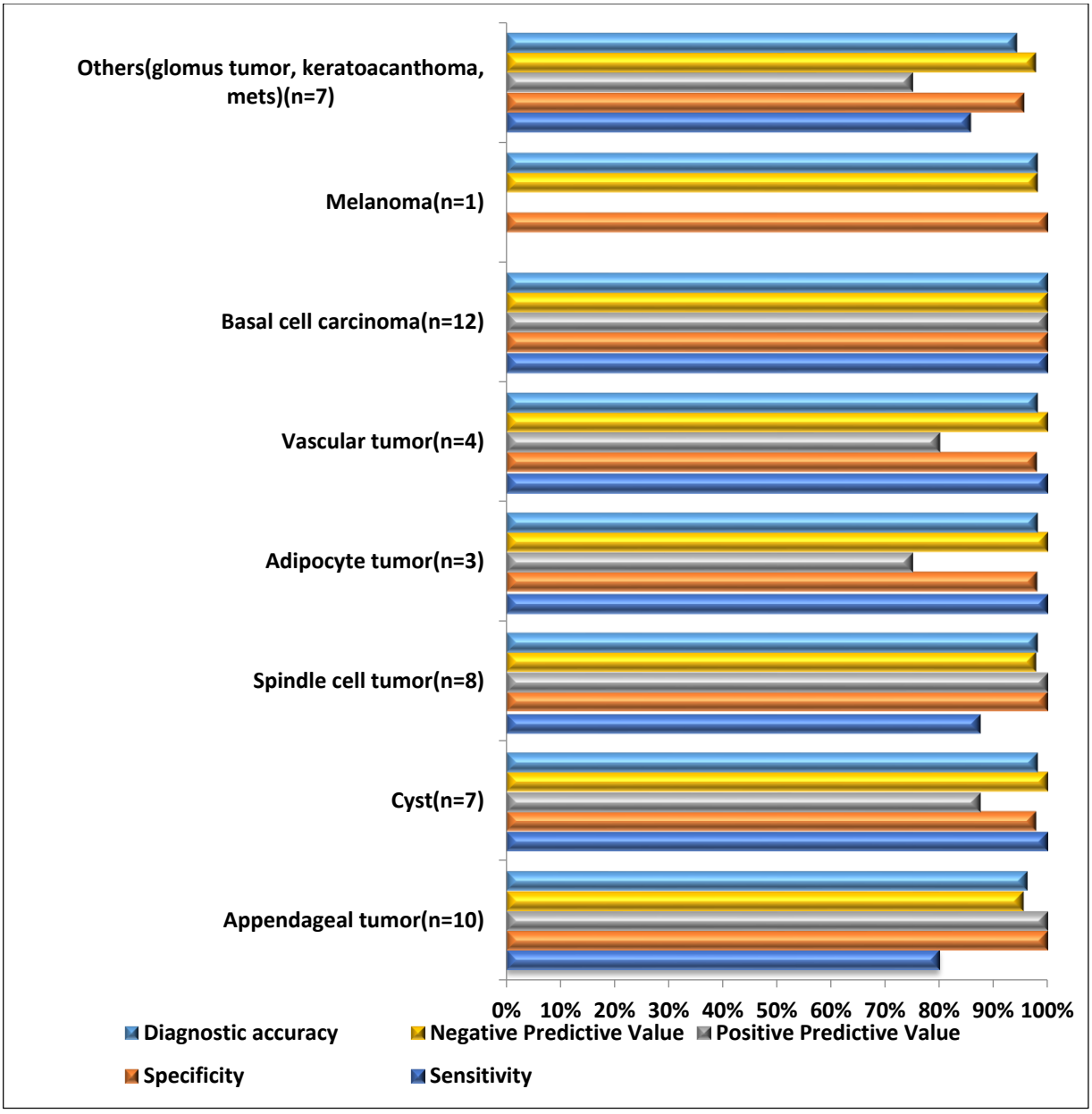


Figure 20 :- Sensitivity, specificity, positive predictive value and negative predictive value of USG for predicting various diseases after taking histopathology as gold standard

CORRELATION OF CLINICAL SIZE (mm) AND HFUS SIZE(mm) OF TUMOR.

Table no. 11: Correlation coefficient of clinical size (mm) and HFUS size(mm) of tumor.

Variables	**USG width(mm)**
Clinical width(mm)	
Correlation coefficient	0.993
P value	<0.0001

Spearman rank correlation coefficient

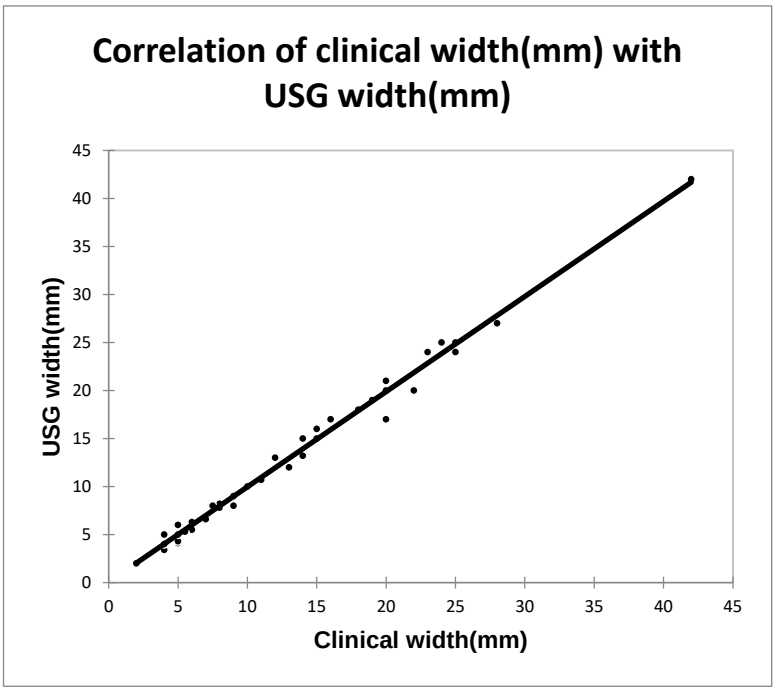


Figure 21 : Scatter diagram depicting correlation of clinical size(mm) with HFUS size(mm).

Significant positive correlation was seen between clinical width(mm) with USG width(mm) with correlation coefficient of 0.993.

CORRELATION OF HFUS DEPTH(mm) WITH HISTOPATHOLOGY DEPTH(mm)

Table no. 12:- correlation coefficient of depth on HFUS and HPE

Variables	**HPE depth(mm)**
USG depth(mm)	
Correlation coefficient	0.976
P value	<0.0001

Spearman rank correlation coefficient

Table no 13 :- Intraclass correlation of HFUS depth(mm) with HPE depth(mm).

USG depth(mm) and HPE depth(mm)	**Intraclass correlation**	**95% Confidence Interval**
Single measures	0.9868	0.9771 to 0.9924
Average measures	0.9933	0.9884 to 0.9962

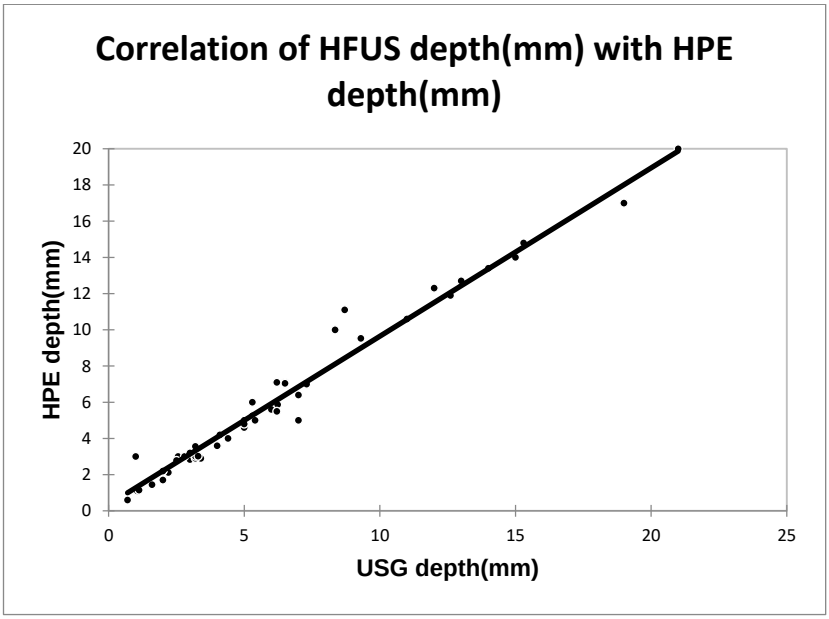


Figure 22 :-Scatter diagram -Correlation of USG depth(mm) with HPE depth(mm).

Significant positive correlation was seen between HFUS depth(mm) with HPE depth(mm) with spearman correlation coefficient of **0.976**. Excellent intraclass correlation was found to exist between HFUS depth(mm) with HPE depth(mm) (ICC: single measure:-0.9868, average measure:-0.9933)

VASCULARITY AND LEVEL OF INVASION ON HFUS AND HISTOPATHOLOGY

Table no.14 :-Inter-rater kappa agreement between HFUS vascularity and HPE vascularity.

USG vascularity	HPE vascularity		Total	P value	Kappa
	No(n=31)	Yes(n=21)			
No	14 (26.92%)	1 (1.92%)	15 (28.85%)	0.002	0.360
Yes	17 (32.69%)	20 (38.46%)	37 (71.15%)		
Total	31 (59.62%)	21 (40.38%)	52 (100.00%)		

Table no.15 :- Inter-rater kappa agreement between HFUS level of invasion and HPE level of invasion.

USG level of invasion	HPE level of invasion				Total	P value	Kappa
	Dermis (n=20)	Subcutis(n=7)	Epidermis+dermis (n=23)	Dermis+subcutis (n=2)			
Dermis	11 (21.15%)	1 (1.92%)	3 (5.77%)	0 (0%)	15 (28.85%)	<0.001	0.452
Subcutis	1 (1.92%)	5 (9.62%)	0 (0%)	1 (1.92%)	7 (13.46%)		
Epidermis+dermis	8 (15.38%)	1 (1.92%)	18 (34.62%)	1 (1.92%)	28 (53.85%)		
Dermis+subcutis	0 (0%)	0 (0%)	2 (3.85%)	0 (0%)	2 (3.85%)		
Total	20 (38.46%)	7 (13.46%)	23 (44.23%)	2 (3.85%)	52 (100%)		

Among 31 patients detected without vascularity, 14 patients had similar findings in USG. Among 21 patients detected with vascularity, 20 patients had similar findings in USG. Overall concordance rate was 65.38% and overall discordance rate was 34.61% between HPE vascularity and USG vascularity. Sensitivity of 95.24%(76.18% to 99.88%) and specificity of 45.16% 45.16%(27.32% to 63.97%) in USG predicting vascularity was calculated with a diagnostic accuracy of 65.38%.

Fair agreement exist between HPE vascularity and USG vascularity with kappa 0.36 and p value 0.002.

Among 20 patients with involvement of dermis in HPE, 11 patients had similar findings in USG. Among 7 patients with involved subcutis via HPE, 5 patients had similar findings in USG. Among 23 patients with involvement of both epidermis and dermis via HPE, 18 patients had similar findings in USG. Among 2 patients in which both dermis and subcutis were involved via HPE, 0 patient had similar findings in USG. Overall concordance rate was 65.39% and overall discordance rate was 34.60% between HPE level of invasion and USG level of invasion. **Moderate agreement was found to exist between HPE level of invasion and USG level of invasion** with kappa 0.452 and p value <.0001.

ASSOCIATION BETWEEN HFUS CONSISTENCY WITH CLINICAL CONSISTENCY

Table no. 16:-Association of USG consistency with clinical consistency.

USG consistency	Soft(n=27)	Firm(n=23)	Hard(n=2)	Total	P value
Solid	18 (66.67%)	19 (82.61%)	2 (100%)	39 (75%)	0.702*
Cystic	5 (18.52%)	3 (13.04%)	0 (0%)	8 (15.38%)	
Semisolid	4 (14.81%)	1 (4.35%)	0 (0%)	5 (9.62%)	
Total	27 (100%)	23 (100%)	2 (100%)	52 (100%)	

*** Fisher's exact test**

Distribution of USG consistency was comparable with clinical consistency {Soft vs Firm vs Hard}. (Solid:- 66.67% vs 82.61% vs 100% respectively, Cystic:- 18.52% vs 13.04% vs 0% respectively, Semisolid:- 14.81% vs 4.35% vs 0% respectively) (p value=0.702).

ASSOCIATION OF USG SATELLITE LESION WITH CLINICAL SATELLITE LESION.

Table no.17 :-Association of USG satellite lesion with clinical satellite lesion.

USG satellite lesion	Clinical satellite lesion		Total	P value
	No(n=46)	Yes(n=6)		
No	41 (89.13%)	0 (0%)	**41 (78.85%)**	**<.0001***
Yes	5 (10.87%)	6 (100%)	**11 (21.15%)**	
Total	46 (100%)	6 (100%)	**52 (100%)**	

*** Fisher's exact test**

Proportion of patients with USG satellite lesion was significantly lower as compared to with clinical satellite lesion. (10.87% vs 100% respectively). (p value <0.0001)

ASSOCIATION OF USG SHAPE WITH CLINICAL MORPHOLOGY

Table no. 18:-Association of USG shape with clinical morphology.

USG shape	Nodule (n=38)	Papule (n=6)	Plaque (n=7)	Noduloplaque (n=1)	Total	P value
Oval	15 (39.47%)	6 (100%)	2 (28.57%)	1 (100%)	**24 (46.15%)**	**0.03***
Round	9 (23.68%)	0 (0%)	0 (0%)	0 (0%)	**9 (17.31%)**	
Irregular	14 (36.84%)	0 (0%)	5 (71.43%)	0 (0%)	**19 (36.54%)**	
Total	38 (100%)	6 (100%)	7 (100%)	1 (100%)	**52 (100%)**	

*** Fisher's exact test**

Proportion of patients with USG shape:- round was significantly higher in nodule as compared to papule, plaque and noduloplaque. (Round:- 23.68% vs 0%, 0% and 0% respectively). Proportion of patients with USG shape:- oval was significantly higher in papule

and noduloplaque as compared to nodule and plaque. (Oval:- 100%, 100% vs 39.47%, 28.57% respectively). Proportion of patients with USG shape:- irregular was significantly higher in plaque as compared to nodule, papule and noduloplaque. (Irregular:- 71.43% vs 36.84%, 0% and 0% respectively). (p value=0.03)

SUBGROUP ANALYSIS OF FEW TUMOR GROUPS

BASAL CELL CARCINOMA

Table no. 19 :-Distribution of dermoscopy features of Basal cell carcinoma.

Dermoscopy features of Basal cell carcinoma	Frequency	Percentage
Color		
Skin color	5	41.67%
Erythematous	2	16.67%
Hyperpigmented	5	41.67%
Arborizing vessel	11	91.67%
Linear vessel	10	83.33%
Dotted vessel	2	16.67%
Lacunae vessel	7	58.33%
Polymorphous vessel	6	50.00%
Clods	12	100.00%
Dots	3	25.00%
Pigment network	7	58.33%
Negative pigment network	0	0.00%
Homogeneous pattern	12	100.00%
Streaks	8	66.67%

In all lesions of BCC, Clods were present and pattern was homogeneous gray white areas with streaks. In vessel morphology, the most common pattern observed was arborizing vessel [11(91.67%)] followed by linear vessel [10(83.33%)], lacunae vessel [7(58.33%)], polymorphous vessel [6(50.00%)], dotted vessel [2(16.67%)]. Blue grey areas and leaf like areas were also present in few lesions.

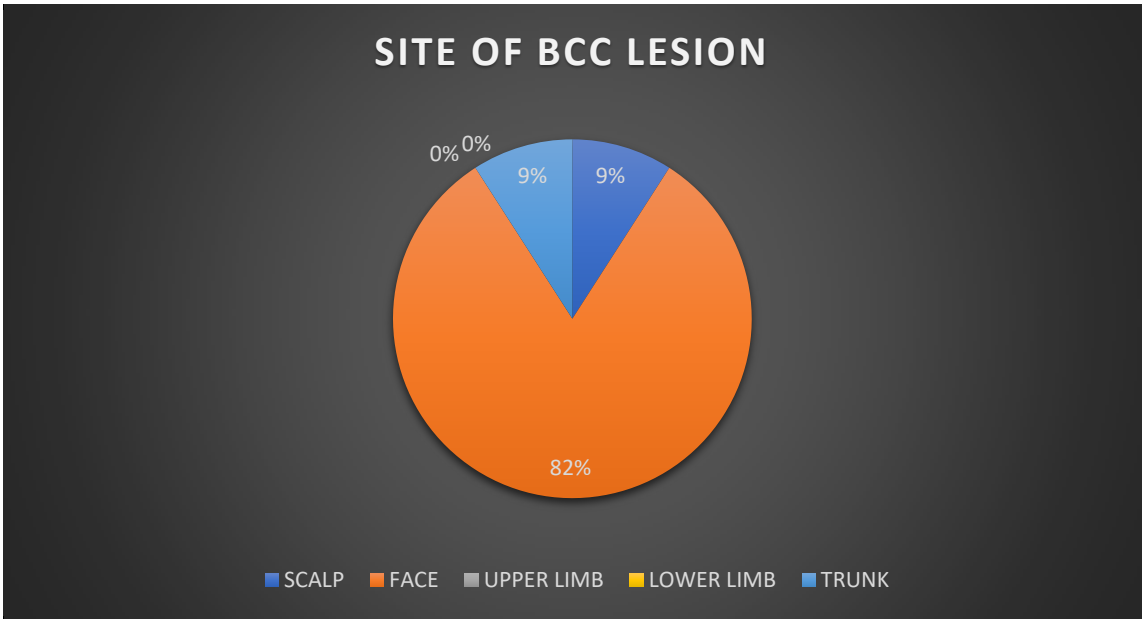


Figure 23: Pie chart showing site of BCC

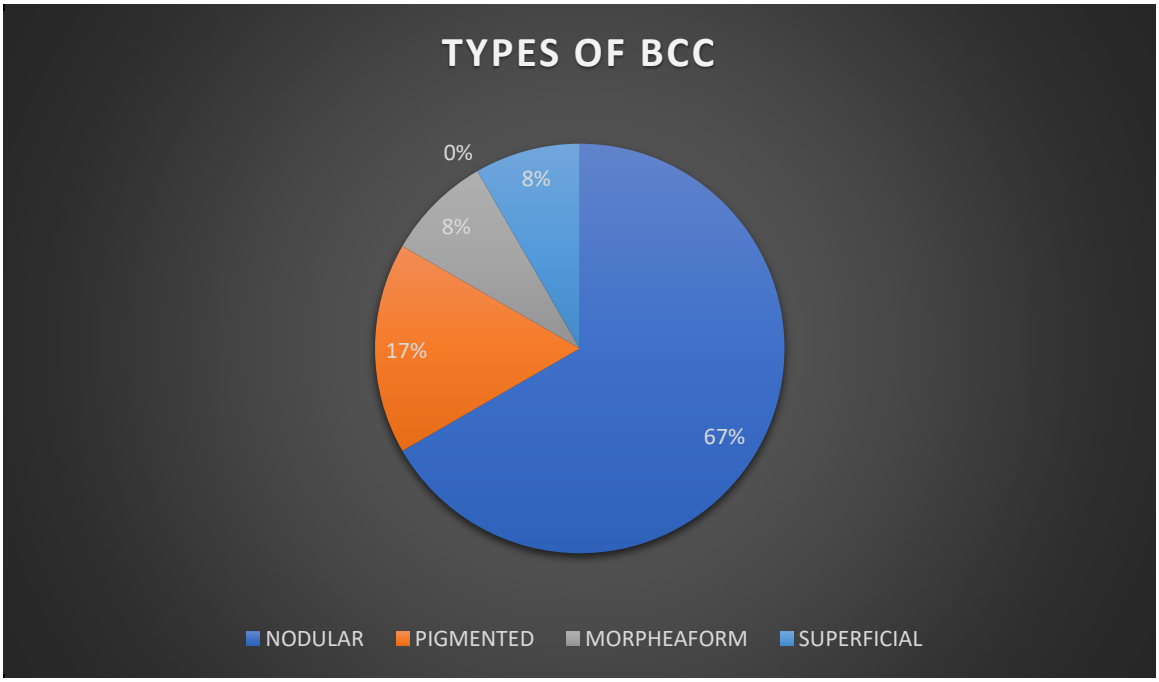


Figure 24: Pie chart showing Type of BCC

Table no.20:-Distribution of USG findings of Basal cell carcinoma.

USG findings of Basal cell carcinoma	Frequency	Percentage
Shape		
Oval	7	58.33%
Irregular	5	41.67%
Consistency		
Solid	12	100.00%
Echogenicity		
Hypoechoic	12	100.00%
Homogeneity		
Heterogenous	6	50.00%
Homogenous	6	50.00%
Level of invasion		
Dermis	2	16.67%
Epidermis+dermis	10	83.33%
Location of vessels		
No	1	8.33%
Peripheral	3	25.00%
Base	3	25.00%
Central	5	41.67%
Locoregional spread	2	16.67%
Vascularity	11	91.67%
Satellite lesion	6	50.00%
Depth(mm)		
Mean ± SD	3.4 ± 3.4	
Width(mm)		
Mean ± SD	15.43 ± 7.59	

Table no. 21:-Correlation of clinical width(mm) with USG width(mm) in Basal cell carcinoma

Variables	USG width(mm){Basal cell carcinoma}
Clinical width(mm){Basal cell carcinoma}	
Correlation coefficient	0.988
P value	<0.0001

Spearman rank correlation coefficient

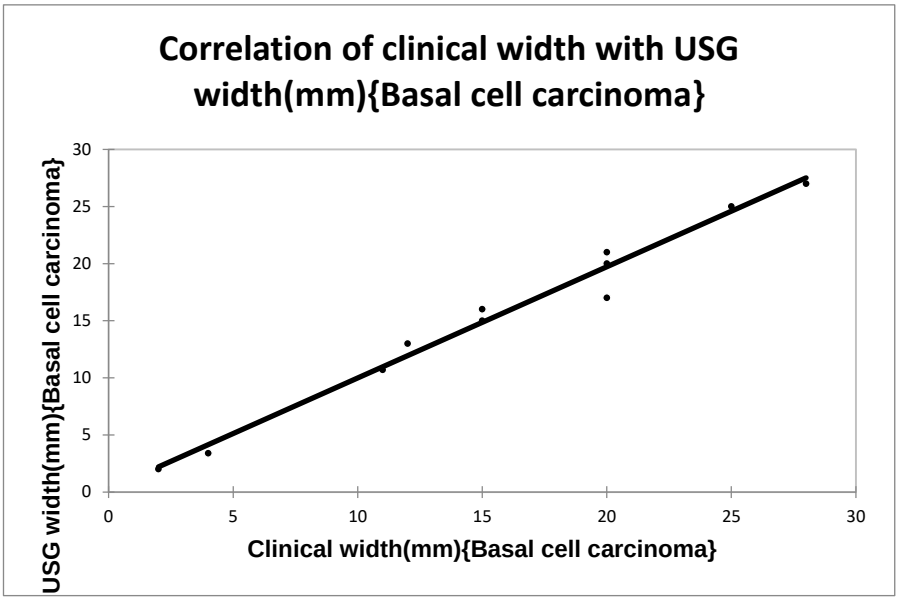


Figure 25 : Correlation of clinical width(mm) with USG width(mm){Basal cell carcinoma}

Table no. 22 :-Correlation of USG depth(mm) with HPE depth(mm) in Basal cell carcinoma.

Variables	HPE depth(mm){Basal cell carcinoma}
USG depth(mm){Basal cell carcinoma}	
Correlation coefficient	0.862
P value	0.001

Spearman rank correlation coefficient

Table no. 23:- Intraclass correlation of USG depth(mm) with HPE depth(mm){Basal cell carcinoma}.

USG depth(mm) and HPE depth(mm){Basal cell carcinoma}	Intraclass correlation	95% Confidence Interval
Single measures	0.9822	0.9411 to 0.9948
Average measures	0.991	0.9696 to 0.9974

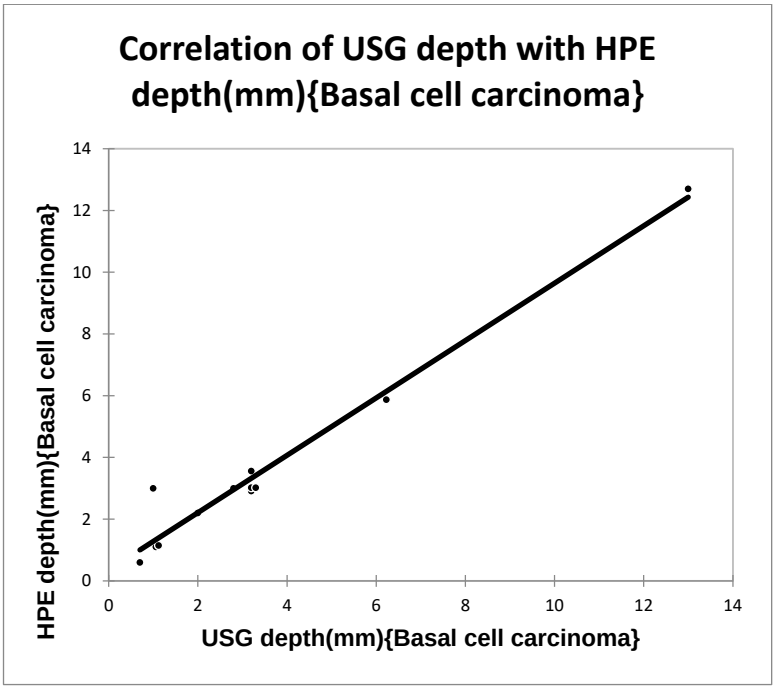


Figure 26 :-Correlation of USG depth(mm) with HPE depth(mm){Basal cell carcinoma}

Significant positive correlation was seen in BCC between clinical width(mm) with USG width(mm) with correlation coefficient of 0.988.

Significant positive correlation was seen in BCC between USG depth(mm) with HPE depth(mm) with correlation coefficient of 0.862.

APPENDAGEAL TUMORS

Table no. 24 :-Distribution of dermoscopy features of appendageal tumor.

Dermoscopy features of appendageal tumor	Frequency	Percentage
Color		
Skin color	9	90.00%
Hyperpigmented	1	10.00%
Arborizing vessel	3	30.00%
Linear vessel	2	20.00%
Dotted vessel	2	20.00%
Lacunae vessel	1	10.00%
Polymorphous vessel	0	0.00%
Clods	6	60.00%
Dots	10	100.00%
Pigment network	6	60.00%
Negative pigment network	0	0.00%
Homogeneous pattern	6	60.00%
Streaks	1	10.00%

In majority of patients, skin colored background was found [9(90.00%)] . In all patients, dots were present followed by clods [6(60.00%)], pigment network [6(60.00%)], homogeneous pattern [6(60.00%)], and streaks [1(10.00%)]. In vasculature, arborizing vessel [3(30.00%)], linear vessel [2(20.00%)], dotted vessel [2(20.00%)], lacunae vessel [1(10.00%)] were present.

Table no.25 :-Distribution of USG findings of appendageal tumor.

USG findings of appendageal tumor	Frequency	Percentage
Shape		
Oval	7	70.00%
Round	1	10.00%
Irregular	2	20.00%
Consistency		
Solid	8	80.00%
Cystic	1	10.00%
Semisolid	1	10.00%
Echogenicity		
Hypoechoic	8	80.00%
Hyperechoic	2	20.00%
Homogeneity		
Heterogenous	3	30.00%
Homogenous	7	70.00%
Level of invasion		
Dermis	6	60.00%
Subcutis	1	10.00%
Epidermis+dermis	3	30.00%
Location of vessels		
No	6	60.00%
Peripheral	2	20.00%
Central	1	10.00%
Linear	1	10.00%
Locoregional spread	1	10.00%
Vascularity	5	50.00%
Depth(mm)		
Mean ± SD	6.93 ± 5.7	
Width(mm)		
Mean ± SD	12.78 ± 8.32	

Most of the lesions were oval[7(70.00%)], solid[8(80.00%)], homogenously[7(70.00%)], hypoechoic [8(80.00%)] on ultrasonography. In majority [6(60.00%)] of patients, level of invasion was dermis followed by epidermis and dermis both[3(30.00%)]. Level of invasion was till subcutis in only 1 out of 10 patients (10.00%). Mean value of depth(mm) and width(mm) of study subjects was 6.93 ± 5.7 and 12.78 ± 8.32 with median(25th-75th percentile) of 5.3(4.1-6.6) and 9.1(6.125-19.75) respectively.

Table no. 26:-Distribution of HPE findings of appendageal tumor.

HPE findings of appendageal tumor	Frequency	Percentage
Level of invasion		
Dermis	6	60.00%
Epidermis and dermis	4	40.00%
Tumor type		
Benign	10	100.00%
Depth(mm)		
Mean ± SD	**6.38 ± 5.25**	

In majority [6(60.00%)] of patients, level of invasion was dermis. Level of invasion was epidermis+dermis in only 4 out of 10 patients (40.00%). All lesions were benign and Mean value of depth(mm) of study subjects was 6.38 ± 5.25.

Table no. 27 :-Correlation of clinical width(mm) with USG width(mm){Appendageal tumor}.

Variables	USG width(mm){Appendageal tumor}
Clinical width(mm){Appendageal tumor}	
Correlation coefficient	0.988
P value	<0.0001

Spearman rank correlation coefficient

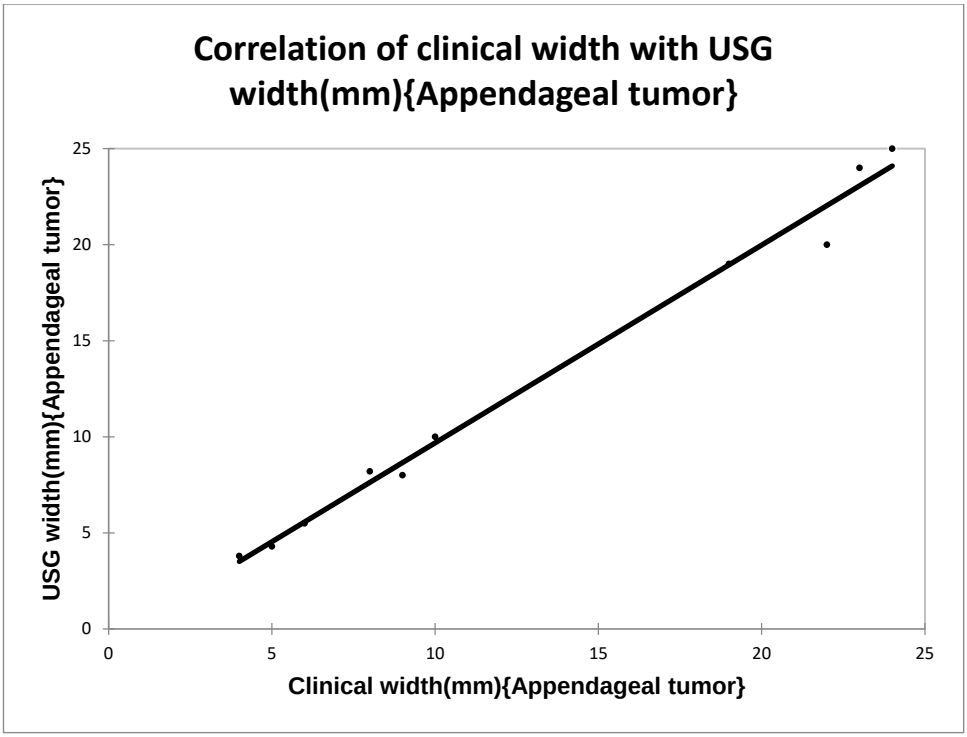


Figure 27:-Scatter diagram-Correlation of clinical width(mm) with USG width(mm){Appendageal tumor}.

Table no. 28:-Correlation of USG depth(mm) with HPE depth(mm){Appendageal tumor}.

Variables	HPE depth(mm){Appendageal tumor}
USG depth(mm){Appendageal tumor}	
Correlation coefficient	0.896
P value	0.001

Spearman rank correlation coefficient

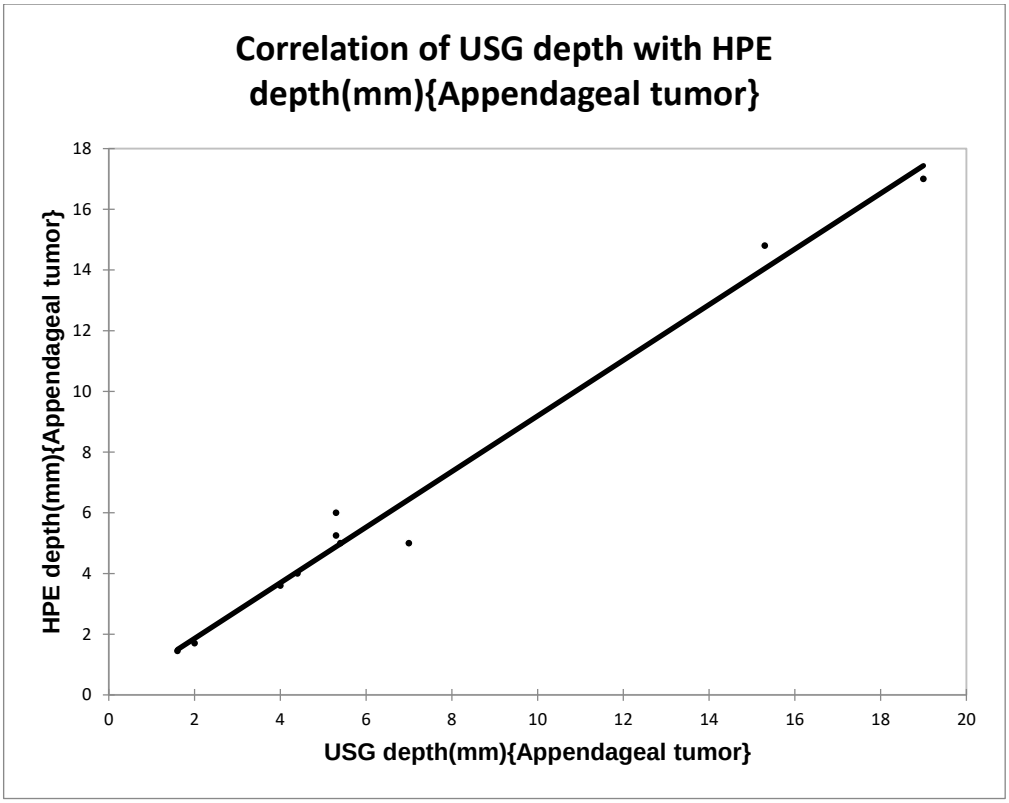


Figure 28 :- Scatter diagram -Correlation of USG depth(mm) with HPE depth(mm){Appendageal tumor}.

Significant positive correlation was seen between clinical width(mm) with USG width(mm) with correlation coefficient of 0.988 in appendageal tumor.

Significant positive correlation was seen between USG depth(mm){Appendageal tumor} with HPE depth(mm){Appendageal tumor} with correlation coefficient of 0.896.

SPINDLE CELL TUMOR

Table no. 29 :-Distribution of dermoscopy features of Spindle cell tumor.

Dermoscopy features of Spindle cell tumor	Frequency	Percentage
Color		
Skin color	3	37.50%
Erythematous	1	12.50%
Hyperpigmented	4	50.00%
Arborizing vessel	0	0.00%
Linear vessel	0	0.00%
Dotted vessel	1	12.50%
Lacunae vessel	1	12.50%
Polymorphous vessel	0	0.00%
Clods	5	62.50%
Dots	6	75.00%
Pigment network	8	100.00%
Negative pigment network	0	0.00%
Homogeneous pattern	8	100.00%
Streaks	5	62.50%

In 4(50.00%) patients, color was hyperpigmented followed by skin color [3(37.50%)]. In all patients, Pigment network was present and pattern was homogeneous followed by dots [6(75.00%)], clods [5(62.50%)], streaks [5(62.50%)].

Table no. 30:-Distribution of USG findings of Spindle cell tumor.

USG findings of Spindle cell tumor	Frequency	Percentage
Shape		
Oval	3	37.50%
Irregular	5	62.50%
Consistency		
Solid	8	100.00%
Echogenicity		
Hypoechoic	7	87.50%
Hyperechoic	1	12.50%
Homogeneity		
Heterogenous	2	25.00%
Homogenous	6	75.00%
Level of invasion		
Dermis	1	12.50%
Subcutis	1	12.50%
Epidermis+dermis	6	75.00%
Location of vessels		
No	3	37.50%
Base	4	50.00%
Hypervascular	1	12.50%
Vascularity	5	62.50%
Depth(mm)		
Mean ± SD	8.36 ± 5.5	
Width(mm)		
Mean ± SD	12.96 ± 12.52	

In majority [5(62.50%)] of patients, shape was irregular which is mostly solid in consistency. Hypoechoic [7(87.50%)] lesions are predominant which are homogenous. Lesions were present in epidermis and dermis in 6 out 8 patients. Vascularity was visible on color doppler in 5 (62.50%) out of 8 patients majorly at base.

Mean value of depth(mm) and width(mm) of study subjects was 8.36 ± 5.5 and 12.96 ± 12.52 respectively.

Table no. 31 :-Distribution of HPE findings of Spindle cell tumor.

HPE findings of Spindle cell tumor	Frequency	Percentage
Level of invasion		
Dermis	5	62.50%
Epidermis and dermis	2	25.00%
Dermis and subcutis	1	12.50%
Tumor type		
Benign	8	100.00%
Nuclear atypia	1	12.50%
Vascularity	2	25.00%
Depth(mm)		
Mean ± SD	**8.09 ± 4.88**	

In majority [5(62.50%)] of patients, level of invasion was dermis followed by epidermal and dermal involvement [2(25.00%)]. Level of invasion was dermis and subcutis in only 1 out of 8 patients (12.50%).All lesions were benign . Mean value of depth(mm) of study subjects was 8.09 ± 4.88 .

Table no. 32:-Correlation of clinical width(mm) with USG width(mm){Spindle cell tumor}.

Variables	USG width(mm){Spindle cell tumor}
Clinical width(mm){Spindle cell tumor}	
Correlation coefficient	0.982
P value	0.0004

Spearman rank correlation coefficient

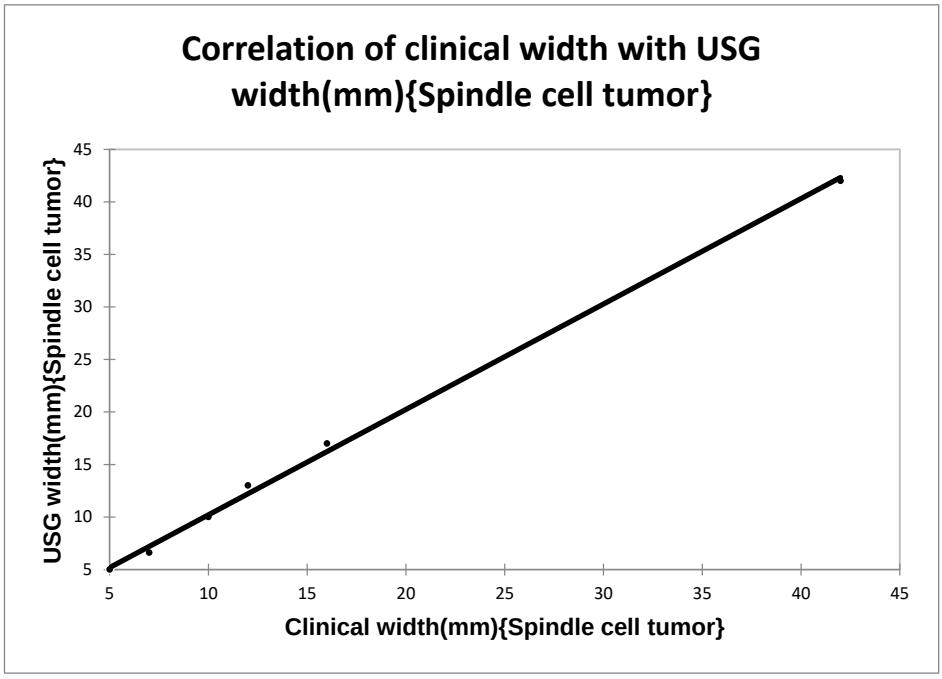


Figure 29 :- Scatter diagram -Correlation of clinical width(mm) with USG width(mm){Spindle cell tumor}.

Significant positive correlation was seen between clinical width(mm) with USG width(mm){Spindle cell tumor} with correlation coefficient of 0.982.

Table no. 33:-Correlation of USG depth(mm) with HPE depth(mm){Spindle cell tumor}.

Variables	HPE depth(mm){Spindle cell tumor}
USG depth(mm){Spindle cell tumor}	
Correlation coefficient	1.000
P value	<0.0001

Spearman rank correlation coefficient

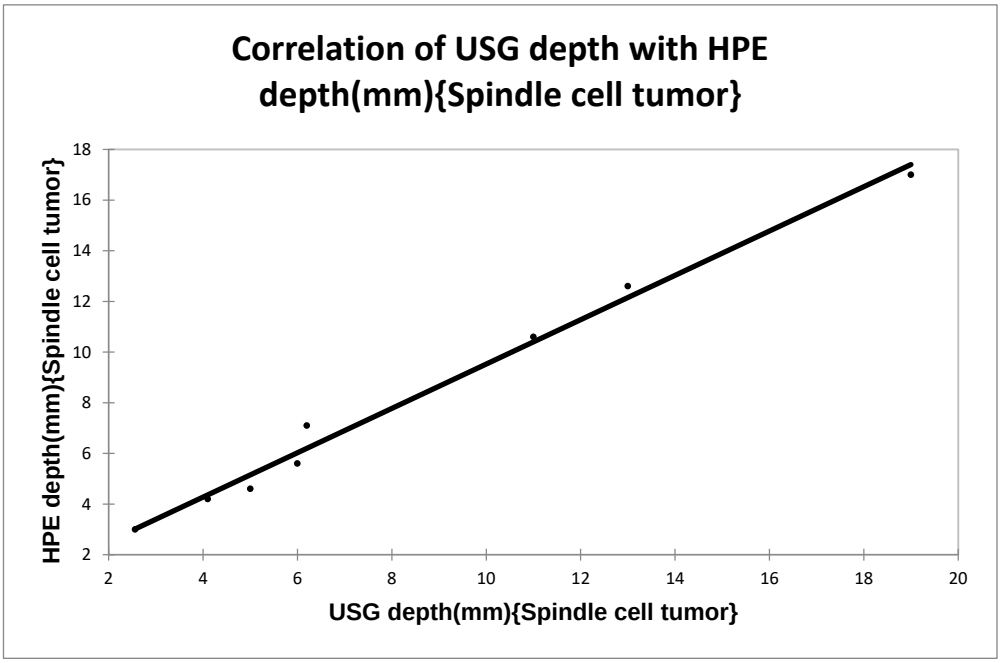


Figure 30:-Scatter diagram -Correlation of USG depth(mm) with HPE depth(mm){Spindle cell tumor}.

Significant positive correlation was seen between USG depth(mm) with HPE depth(mm){Spindle cell tumor} with correlation coefficient of 1.

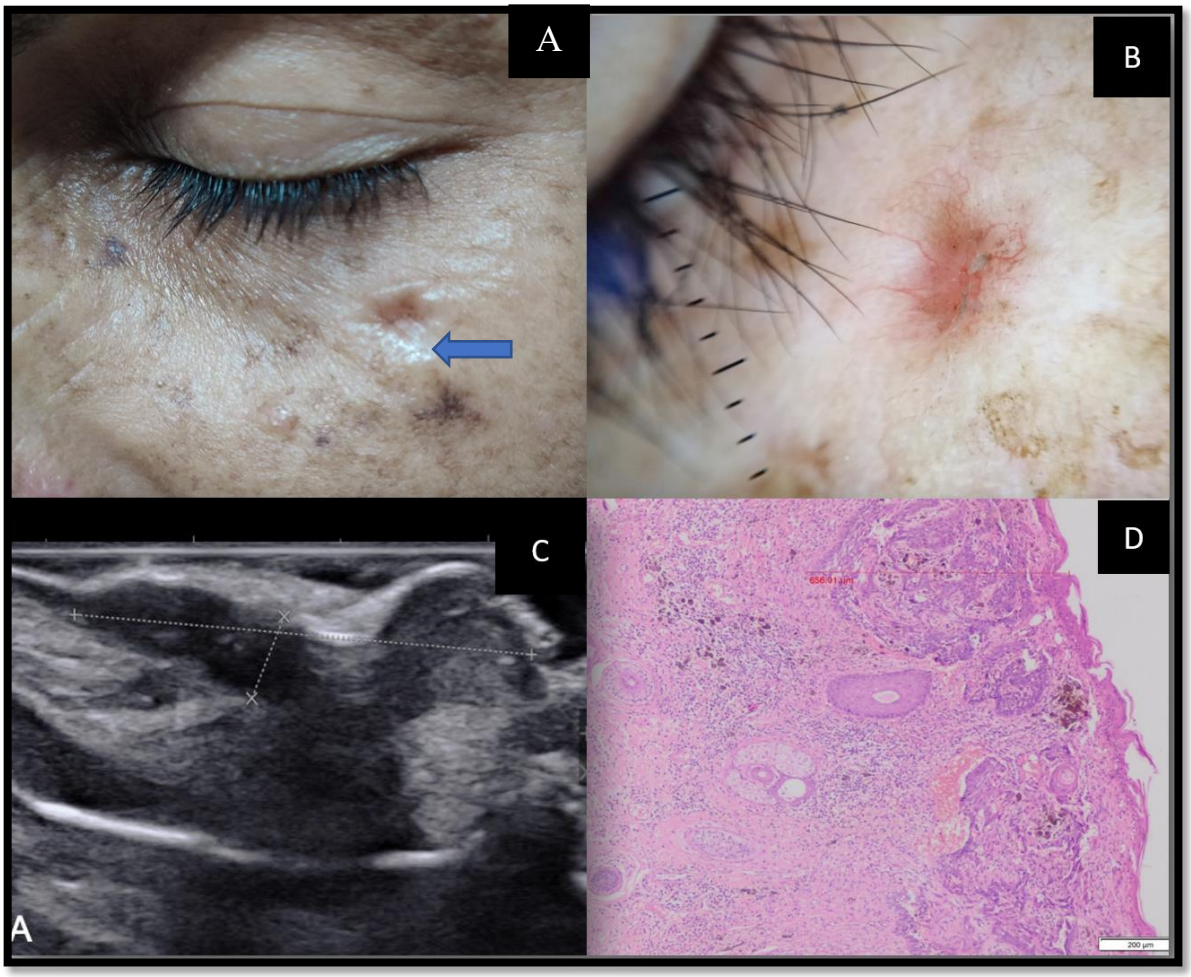


Figure 31 :BASAL CELL CARCINOMA A: Ill defined skin colored to erythematous plaque with raised margins(blue arrow) B: skin colored background with arborizing and linear vessels. C: solid hypoechoic mass lesion is seen in dermis . D: The dermis shows tumour comprising of irregular lobules and nests of basaloid cells(red dotted lines showing depth measurement) (patient 22)

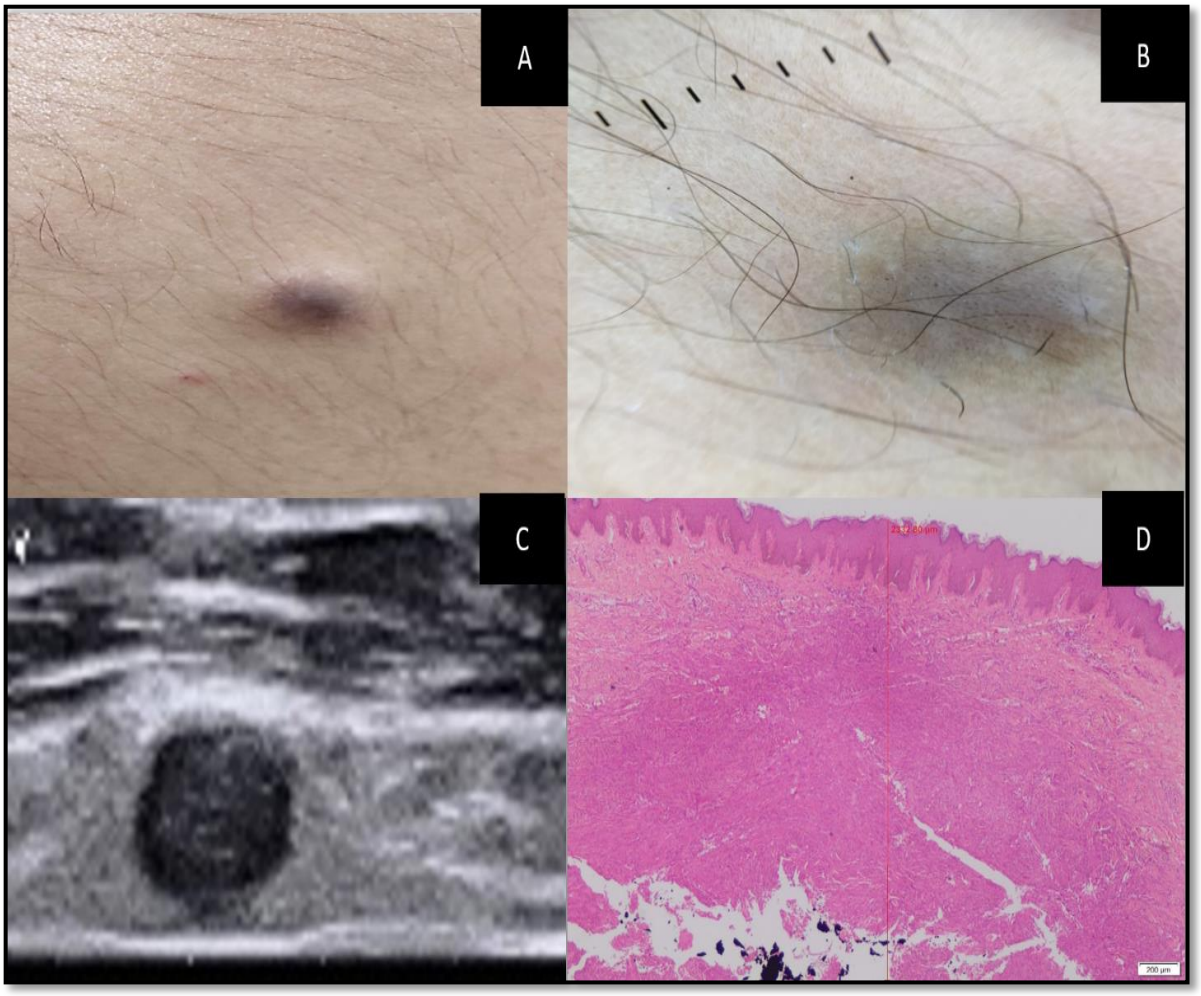


Figure 32:DERMATOFIBROMA A : Well defined hyperpigmented nodule over right forearm. B: dermoscopy shows brown colored background with pigment network, small whitish homogenous areas and streaks C: An oval hypoechoic lesion is seen in dermis with no significant vascularity. D: dermis shows a poorly circumscribed tumor arranged in short fascicles and vague storiform pattern (patient 25)

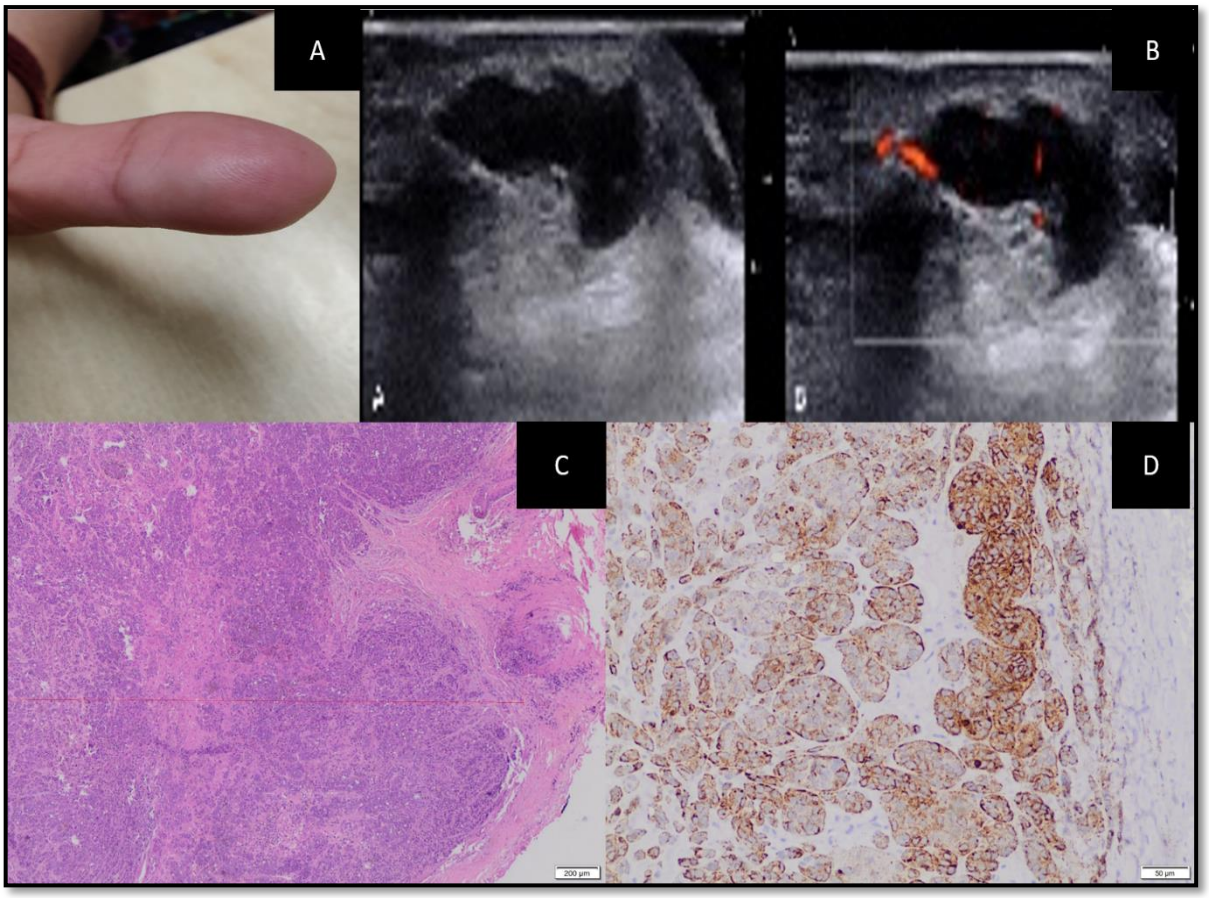


Figure 33: MALIGNANT MELANOMA A :Patient complained of pain over left thumb. Dermoscopy did not show significant findings.B: An irregular solid hypoechoic mass lesion is seen in dermis and subcutaneous tissue planes with increased vascularity. C: H&E- tumour comprising of small sheets, nests, trabeculae and singly scattered cells displaying moderate anisonucleosis, round to irregular nuclei, coarse chromatin, prominent nuclei and moderate amount of cytoplasm. Intracellular as well as extracellular melanin noted. D: tumour cells showing expression of Melan-A and HMB45 (patient 28)

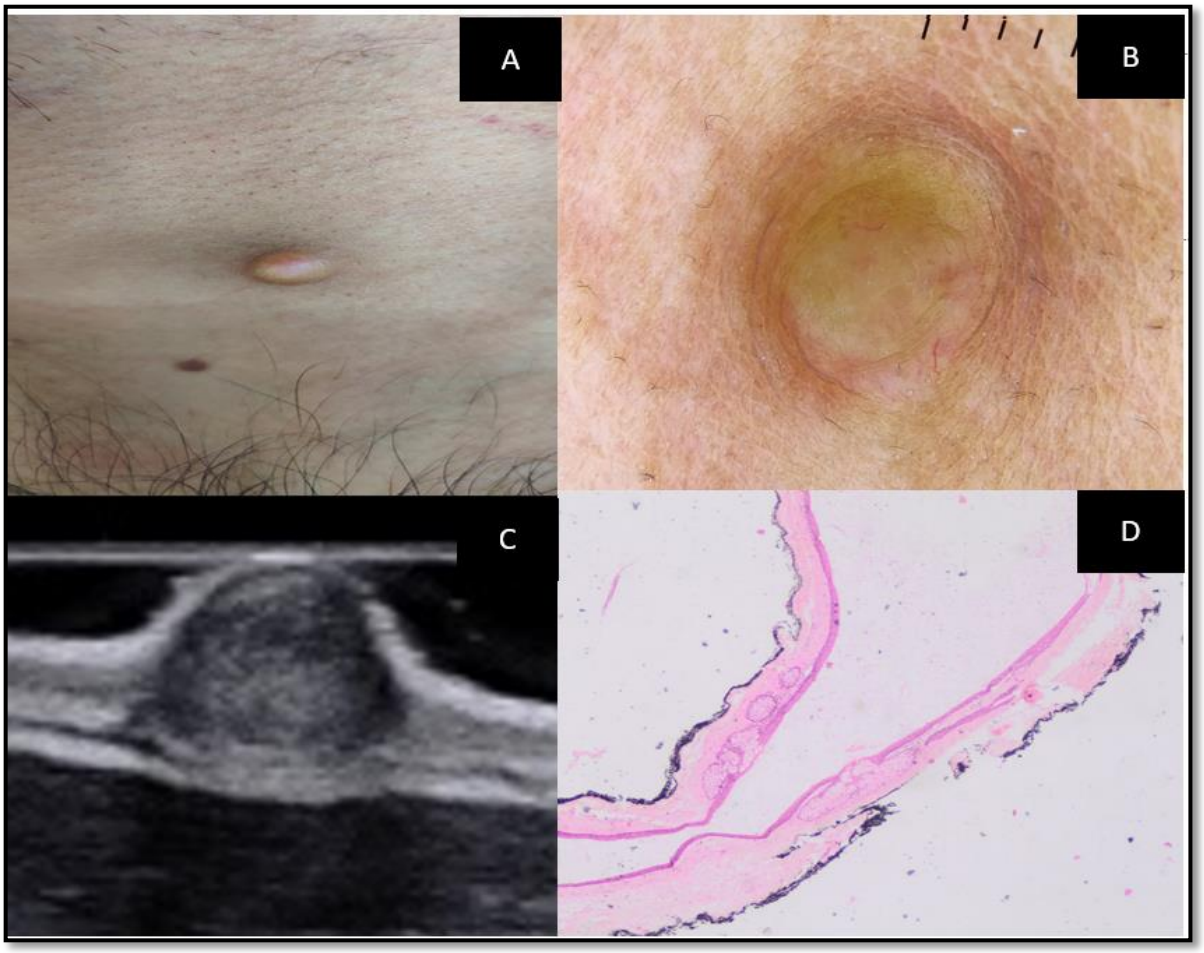


Figure 34 : PILAR CYST A : skin colored nodule present over anterior aspect of neck B: Dermoscopy showing yellow structureless areas with telangiectasias C: A well defined hypoechoic lesion is seen in dermis with absence of internal vascularity. D: fibrocollageneous cyst wall lined by stratified squamous epithelium, devoid of granular layer (patient 3)

DISCUSSION

DISCUSSION

The skin is a key site for benign and malignant neoplasms. Despite their lack of biological significance, patients may experience severe psychological distress because of benign epithelial neoplasms. Clinically, they can be difficult to differentiate from malignancy, especially when they are pigmented or inflammatory, and histologic evaluation of a biopsy specimen is often necessary to make a clear diagnosis and permit proper action and follow-up.[53]

Fifty-two patients with suspected benign and malignant skin tumors were recruited from Dermatology, Venereology, and Leprology OPD at AIIMS, Jodhpur between March 2021 and August 2022 as per the selection criteria. Clinical examination and dermoscopy of the lesions was performed followed by high-frequency ultrasonography and histopathology.

The ages of the patients ranged from 18 to 80 years, with a mean age of 36.81 ± 18.7 years. The majority of the patients (25.00%) were between the ages of 21 to 30 years, followed by those between the ages of 18 to 20 (23.08%). In a four-year study of clinicopathological characteristics of skin tumors in northern India by Goel et al., the average age of benign and malignant skin tumors was determined to be 40.3±19.9 and 60.8±14.8 years, respectively.[53] Our study's mean age was lower than that of similar studies because benign tumors outnumbered malignant ones, and it is generally found that benign tumors tend to present at a younger age.

In our analysis, there were 73.08% benign tumors and 26.92% malignant tumors which was in concordance to a study conducted by Har-Shai et al. in which it was observed that 64.4% of tumors were benign or premalignant, whereas 31.6% were malignant.[54]. In contrast, in a research by Goel et al., the proportions of benign and malignant lesions were comparable at 53% and 47%, respectively.[53].

There were more female than male, with 61.54% of patients being women and 38.46% being men. The number of female to male was about 1.5 to 1. In contrast, males were more common in earlier studies. In a study by Goel et al., the ratio of number of men to women was 1.15:1.[53] In accordance with the findings of our analysis, more women were present in a study conducted by Lal et al., which had a male to female involvement ratio of 0.79:1.[55]

In our research, nodule was found to be the most common morphology (73.08%), followed by plaque (13.46%) and papule (11.54%). Nodules and papules are more prevalent due to the prevalence of benign lesions, as Khandpur et al stated that benign lesions are smoother, nodular and papular.[13]

Lesions were most common on the face (46%), scalp (21.15%), and upper extremities (17.31%). Lower limbs and the trunk (7.69%) were the least frequently involved sites. In prior research, the face (45.7%), followed by the limbs (19%), was the predominant location for benign and malignant skin tumors.[53] Lal et al. also identified the head and neck as the most often affected site. It may be the result of greater sun exposure to the head and neck in this region of the country.[55]

In our study, 23.08 percent of lesions were found to be BCC, followed by appendageal tumors and spindle cell tumors. There were only a few patients who had pyogenic granulomas or lipomas. Only one patient with subungual melanoma was detected.

Our results are consistent with those of Goel et al., who also observed that keratinocytic tumors are the most common kind of neoplasm whereas melanocytic tumors were shown to be more prevalent than appendageal tumors among all benign lesions.[53] Based on a retrospective study conducted over a decade, Khullar G. et al. discovered that BCC outnumbered SCC.[56] Although basal cell carcinoma is the most frequent form of skin cancer worldwide, various Indian studies have suggested that squamous cell carcinoma is the most common form of skin cancer.[57] Sweat gland tumors were the most prevalent appendageal tumors in previous studies (79.8%), followed by follicular tumors (11.6%), and sebaceous tumors (8.3%).[24]

Dermoscopic findings included had predominantly skin-colored and hyperpigmented background. The most noticeable finding was a homogeneous pattern, but clods and pigment network were also present. Basal cell carcinoma has a hyperpigmented and skin-coloured background with homogenous gray-white areas and streaks in the majority of patients. Arborizing vessels and linear vessels were present in 91.67% and 83.33% of lesions, respectively. Pigment network was also seen in 58% of lesions. Approximately 60.7% of all BCC were identified as having arborizing vessels and then short fine telangectasias. The predominant pigmented structures in BCC are blue-gray ovoid nests that correlate to homogeneous pattern and clods. [58]

In the context of appendageal tumors lesions , 90% of patients had a skin colored background with dots, clods, and pigment network. In literature, most of the findings given are specific for individual tumors and show high dermoscopic variability. In our investigation, we discovered nodular hidradenoma with dots, homogenous regions and a pigment network with arborizing vessels, which is compatible with the description provided by Zaballos et al which includes a homogenous area and white structures. In trichoepithelioma, we identified arborizing vessels, linear vessels, and dots, which are compatible with the literature's description of tiny, thin, in-focus arborizing vessels, glossy white patches, or backgrounds.[59]

On dermoscopy, white homogeneous patches and pigment network were most frequently observed patterns in dermatofibroma. There are dots, clods and streaks in decreasing order of frequency. It corresponds with analysis of 412 patients, the most frequent dermatoscopic pattern noted was a central white patch and peripheral pigment network. [60]

On ultrasonography, the majority of lesions were oval or irregular in shape and mostly solid in consistency. Skin tumors were predominantly hypoechoic (80.77%), only seven (13.46%) out of 52 were hyperechoic, and three were isoechoic (5.77%). Consistent with these results, song et al. found that out of 47 lesions in which echogenicity and homogeneity were assessed, 37 were homogenously hypoechoic, 7 were heterogeneously hypoechoic, and 3 were isoechoic. Most skin cancers, it is stated, manifest as indistinct hypoechoic lesions.[38]

Epidermal with dermal invasion was the most commonly detected pattern on HFUS, followed by only dermal involvement. Subcutis involvement was present in 13.46% of lesions, mainly lipomas and cysts. Vascularity was detected in 71.15% of lesions using color doppler. Ultrasound helps in identifying vascularity, and colour doppler can be used in confirming the diagnosis of a vascular tumour and its attachment to the internal vasculature. We did not find any significant connecting vessels to the tumor.

In many of our cases, ultrasound turned out to be a very helpful tool. Two cases that we were initially diagnosed as neurofibroma and dermatofibroma turned out to be cystic lesions after ultrasonography which helped us to plan surgical excision of the individual lesions..

Since HFUS is a new entity, it is typically used as an adjunctive modality to look for secondary features rather than as a diagnostic tool for skin tumors. In our study, we attempted to correlate the probable diagnosis based on ultrasonography with the confirmatory findings of histopathology. Using inter-rater kappa agreement, we discovered very good agreement in

correlating the ultrasound diagnosis with the final histopathological diagnosis. During the study, one case of nodular hidradenoma was diagnosed as a cystic lesion due to the presence of cystic component in addition to cellular component which was visible on histopathology. Another case which appeared to be squamous cell carcinoma on clinical examination and HFUS due to a heterogeneously hyperechoic lesion with internal vascularity, turned out to be a case of leiomyoma after histopathology. We also detected a rare case of malignant melanoma; clinically, it appeared to be glomus tumour with complaints of excruciating pain while usingzoter that finger. Ultrasonography revealed an irregular hypoechoic, heterogeneous dermal lesion with increased vascularity . The diagnosis of malignant melanoma was made based on the final histopathology and the presence of Melan-A and HMB-45.

Wortsman et al. estimated overall sensitivity of HFUS as 99%, specificity as 100%, and statistical diagnostic certainty was 99%. Although the sample size in our study was insufficient to calculate accurate sensitivity and specificity as a whole, however we still tried to detect them for individual tumor groups. Ultrasonography detected cystic, adipocytic, vascular, and BCC lesions with 100% sensitivity. Spindle cell tumors and appendageal tumors sensitivity was 87.50% and 80% respectively. Specificity for appendageal tumors, spindle cell tumors, BCC was 100%. For cysts 97.78%, adipocytic tumors 97.96%, vascular tumor 97.92 specificity was found. In concordance to the findings seen in our study, Hung et al conducted a study on Ultrasound of Soft-Tissue Tumors, measuring the sensitivity and specificity of the initial ultrasound diagnosis for lipoma were 95.2% and 94.3%, respectively; 73.0% and 97.7% for vascular malformation; and 80.0% and 95.4% for epidermoid cyst, respectively.[61]

Pre-operative colour Doppler ultrasound was a useful and efficient technique for surgical planning; it allowed the analyser to depict skin tumors in a non-invasive manner, thereby streamlining and optimizing treatment approach. On correlating clinical size with ultrasonographic size of tumor, significant positive correlation 0.993 was found. HFUS measurements of BCCs were compared to clinical measurements in three studies. One had greater HFUS measurements [62], another had similar HFUS and clinical measurements [63], and the third had smaller HFUS measurement results [64] According to Marmur et al, there is no statistically significant difference between clinical and ultrasound widths or lengths for basal cell carcinoma and SCC.[65]

Also, when the depth of the lesion was correlated between USG and HPE, a significant positive correlation of 0.976 was observed, with an excellent intraclass correlation of 0.9868. In a study conducted by Kim et al., there was a strong correlation in depth between ultrasonography and histopathology, with Spearman's rank correlation coefficient 0.842.[49] Kashani et al., on the contrary observed a lower mean depth of tumor in HFUS as compared to what the dermatopathologist measured, with only a moderate correlation of 0.45 in depth using a 50Mhz probe.[8] We found a mean depth of 6.55+/-5.06 (mm) on USG and 6.44 +/-4.76 (mm) on HPE, which is consistent with Kim et al's finding that ultrasonography slightly overestimates measurement. [49] This overestimation is usually attributed to sebaceous gland hypertrophy and inflammatory infiltrate surrounding the tumor which forms a hypoechoic shadow in a few cases. Also it can represent tissue shrinkage that happened while the histopathologic slides were being made, or the fact that tissue measurements weren't taken at the exact same point along the often uneven borders of neoplastic lesions.[9]

The vascularity of skin lesions, a key trait in determining if tumors are benign or malignant, may be identified preoperatively with the use of an ultrasound scan. Identification of vascularity for the skin lesions showed a 44% (17/39 lesions) vascularity, with 64% (25/39 lesions) showing no vascularity among the malignant group. In the benign group, 25% (2/8 lesions) displayed prominent vascularity, while 75% (6/8 lesions) showed no vascularity.[38] Even though the primary goal of our study was not to distinguish benign and malignant skin tumors based on USG vascularity, we still managed to detect that 13 (92%) of 14 malignant tumors had significant vascularity on USG. In our study, USG overestimated vascularity and only fair agreement was measured correlating HPE and USG vascularity with kappa 0.36 and p value of 0.002. This can be attributed to USG's higher sensitivity of detecting flow on color doppler that were not reported significantly on histopathology reports.

USG detects not only the width and length of a skin tumour, which can be seen with the naked eye, but also its depth and the likelihood of spread to deeper structures. In our study no tumor had an extent beyond subcutis in the adjacent areas such as cartilage, bone or muscles. We found Moderate agreement between HPE level of invasion and USG level of invasion with kappa 0.452 and a statistically significant p value <.0001. This can be attributed to the inability of ultrasound to distinguish clearly between dermis and subcutis due to the disrupted architecture of skin in neoplastic tissue reaction.

Locoregional spread was found on USG in 6 patients of BCC, keratoacanthoma, cutaneous metastasis, and trichoepithelioma. In our study, locoregional spread was defined as either internal structure invasion or surrounding tissue involvement, or lesions present in the surrounding area related to primary pathology which were not detected on clinical examination.

In subgroup analysis, 82% of BCC lesions were present over face, followed by scalp and trunk in 9% of lesions. The most common type of BCC was nodular (67%), followed by pigmented (17%), morpheaform (8%), and superficial (8%). Adinarayan, and Baruah also reported nodular as the most common histopathologic subtype of BCC in their studies.[57,66] On HFUS, majority of lesions of BCC were found to be oval to irregular in shape, solid, hypoechoic, and had varying blood flow. Half of the lesions were heterogenous, and the other half were homogenous. This was consistent with the study by Bobadilla et al. in which sonography showed solid, oval-shaped tumor with uneven edges in all cases. Two of the 12 lesions were found to have spread to locoregional areas. All of the tumors had arterial blood vessels inside and around them, mostly in the deep parts of the tumors.[9] Mean depth calculated was 3.4 ± 3.4 (mm) on HFUS and on HPE was 3.51 ± 3.2 in our study. Significant positive correlation was seen in BCC between USG depth(mm) with HPE depth(mm) with correlation coefficient of 0.862. Significant positive correlation was seen in BCC between clinical width(mm) with USG width(mm) with correlation coefficient of 0.988. Depth was measured by histology and ultrasound and Mean USG depth was 3.7 +/-1.1 mm and 3.9 +/-1.0 mm on HPE. All except two cases had a very good correlation (ICC) between ultrasound and histology.

Dermoscopy has shown to be valuable in the diagnosis of skin lesions. Histopathological and dermoscopic correlation have been assessed in many studies. In our study BCC had arborizing and linear vascularity in majority of cases which can be correlated with increased vascularity in papillary dermis. Also, clods and homogenous areas (concordant with tumor nests in dermis) was also seen in many cases. Histopathologically, arborizing vessels correspond to dermal dilated vessel [67] and short, thin telangiectasias correspond to telangectatic vessels in the papillary dermis. Blue-gray ovoid nests correspond to substantial tumor nests that invade the dermis and contain pigment aggregates and dots with tiny tumor nests in the papillary and reticular dermis. [58]

Skin tumors are a diverse group with varying clinical presentations. They frequently pose a diagnostic challenge to the clinician. Histopathological analysis is the current diagnostic gold standard. However , dermoscopy and HFUS have been utilised to hasten the diagnosis and improve pre-operative evaluation. Similarly in our research, dermoscopy proved to be a valuable aid in diagnosis of skin tumors. In addition, HFUS assisted in analysing extension of tumor, the depth to which it penetrated, and the blood flow in the lesion using Color Doppler examination. Although HFUS cannot be used to establish a diagnosis, it can allow for a thorough preoperative evaluation of the tumor. Patients who are reluctant to undergo a biopsy straightaway may also benefit from its use. It can provide clues regarding the type of tissue and whether or not critical structures beneath or around it are involved non-invasilvely. Incomplete excision is a common problem with facial tumors because of their locations. Our research shown that the linear hockey stick probe could be used to access all anatomical areas, including eyelids, nose and post auricular region , which is very helpful because these are the most prevalent places where skin malignancies arise.

Although earlier researches have mostly focused on NMSCs, our study expands potential literature on value of HFUS in diagnosing a wide range of skin malignancies. It emphasised the need of ultrasound before surgery since it can provide an approximate depth estimate that can be utilized during the excision process.

As dermoscopy is only capable of visualising the epidermis and papillary dermis, it was challenging to correlate it with ultrasonography, which focuses primarily on dermal and subcutaneous findings. And ultrasonography is an operator-dependent tool; even though a single operator performed all USGs in our study, a learning curve is still required to perform USG and make a diagnosis after analysis. In addition, ultrasonography was not possible for very small lesions due to the inability to localise the lesion. Ultrasound detected vascularity in significantly more patients than histopathology. Future research will require a larger sample size due to the heterogeneity of our data and the small number of patients in each category.

CONCLUSION

CONCLUSION

We conducted a cross sectional observational study on patients with benign and malignant skin tumors. A total of 52 patients were recruited in the study as per the selection criteria. We took relevant history, performed clinical examination, dermoscopy with photographic documentation, and ultrasonographic and histopathological examinations. During ultrasonography, relevant findings were noted and biopsy was sent to make the final diagnosis of the lesion.

We found that skin tumors affected people in all age groups. However, a female preponderance was noted in our study. Benign tumors are more common in younger people than malignant tumors. The most common site was the face and the most common type of skin tumors found were keratinocytic tumors. Benign tumors outnumbered malignant ones, although BCC individually was the most common type of tumor observed. Other tumors detected in the study were mostly benign.

Dermoscopy revealed that the majority of tumors are skin-colored or hyperpigmented with BCC exhibiting typical findings of homogenous patterns and clods areas that are concordant with dermal tumor nests and arborizing vessels with increased papillary dermal vascularity.

The majority of skin tumors were described as hypoechoic, homogenous, oval to irregular-shaped solid lesions by HFUS. Lesions were involving epidermis and dermis in the most of the cases with vascularity present in a substantial number of lesions. HFUS was found to have very good agreement in correlating the diagnosis with the final histopathological diagnosis. BCC demonstrated the highest sensitivity and specificity. Cysts, lipoma, pyogenic granuloma had a higher sensitivity whereas appendageal tumors and spindle cell tumors were found to have a higher specificity.

Statistically significant correlation was noted between clinical size and ultrasonographic size and between USG depth and HPE depth which highlight the pre-surgical role of ultrasonography.

Vascularity was found to have a fair agreement when correlation was analysed between HFUS and HPE. HFUS was found to have greater sensitivity and lesser specificity in detecting vascularity. The levels of invasion on HFUS and HPE showed moderate agreement

with a statistically significant correlation. 6 patients had locoregional spread resulting in better planning of excision.

In subgroup analysis, BCC was seen as an oval to irregular, solid, hypoechoic lesion with increased vascularity. Statistically significant correlation was detected between depth measured between HFUS and HPE.

Our research expands the non-invasive diagnostic approach for skin tumors with the help of dermoscopy and HFUS by detecting tumor size, location, vascularity, and invasion which can eventually lead to better preoperative planning.

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ANNEXURES

ANNEXURE 1

ETHICAL CLEARANCE CERTIFICATE

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2021/3474 **Date: 12/03/2021**

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2021/3309**

Project title: **"High frequency ultrasonography of benign and malignant skin tumors and its correlation with histopathology and dermoscopy"**

Nature of Project:	**Research Project Submitted for Expedited Review**
Submitted as:	**M.D. Dissertation**
Student Name:	**Dr. Priyanka Karadia**
Guide:	**Dr. Anil Budania**
Co-Guide:	**Dr. Taruna Yadav, Dr. Abhishek Bhardwaj, Dr. Prakash Kala, Dr. Vikarn Vishwajeet, Dr. Saurabh Singh, Dr. Anupama Bains & Dr. Suman Patra**

Institutional Ethics Committee after thorough consideration accorded its approval on above project.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

Please Note that this approval will be rectified whenever it is possible to hold a meeting in person of the Institutional Ethics Committee. It is possible that the PI may be asked to give more clarifications or the Institutional Ethics Committee may withhold the project. The Institutional Ethics Committee is adopting this procedure due to COVID-19 (Corona Virus) situation.

If the Institutional Ethics Committee does not get back to you, this means your project has been cleared by the IEC.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Praveen Sharma
Member Secretary

Member secretary
Institutional Ethics Committee
AIIMS,Jodhpur

Basni Phase-2, Jodhpur, Rajasthan-342005; **Website:** www.aiimsjodhpur.edu.in; **Phone:** 0291-2740741 Extn. 3109
E-mail : ethicscommittee@aiimsjodhpur.edu.in; ethicscommitteeaiimsjdh@gmail.com

ANNEXURE 2

CASE SHEET PROFORMA

Name: ID:
Age / Sex: Address:

1. Education status: :
2. Occupation:
3. Marital status: Unmarried Married
4. Age of onset:
5. Total duration of illness:
6. Presenting complaints:
……
…….
……
…….
7. . H/O diabetes/ hypertension/ tuberculosis/ thyroid illness: Yes/No
If, yes→ Specify: Duration: Treatment taken:
8. H/O Previous treatment (including surgical history):

9. H/O HIV/HBV/HCV:
If yes , Specify:
10. H/O smoking/ Alcohol: Yes/No If, yes→ Duration:
11. H/O any other cutaneous illness: Yes/No If,yes→Details:
12. H/O any bleeding disorders :
13. Drug history :

Examination:

General Examination:
BP :
PR:
RR:
Temperature:

Any significant finding:

Cutaneous examination:
Lesion
morphology:……
…..
Site of the lesion:
Size of the lesion:
Number :
Consistency / induration of lesion :
Surface changes:
Any signs of infection : pus discharge / warmth
Tenderness:
Any other findings:

INVESTIGATIONS :

DERMOSCOPY :
……
……..

COLOR	
VESSELS	Arborization/lacunae/serpentine/dotted/comma/hairpin/glomerular/ crown/ polymorphous
CLODS /DOTS/GLOBULES	
HOMOGENOUS PATTERN	
PIGMENT NETWORK	
NEGATIVE PIGMENT NETWORK	
STREAKS	
HAIR	
SCALES{IF PRESENT}	
ANY OTHER FINDINGS	
SATELLITE LESIONS IN EPIDERMIS OR DERMIS{IF PRESENT}	

ULTRASOUND:……

SHAPE	
DIMENSIONS : DEPTH WIDTH OR DIAMETER	
CONSISTENCY : SOLID/SEMISOLID/CYSTIC	
ECHOGENICITY	
HOMOGENEITY	

LEVEL OF INVASION :TILL EPIDERMIS/DERMIS/SUBCUTIS / MUSCLE/BONE	
VASCULARITY AND ITS LOCATION	
SATELLITE LESIONS {IF ANY}	
EPIDERMAL FINDINGS	
DERMAL FINDINGS	
LOCOREGIONAL SPREAD	

HISTOPATHOLOGY:……
……..

DIMENSIONS :DEPTH WIDTH OR DIAMETER	
LEVEL OF INVASION	
ATYPIA / N/C RATIO	
VASCULARITY	
COMPOSITION : TYPE OF CELLULAR MORPHOLOGY	
EPIDERMAL FINDINGS	
DERMAL FINDING	
TYPE OF TUMOR	
SUBCUTIS FINDINGS	

Any other significant findings:

ANNEXURE 3

PATIENT CONSENT FORM

I ……, age/sex ……
D/S/W of…….. ,R/O
……ID……
file number …….. ,contact number…….
Hereby declare that I authorize the doctor of Department of Dermatology, AIIMS , Jodhpur to perform ultrasonography and tissue biopsy on me.
I give my full, free, voluntary consent to be a part of the study " **High frequency ultrasonography of benign and malignant skin tumors and its correlation with histopathology and dermoscopy**"

- I understand I will have to undergo ultrasonographic examination and tissue biopsy .
- I am aware that tissue biopsy is a invasive surgical procedure where the tumor tissue will be removed under local anaesthesia for laboratory analysis. I understand that this will need stitches for closure of the incision.
- I am aware that the tissue biopsy can produce but are not limited to the following common side effects: pain, bleeding, swelling, wound infection, scarring, irritation due to antiseptics and sutures, nerve damage and delayed healing. I understand that these side effects can last for couple of days. I understand that there are some risks and complications that can occur from a tissue biopsy that can interrupt my daily life, work routine or social life. These may include but are not limited to- prolonged pain, scarring and infection .
- I give consent for my photographs taken during the clinical and dermatoscopic examination. Photos will be retained as a part of my file and used for future scientific publications , under seal of my anonymity.
- I have read and understood all information presented to me before signing this consent .i have had opportunity to ask question regarding ultrasound and tissue biopsy and its side effects .
- I hereby and forever discharge my treating doctor and technicians from all claims, demands, actions, and cause of action arising out of the procedure performed.
  I understand that my participation is voluntary and I am aware of my right to opt out of the study at any time without giving any reason.

Signed …… Witness ……...
(patient or person legally authorized for the patient) (to patient's sign)to consent
Full name: ……. Full name……..
Date: ……. Date……..
This to certify that the above consent has been obtained in my presence.

Date : _____ _____

Place : _____ Name & Signature of PG Student

ANNEXURE 4

<u>रोगी सहमति</u> पत्र

मैं ....., उम्र / लिंग .....
पुत्र/पुत्री/ पत्नी श्री..... .., निवासी ..... ID .....।
फ़ाइल नंबर ...., संपर्क नंबर .....।
मैं यह घोषित करता/करती हूं कि मैं त्वचाविज्ञान विभाग, एम्स, जोधपुर के डॉक्टर को अधिकृत करता/ करती हूं कि वे मुझ पर अल्ट्रासोनोग्राफी और टिशू बायोप्सी करें। उपरोक्तअध्ययन "– बिनाइन और मालिगनेंट त्वचा ट्यूमर की हाई फ्रिकवेंसी की अल्ट्रासोनोग्राफी ,हिस्टोपैथोलॉजी और डर्मोस्कोपी के बीच सहसंबंध ।"(

High frequency ultrasonography of benign and malignant skin tumors and its correlation with histopathology and dermoscopy) का एक हिस्सा बनने के लिए मेरी पूर्ण, स्वतंत्र, स्वैच्छिक सहमति देता हूँ।

- मैं समझता हूं कि मुझे अल्ट्रासोनोग्राफिक परीक्षा और टिशू बायोप्सी से गुजरना होगा।
- मुझे पता है कि टिशू बायोप्सी एक शल्य प्रक्रिया है जहां प्रयोगशाला विश्लेषण के लिए स्थानीय एनेस्थीसिया के तहत गांठ को हटा दिया जाएगा। मैं समझता हूं कि चीरा बंद करने के लिए टांके लगाने की जरूरत होगी।
- मुझे पता है कि टिशू बायोप्सी निम्नलिखित दुष्प्रभाव हो सकते हैं: दर्द, रक्तस्राव, सूजन, घाव संक्रमण, जख्म, एंटीसेप्टिक्स और टांके के कारण जलन, तंत्रिका क्षति और घाव भरने में अधिक समय लगना। मैं समझता हूं कि ये दुष्प्रभाव कुछ दिनों तक रह सकते हैं। मैं समझता हूं कि कुछ जोखिम और जटिलताएं हैं जो एक टिशू बायोप्सी से हो सकती हैं जो मेरे जीवन ,कार्य दिनचर्या या सामाजिक जीवन को बाधित कर सकती हैं।
- मैं नैदानिक और डर्मेटोस्कोपिक परीक्षा के दौरान ली गई मेरी तस्वीरों के लिए सहमति देता हूं। मेरी गुमनामी की मुहर के तहत तस्वीरों को मेरी फ़ाइल के एक हिस्से के रूप में रखा जाएगा और भविष्य के वैज्ञानिक प्रकाशनों के लिए उपयोग किया जाएगा।
- मैंने इस सहमति पर हस्ताक्षर करने से पहले मेरे सामने प्रस्तुत सभी सूचनाओं को पढ़ा और समझा है। मुझे अल्ट्रासाउंड और ऊतक बायोप्सी के बारे में और उनके दुष्प्रभावों के बारे में सवाल पूछने का पर्याप्त अवसर मिला है।
- मैं एतद्द्वारा और हमेशा के लिए अपने उपचार करने वाले डॉक्टर और तकनीशियनों को सभी दावों, मांगों, कार्यों और प्रदर्शन की प्रक्रिया से उत्पन्न होने वाले कार्यों के कारण से मुक्ति देता हूं।

मैं समझता हूं कि मेरी भागीदारी स्वैच्छिक है और मुझे किसी भी कारण दिए बिना किसी भी समय अध्ययन से बाहर निकलनेका मेराअधिकार है।

हस्ताक्षरित .....
(रोगी या व्यक्ति कानूनी रूप से अधिकृत है रोगी के लिए सहमति)
पूरा नाम: .....
दिनांक: .....

साक्षी .....
(रोगी के संकेत के लिए)
पूरा नाम: .....
दिनांक: .....

यह प्रमाणित करने के लिए कि मेरी उपस्थिति में उपरोक्त सहमति प्राप्त की गई है

तारीख : _____

_____

जगह : _____

पीजी छात्र के हस्ताक्षर

ANNEXURE 5

PATIENT INFORMATION SHEET (PIS)

This document has been given to provide more information about the disease and this research is related to correlation of ultrasonographic findings of skin tumors with histopathology and dermoscopy.

The current research project is titled **- High frequency ultrasonography of benign and malignant skin tumors and its correlation with histopathology and dermoscopy**.

Skin tumors are the abnormal growth of the skin cells .

Ultrasonography uses sound waves to visualize internal parts of our body which are not visible to the naked eyes. It uses a small probe called a transducer and gel placed directly on the skin.

A skin biopsy is a routine investigation that helps us to diagnose skin conditions. A biopsy is where a small sample of skin is removed under local anaesthetic in order for it to be looked at under the microscope.

The basic goal of this research is to correlate the findings of ultrasonography, histopathology and dermoscopy in skin tumors.

The patient is also informed that all the information given by him will be kept confidential. The patient also reserves the right that during this research, patient can withdraw the consent & can be out of this research without explaining the reasons.

Principal investigator: Dr. Priyanka Karadia Contact number: 9920710040

ANNEXURE 6

रोगी सूचना पत्रक (पीआईएस)

यह दस्तावेज़ रोग के बारे में अधिक जानकारी प्रदान करने के लिए दिया गया है और यह अनुसंधान हिस्टोपैथोलॉजी और डर्मोस्कोपी के साथ त्वचा के ट्यूमर के अल्ट्रासोनोग्राफिक निष्कर्षों के सहसंबंध से संबंधित है।

वर्तमान अनुसंधान परियोजना का शीर्षक है – **बिनाइन और मालिगनेंट त्वचा ट्यूमर की हाई फ्रिकवेंसीकी अल्ट्रासोनोग्राफी ,हिस्टोपैथोलॉजी और डर्मोस्कोपी के बीच सहसंबंध** । (**High frequency ultrasonography of benign and malignant skin tumors and its correlation with histopathology and dermoscopy)**

त्वचा के ट्यूमर त्वचा कोशिकाओं की असामान्य वृद्धि है।

अल्ट्रासोनोग्राफी हमारे शरीर के आंतरिक भागों को देखने के लिए ध्वनि तरंगों का उपयोग करती है जो नग्न आंखों को दिखाई नहीं देती हैं। यह एक छोटे प्रोब का उपयोग करता है जिसे ट्रांसड्यूसर कहा जाता है।

त्वचा बायोप्सी एक नियमित जांच है जो हमें त्वचा की स्थिति का निदान करने में मदद करती है। एक बायोप्सी वह जांच है जहां त्वचा के एक छोटे नमूने को स्थानीय एनेस्थीसिया के तहत हटा दिया जाता है ताकि इसे माइक्रोस्कोप के नीचे देखा जा सके।

इस शोध का मूल लक्ष्य स्किन ट्यूमर में अल्ट्रासोनोग्राफी, हिस्टोपैथोलॉजी और डर्मोस्कोपी के निष्कर्षों का सहसंबंध है।

रोगी को यह भी सूचित किया जाता है कि उसके द्वारा दी गई सभी जानकारी को गोपनीय रखा जाएगा। रोगी को यह अधिकार भी है कि इस शोध के दौरान, रोगी बिना कारण बताए सहमति को वापस ले सकता है और इस शोध से बाहर हो सकता है।

सिद्धांत अन्वेषक: डॉ प्रियंका कराडिया संपर्क नंबर: 9929710040

ANNEXURE 7

MASTER CHART WITH IMPORTANT KEY WORDS

Si. No.	VARIABLE	CODING
1.	Diagnosis	Appendageal Tumor-1 Cyst-2 Spindle Cell Tumor-3 Adipocyte Tumor-4 Vascular Tumor-5 Basal Cell Carcinoma-6 Melanoma-7 Others(Glomus Tumor, Keratoacanthoma, Mets, dermal melanocytic nevus)-8
2.	Address	Rural-1 Urban-2
3.	Sex	Male-1 Female-2
4.	Education	Illiterate-1 Literate-2
5.	Occupation	Housewife-1 Student-2 Businessman-3 Skilled Worker-4 Semiskilled Worker-5 Professional-6 Unemployed-7
6.	Site	Scalp-1 Face-2 Upper Limb-3 Lower Limb-4 Trunk-5 Genitelia-6
7.	Size	<1cm-1 1-3cm-2 >3cm-3
8.	Color	Erythematous-1 Skin Colored-2 Hyperpigmented-3 Violaceous-4
9.	Morphology	Nodule-1 Papule-2 Plaque-3 Noduloplaque-4
10.	Specific morphology	Exophytic-1 Raised-2 Deep-3

11.	Consistency	Soft-1 Firm-2 Hard-3
12.	Tenderness	Yes-1 No-2
13.	Satellite lesions	Yes-1 No-2
14.	Comorbidities	Hypertension-1 Diabetes Mellitus-2 Thyroid-3 No-4
15.	Viral markers	Yes-1 No-2
16.	Bleeding diathesis	Yes-1 No-2
17.	Dermoscopy color	Skin Color-1 Erythematous-2 Hyperpigmented-3
18.	Dermoscopy arborizing vessel	Yes-1 No-2
19.	Dermoscopy Lacunae	Yes-1 No-2
20.	Dermoscopy linear Vessel	Yes-1 No-2
21.	Dermoscopy Dotted Vessel	Yes-1 No-2
22.	Dermoscopy Polymorphous	Yes-1 No-2
23.	Dermoscopy Clods	Yes-1 No-2
24.	Dermoscopy Dots	Yes-1 No-2
25.	Dermoscopy Pigment Network	Yes-1 No-2
26.	Dermoscopy Homogenous Pattern	Yes-1 No-2
27.	Dermoscopy Streaks	Yes-1 No-2
28.	USG Shape	Oval-1 Round-2 Irregular-3
29.	USG_Consistency	Solid-1 Cystic-2 Semisolid-3
30.	USG Echogenicity	Hypoechoic-1 Hyperechoic-2 Isoechoic-3
31.	USG Homogeneity	Yes (Homo)-1 No(Hetero)-2
32.	USG Locoregional Spread	Yes-1 No-2
33.	USG Level of Invasion	Epidermis-1 Dermis-2 Subcutis-3 Epidermis+Dermis-4 Dermis+Subcutis-5
34.	USG Vascularity	Yes-1 No-2
35.	USG Location vessel	Peripheral-1 Base-2 Central-3 Hypervascular-4 Linear-5

		No-6
36.	Satellite Lesion	Yes-1 No-2
37.	HPE Level Of Invasion	Epidermis-1 Dermis-2 Subcutis-3 Epidermis+Dermis-4 Dermis+Subcutis-5
38.	HPE Nuclear Atypia	Yes-1 No-2
39.	HPE Vascularity	Yes-1 No-2
40.	Tumor_Type	Benign-1 Malignant-2

S.No.	Final_diagnosis_hpe	provisional_clinical_diagnosis	USG_diagnosis	final_diagnosis_hpe_code	age (years)	address	sex	education	occupation	duration of illness(month)	site of lesion	clinical width	size of lesion	color of lesion	morphology	specific morphology	consistency	tenderness	satellite lesion	comorbidities	viral_markers	bleeding disorder	Dermoscopy color	Dermoscopy arborizing vessel	Dermoscopy linear Vessel	Dermoscopy Dotted Vessel	Dermoscopy Lacunae	Dermoscopy Polymorphous	Dermoscopy Clods	Dermoscopy Dots	Dermoscopy Pigment Network	Dermoscopy Homogenous Pattern	Dermoscopy Streaks	USG shape	USG depth(mm)	USG width(mm)	USG consistency	USG echogenicity	USG homegeneity	USG locoregional_spread	USG level of invasion	USG vascularity	USG Location vessels	USG satellite lesion	HPE depth(mm)	HPE level of invasion	HPE nuclear atypia	HPE vascularity	HPE tumor type
1	eccrine origin tumor	1	1	**1**	46	1	2	1	1	60	2	9	1	1	1	2	1	2	2	4	2	2	1	1	2	2	2	2	2	1	2	1	2	1	5.3	8	1	1	1	2	2	1	1	2	6	2	2	1	1
2	pigmented nodular hidradenoma	1	1	**1**	20	1	2	2	2	8	2	22	2	3	1	2	2	2	2	4	2	2	3	1	2	2	2	2	1	1	2	1	2	1	7	20	1	2	2	2	4	1	5	2	5	4	2	1	1
3	pilar cyst	3	2	**2**	23	2	1	2	2	60	2	8	1	2	1	2	1	2	2	4	2	2	1	2	1	2	2	2	2	2	1	1	2	1	5	7.8	2	1	1	2	4	2	6	2	5	4	2	2	1
4	dermatofibroma	3	3	**3**	24	2	2	1	2	12	4	5	1	3	1	3	2	1	2	4	2	2	3	2	2	2	2	2	2	1	1	1	1	1	5	5	1	1	1	2	2	2	6	2	4.6	2	2	2	1
5	fibroepithelial polyp	1	4	**1**	62	2	1	2	6	36	1	6	2	2	1	2	1	2	2	2	2	2	1	2	2	2	2	2	2	1	1	2	2	2	4.4	5.5	1	2	1	2	2	2	6	2	4	2	2	2	1
6	melanocytic nevus	8	8	**8**	22	2	2	1	2	180	2	5	1	3	1	2	1	2	2	4	2	2	3	2	2	2	2	2	1	2	1	2	2	1	2.2	4.1	1	1	1	2	2	2	6	2	2.12	2	2	2	1
7	pilar cyst	2	2	**2**	48	2	2	2	1	72	1	14	2	1	1	2	2	1	1	2	2	2	1	2	2	2	2	1	1	1	2	2	2	2	8.35	13.2	2	2	2	1	2	1	1	1	10	3	2	1	1
8	epidermal inclusion cyst	2	2	**2**	25	1	1	2	6	120	1	13	2	2	1	2	2	2	2	4	2	2	1	2	2	2	2	2	1	2	1	1	2	2	8.7	12	2	2	2	2	3	1	1	2	11.1	3	2	1	1
9	BCC	6	6	**6**	80	2	2	1	1	60	2	15	2	1	3	2	2	2	1	2	2	2	2	1	2	2	1	1	1	2	1	1	2	3	3.2	15	1	1	1	1	4	1	3	1	3.56	4	2	1	2
10	lipoma	4	4	**4**	26	2	1	2	2	18	3	20	2	2	1	3	1	2	2	4	2	2	1	2	2	2	2	2	2	1	2	2	2	2	12.6	20	3	3	1	2	3	2	6	2	11.9	3	2	2	1
11	epidermal inclusion cyst	2	2	**2**	21	1	2	2	2	6	2	14	2	2	1	3	1	2	2	3	2	2	1	2	2	2	2	2	1	1	1	2	2	2	6.5	15	2	1	1	2	2	1	1	2	7.1	2	2	2	1
12	pyogenic granuloma	5	5	**5**	18	1	1	2	2	2	1	20	2	1	1	1	1	2	2	3	2	2	2	2	2	1	1	1	1	2	1	1	2	3	6.5	20	1	1	1	2	2	1	3	2	7.04	4	2	1	1
13	trichoepithelioma	1	1	**1**	29	2	2	2	6	12	2	4	1	2	2	2	1	2	2	4	2	2	1	1	1	2	2	2	1	1	2	2	2	1	1.6	3.8	1	1	1	1	2	2	6	1	1.45	2	2	2	1
14	leiomyoma	8	8	**3**	33	1	2	2	6	12	4	16	3	1	3	3	2	2	2	1	2	2	2	2	2	1	1	2	1	2	1	1	2	3	2.56	17	1	2	2	2	4	1	2	2	3	4	1	1	1
15	BCC	6	6	**6**	80	2	2	1	1	60	2	15	2	2	3	2	2	2	1	2	2	2	1	1	2	1	1	2	1	2	1	1	2	3	1.06	16	1	1	2	1	4	1	2	1	1.1	4	2	1	2
16	nevus sebaceous	1	1	**1**	18	1	1	2	2	84	2	24	3	3	3	2	1	2	2	4	2	2	1	2	2	2	2	2	1	1	1	1	1	3	5.3	25	3	1	2	2	4	2	6	1	5.25	4	2	2	1
17	dermal melanocytic nevus	8	8	**8**	31	2	2	2	1	180	2	6	1	2	1	2	1	2	2	1	2	2	1	2	1	2	2	2	1	1	1	1	2	1	3.4	6.3	1	1	1	2	5	1	2	2	2.9	4	2	1	1
18	BCC	6	6	**6**	44	1	2	1	1	180	2	4	1	1	2	2	2	2	1	1	2	2	2	1	1	1	1	1	1	2	2	1	1	1	1	3.4	1	1	1	2	2	1	1	1	3	4	1	1	2
19	lipoma	4	4	**4**	20	2	1	2	2	120	3	15	2	2	1	3	1	2	2	4	2	2	1	2	2	2	2	2	2	1	2	1	2	2	12	16	1	3	1	2	3	2	6	2	12.3	3	2	2	1
20	syringocystadenoma papilliferum	1	1	**1**	20	2	1	2	2	60	1	5	1	1	2	2	1	2	2	4	2	2	1	2	2	1	1	2	1	1	1	1	2	1	4	4.3	1	1	1	2	4	1	3	2	3.6	4	2	1	1
21	lipoma	4	4	**4**	27	2	1	2	2	12	3	10	2	2	1	3	1	2	2	4	2	2	1	2	2	2	2	2	2	1	2	1	2	1	14	10	1	3	1	2	3	1	6	2	13.4	3	2	2	1
22	BCC	6	6	**6**	44	1	2	1	1	24	2	2	1	2	2	2	2	2	1	1	2	2	1	1	1	2	2	2	1	1	1	1	2	1	0.7	2	1	1	1	2	2	1	1	1	0.6	2	2	2	2
23	epidermal inclusion cyst	3	2	**2**	18	1	2	2	2	12	2	4	1	2	2	2	1	2	2	4	2	2	1	2	1	2	2	2	1	1	1	2	2	1	3	4	2	1	1	2	4	1	1	2	2.84	4	2	2	1
24	pyogenic granuloma	5	5	**5**	18	1	1	2	2	2	2	5.5	2	1	1	1	1	2	2	4	2	2	2	2	2	1	1	2	1	2	2	1	2	3	2.5	5.3	1	1	2	2	4	1	2	2	2.78	4	2	1	1
25	dermatofibroma	3	3	**3**	18	2	2	2	2	12	3	7	2	2	1	3	2	2	2	4	2	2	3	2	2	2	2	2	2	1	1	1	1	1	6	6.6	1	1	1	2	4	2	6	2	5.6	2	2	2	1
26	neurofibroma	3	3	**3**	44	2	1	2	5	24	3	5	2	2	1	3	1	2	2	1	2	2	3	2	2	2	2	2	1	1	1	1	2	1	6.2	5.1	1	1	1	2	4	1	2	2	7.1	2	2	2	1
27	glomus tumor	8	8	**8**	35	2	2	2	1	12	3	2	1	4	1	3	1	1	2	3	2	2	2	2	2	1	1	2	2	2	2	1	2	3	3.2	2	3	1	2	2	5	1	2	2	3	4	2	1	1
28	malignant melanoma	8	8	**7**	41	2	2	2	1	7	3	22	2	2	1	3	1	1	2	4	2	2	1	2	2	2	2	2	2	2	2	2	2	3	7	20	1	1	2	2	4	1	4	2	6.4	3	1	1	2
29	Keratoacanthoma	8	8	**8**	75	1	1	1	7	4	1	24	2	1	1	1	3	2	2	1	2	2	1	1	1	2	2	2	2	2	2	1	2	3	15	25	1	1	2	1	4	1	3	1	14	4	2	2	2
30	bcc	6	6	**6**	51	1	2	1	1	24	5	12	2	3	1	2	2	2	2	4	2	2	1	1	1	2	2	2	1	1	1	1	2	1	6.23	13	1	1	1	2	4	1	2	1	5.87	4	2	1	2
31	dermatofibroma	3	3	**3**	35	2	2	2	6	6	3	5	2	2	1	3	2	2	2	4	2	2	3	2	2	2	2	2	1	2	1	1	1	3	13	5	1	1	1	2	4	1	2	2	12.6	4	2	2	1
32	bcc	6	6	**6**	70	2	2	1	1	24	2	28	2	3	3	2	2	2	1	4	2	2	1	1	1	2	1	2	1	2	2	1	1	1	2.8	27	1	1	2	2	4	1	1	1	3	4	2	2	2
33	bcc	6	6	**6**	60	1	2	1	1	36	2	11	2	3	1	2	2	2	2	4	2	2	1	1	1	2	2	2	1	2	2	1	1	1	3.2	10.7	1	1	2	2	4	2	6	2	2.91	4	2	2	2
34	pyogenic granuloma	5	5	**5**	45	2	1	2	5	12	2	4	1	1	1	1	1	2	2	1	2	2	2	2	1	2	1	2	1	2	1	1	2	1	2	5	3	1	2	2	4	1	4	2	2.2	2	2	1	1
35	epidermal inclusion cyst	2	2	**2**	30	1	1	2	6	6	2	10	1	2	1	2	1	2	2	4	2	2	1	2	2	2	2	2	1	2	1	1	2	2	5	10	2	2	2	2	4	2	6	2	4.8	2	2	2	1
36	dermal melanocytic nevus	8	8	**8**	39	2	2	2	1	12	1	9	1	2	1	2	1	2	2	4	2	2	3	2	2	2	2	2	1	1	1	1	2	1	7.3	9	1	1	1	2	2	2	6	2	7	2	2	2	1
37	bcc	6	6	**6**	54	1	2	1	1	30	2	15	2	3	3	2	2	2	2	2	2	2	3	2	1	2	1	2	1	2	2	1	1	3	1.12	15	1	1	2	2	4	1	3	2	1.15	2	1	2	2
38	epidermal inclusion cyst	3	2	**2**	19	2	2	2	2	24	2	18	1	2	1	3	2	2	2	4	2	2	1	2	1	2	2	2	2	1	2	1	2	2	9.3	18	2	1	1	2	2	1	1	2	9.53	2	2	2	1
39	bcc	6	6	**6**	79	2	2	1	1	60	1	20	2	3	1	2	2	2	2	1	2	2	3	1	1	2	1	1	1	2	1	1	1	3	3.2	20	1	1	2	2	4	1	3	2	3.02	4	2	2	2
40	nodular hidradenoma	1	2	**1**	21	2	1	2	2	12	2	19	2	1	1	3	1	2	2	4	2	2	1	2	1	2	2	2	2	1	1	2	2	1	5.4	19	2	1	2	2	3	1	1	2	5	2	2	2	1
41	schwannoma	3	3	**3**	25	1	1	2	2	120	5	42	3	2	1	3	1	2	2	4	2	2	1	2	2	2	2	2	1	1	1	1	2	3	19	42	1	1	2	2	3	1	4	2	17	5	2	1	1
42	bcc	6	6	**6**	40	1	2	2	1	12	2	20	2	3	3	2	2	2	2	4	2	2	3	1	1	2	2	1	1	1	2	1	1	1	2	17	1	1	1	2	4	1	3	2	2.2	4	2	2	1
43	dermatofibroma	3	3	**3**	18	2	2	2	2	12	4	10	1	3	1	3	2	2	2	4	2	2	1	2	2	2	2	2	1	1	1	1	1	3	4.1	10	1	1	1	2	4	1	2	2	4.2	2	2	2	1
44	metastatic glial tumor	8	5	**8**	18	1	1	2	2	18	1	5	2	1	1	1	3	1	2	4	2	2	1	1	1	2	2	1	1	1	1	1	2	3	3	6	1	2	2	1	4	1	2	1	3.2	5	1	1	2
45	trichofolliculoma	1	1	**1**	30	2	1	2	6	12	1	8	2	1	1	2	1	2	2	4	2	2	1	2	2	2	2	2	1	1	2	1	2	3	2	8.2	1	1	1	2	2	1	6	2	1.7	2	2	2	1
46	dermatofibroma	3	3	**3**	23	2	2	2	2	18	4	12	2	1	1	3	2	1	2	4	2	2	1	2	2	2	2	2	2	1	1	1	1	3	11	13	1	1	1	2	4	2	6	2	10.6	2	2	2	1
47	glomus tumor	8	8	**8**	37	2	2	2	1	24	3	7.5	1	2	1	3	2	1	2	4	2	2	1	2	2	2	1	2	2	2	2	1	2	2	6.2	8	1	1	1	2	3	1	1	2	5.5	3	2	2	1
48	pyogenic granuloma	5	5	**5**	32	1	1	2	1	12	5	25	2	1	1	1	2	1	2	4	2	2	2	2	1	2	1	2	1	2	1	1	2	3	21	24	3	1	2	2	4	1	4	2	20	2	2	1	1
49	appendageal tumor	1	1	**1**	33	1	2	1	1	6	2	23	1	1	2	2	1	2	2	4	2	2	1	2	2	2	2	2	2	1	1	1	2	1	19	24	1	1	1	2	2	2	6	2	17	2	2	1	1
50	bcc	6	6	**6**	52	2	2	1	1	16	5	25	2	3	4	2	1	2	2	3	2	2	3	1	1	2	2	1	1	2	1	1	1	1	13	25	1	1	1	2	4	1	2	2	12.7	4	1	1	2
51	pilomatricoma	2	1	**1**	18	1	2	2	2	8	2	10	1	1	1	2	1	1	2	4	2	2	1	2	2	1	2	2	1	1	1	2	2	1	15.3	10	1	1	1	2	2	2	6	2	14.8	4	2	2	1
52	bcc	6	6	**6**	75	2	1	1	7	60	1	20	2	3	1	2	2	2	2	1	2	2	3	1	1	2	1	1	1	2	1	1	1	3	3.3	21	1	1	2	2	4	1	3	2	3.02	4	2	2	2