Nephrogenic Fibrosing Dermopathy (NFD) is a newly emerging term that was first introduced by **cowper and colleagues** denoting the acquired, idiopathic cutaneous fibrosing disorder occurring exclusively in the setting of renal dysfunction **(Cowper et al.,2000).**

In contrast with the original description of (NFD) as a purely cutaneous disorder , subsequent reports revealed that the disorder displays an evidence of systemic involvement which prompted the name of the disease to be changed to Nephrogenic Fibrosing Dermopathy/Nephrogenic Systemic Fibrosis (NFD/NSF). At this point ,it appears that (NSF) is a systemic disorder with its most prominent and visible effects in the skin **(Cowper, 2007).**

Despite the extensive epidemiologic and histopathologic studies , the precise sequence of events that culminate in (NFD/NSF) remains to be established , however, since the identification of the NSF-gadolinium link in 2006, the understanding of NSF has changed radically ***(Scheinfeld et al., 2008)*** .

In addition to several reports on the epidemiologic association of GBCM exposure and NSF,demonstration of gadolinium in NSF tissues has strengthened the causal associative Gd3/NSF link***(High et al., 2007)***.

Conducted investigations in the NSF registry suggest that the cells responsible for the fibrosis seen in NSF are newly characterized cells involved in wound healing and tissue remodeling namely circulating Fibrocytes (cF),which are aberrantly recruited to the skin and other systemic sites by a process initiated by renal dysfunction and likely triggered or exacerbated by endothelial damage **(*Cowper , 2007).***

The cause is almost certainly multifactorial, requiring renal disease for initiation i.e : renal dysfunction, with or without renal replacement therapy,is a prerequisite for NFD/NSF to develop **(Cassis *et al*. ,2006).**

So far, there is no clear cutt-off answer about the exact degree of renal insufficiency that sets up the development of NFD\NSF ,however, risk factors include: advanced chronic kidney disease (CKD stage 4 and 5) and acute kidney injury (AKI) ***(Scheinfeld et al., 2008).***

The US food and Drug Administration (FDA) has updated its public health advisory about patients at risk of (NFD/NSF)to include patients with moderate renal insufficiency (CKD stage 3) **(CDC ,2007) .**

In 2007, ***Swaminathan and Shah*** ., Proposed a unifying model of cumulative risk factors in which the interplay of systemic inflammation and stimulated hematopoietic environment associated with erythropoietin and hyperparathyroidism may tie to a common pathogenic mechanism of fibrogenesis.

Also in ***2007, Perazella*** suggested that : prolonged tissue exposure to gadolinium occurs in patients with CKD/ESRD (reduced renal clearance), which may allow free Gd3 (released from its chelate) to extravasate from abnormal vessels (e.g., from vascular trauma, endothelial dysfunction, chronic edema) and deposit in tissues. Once in tissues, Gd3-containing macrophages produce profibrotic cytokines that act locally and attract (cF), which in turn promote the fibrotic Response .

In their case definition, the CDC defined the clinical characteristic of the disorder as "large areas of hardened skin with slightly raised plaques or confluent papules, with or without pigment alteration and/or with biopsies showing increased numbers of fibroblasts, alteration of the normal pattern of collagen bundles seen in the dermis and often increased dermal deposits of mucin" **(CDC,2002)**.

The unique features of NFD\NSF including : the specific distribution of cutaneous involvement with facial sparing , the occurrence in the setting of renal failure , temporal relation to gadolinium exposure and the unique histopathologic features (i.e. thickened collagen bundles with surrounding clefts, mucin deposition and a proliferation of fibroblasts and elastic fibres with lack of inflammatory cells on biopsy) and its specific immunophenotype profile , distinguish NFD from the other sclerotic and panniculitic cutaneous conditions seen in patients with end-stage renal disease **(Perazella , 2007).**

Work-up for definitive diagnosis of NFD\NSF is established by performing a deep-skin biopsy such as an incisional biopsy or a deep punch biopsy from affected areas ***(Scheinfeld et al., 2008).***

Neither laboratory abnormality nor imaging studies are consistently pecific for NFD\NSF ***(Cowper , 2007).***

The histologic features of cutaneous biopsies vary depending on the age of the lesion. When biopsied early in the disease, the changes may be subtle, with only a scanty proliferation of spindled fibroblasts and

minimal evidence of collagen production appreciated. Older lesions, however, demonstrate more florid numbers of fibroblasts and collagen deposition in the reticular dermis and subcutaneum . The subcutaneous septae may be expanded by this fibrotic process ***(Perazella ,2007).***

Many different treatment options have been explored for NFD/NSF, with varying degrees of success. No single treatment has been proven effective, however, improvement in renal function seems to halt or reverse the process **(Weiss et al., 2007).**

Therapeutic approaches that have shown promise in NFD\NSF include: pentoxifylline **(Cowper et al.,2006)**, plasmapheresis **(Hubbard et al ., 2003),** photodynamic therapy **(Schmook et al.,2005),** UVA-1 phototherapy **(Kafi et al.,2004),** extracorporeal photophoresis**(Lauchli et al.,2004)** and sodium thiosulphate **(Yerram et al.,2007).**

Aim of work is to :

- Give new insights into the available epidemiological data and anecdotal studies researching the possible aetiology and incriminated risk factors and their active interplay that culminate in NFD/ NSF, Specify the unique clinical and histopathological features of the disorder and Outline the proposed treatment modalities and investigational Therapies designed for NFD/NSF.