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### **Original Research Article**

# Histopathological changes in the Liver of fatal burn victims in relation to different survival period

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#### ARTICLE INFO

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#### ABSTRACT

**Background**: Annually about 2 million people suffer from various modes of burn injuries worldwide of whom more than a lakh die. In India about 60,000 people suffer from burns annually, more than 50,000 are treated in hospitals and about 10,000 succumb to thermal injury.

**Aim**: The primary importance of present study is to have a better understanding of changes occurring in this vital organ in relation to survival period of burn victims, to emphasis that hepatic dysfunction is also an important determinant to survival of burn victims.

Setting: Forensic Medicine and Toxicology Department of a tertiary care hospital.

**Materials and Methods:** A descriptive study was performed on 37 burn deceased of both the sexes of different age groups brought into the mortuary of the Department of Forensic Medicine during the period of July 2009 to December 2010. Liver specimens were collected and the H& E stained slides studied separately by two independent observers.

**Results:** Fatty infiltrations in the liver were present at various stages i.e. microvesicular steatosis to macrovesicular steatosis, followed by fatty cyst in victims with survival periods ranging from 2 days to 30 days. Thus as the survival period increased, the proportion of involvement of the hepatic lobule increased with focal / confluent centrilobular hepatocyte necrosis in 54.5% victims of 8-15 days survival and ultimately ended into massive hepatocyte necrosis leading to complete loss of lobular architecture in victims who survived for 16-30 days.

**Conclusion:** The present study indicates that liver damage in the form of hepatic steatosis leading to hepatocyte necrosis and latter complete loss of liver architecture and consecutively hepatic dysfunction occurs with increasing survival period of burn victims therefore, maintenance of Liver integrity and function are crucial for post burn survival.

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### 1. Introduction

Deaths due to burning in India are the problem of great concern. Annually about 2 million people suffer from various modes of burn injuries worldwide of whom more than a lakh die. In India about 60,000 people suffer

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from burns annually, more than 50,000 are treated in hospitals and about 10,000 succumb to thermal injury. <sup>1</sup> Thermal injury produces a profound hypermetabolic and hypercatabolic stress response characterized by increased endogenous glucose production via gluconeogenesis and glycogenolysis, lipolysis and proteolysis. The liver is the central body organ involved in these metabolic responses. It is suggested that the liver, with its metabolic, inflammatory,

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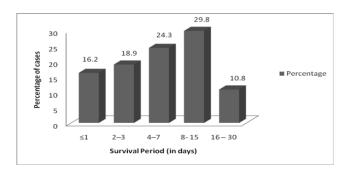
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immune and acute phase functions plays a pivotal role in patient survival and recovery by modulating multiple pathways following thermal injury. An experimental study reported 40% mortality in rats with hepatomegaly and hepatic steatosis, as compared to a control group when exposed to severe burn involving 60% of TBSA. Similar results were also seen in another retrospective study from Price et al. Therefore hepatomegaly, hepatic steatosis and dysfunction are strongly associated with increased mortality after thermal injury.

### 2. Materials and Methods

The various data for histopathological study were collected from 37 cases of both the sexes of different age groups brought into the mortuary of the Department of Forensic Medicine, during the period of July 2009 to December 2010 for medicolegal postmortem examination from various police stations of Varanasi and surrounding regions. Those were autopsied within 6 hrs to 18 hrs after death and no evidence of decomposition and associated any other organ pathology was observed at the time of autopsy. Maximum number of studied cases (11/37) had a survival period of 8-15 days and the minimum (4/37) deceased survived for 16-30 days [Graph 1].



Graph 1: The distribution of cases in different groups based on survival period of the victims

### 2.1. Tissue slide examination

The tissue blocks of about 2x2 cm collected from the most affected region observed during gross examination were fixed and subjected to histological tissue processing, following standard steps. <sup>5</sup> Haematoxylin and Eosin stained slides were prepared and the microscopic features were reviewed by two independent observers to arrive at a consensus; the histomorphologic findings were noted and photographed. These histopathological findings were finally compiled and correlated with the survival period of the

Table 1: Microscopic findings of the Liver Sections in relation to the survival period of the deceased

	Microscopic findings of liver				nS	Survival period (in days)	l (in days)				
	1	=1</th <th></th> <th>2-3</th> <th></th> <th>4-7</th> <th></th> <th>8-15</th> <th></th> <th>16-3(</th> <th></th>		2-3		4-7		8-15		16-3(	
		$(9 = \mathbf{u})$	(9 =	$(\mathbf{n} = 7)$	(7=	(0 = 0)	(6 :	(n = 11)	11)	$(\mathbf{n} = 4)$	<del>4</del> =
			%		%						6
_	Sinusoidal congestion	3	50	9	85.7	0	00	00	00	0	0
2	Central vein congestion	2	33.3	3	42.8	0	00	00	00	0	0
$\mathcal{E}$	Fatty changes										
a.	Microvesicular steatosis	0	00	3	42.8	6	100	2	18.1	0	0
þ.	Macrovesicular steatosis	0	00	0	00	7	77.8	11	100	2	S
·.	Fatty cyst	0	00	0	00	0	00	3	27.3	4	)
4	Hepatocyte necrosis	0	00	0	00	3	33.3	9	54.5	4	$\simeq$
2	Intrahepatic cholestasis	0	00	0	00	5	55.6	2	18.1	0	0

**Table 2:** The distribution of cases based on age of the victims

		<u> </u>
Age group (in years)	No. of cases	Percentage
0 - 15	2	5.4
16 - 30	25	67.6
31 - 45	9	24.3
>45	1	2.7
Total	37	100

**Table 3:** The distribution of cases based on Total body surface area involved in burn victims

Total burn body surface area (in %)	No. of cases	Percentage
<50	1	2.7
51-60	1	2.7
61-70	12	32.5
71-80	3	8.1
81-90	14	37.8
91-100	6	16.2
Total	37	100

victims and attempted to infer the relation of pathological findings in the study with the survival period of the victims. Additionally special Reticulin staining was also done using Gomori's Silver Impregnation method<sup>5</sup> to demonstrate reticular fibers and for better visibility of the actual extent of necrosis of liver tissues and their correlation with the H&E stained tissues sections.

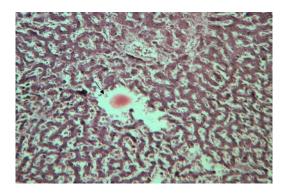
#### 3. Results

Grossly, the liver was slightly enlarged and congested with not much change in gross appearance in victims with survival period of less than 24 hrs. As the survival period increased, liver was markedly enlarged with tense, glistening capsule and rounded margins. The liver had a flabby, spongy consistency and was greasy to touch. The cut surface was yellow to pale yellow and in most cases 75.7 % (28/37) appeared mottled.

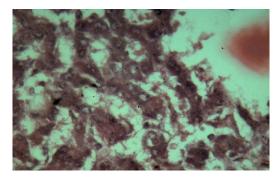
Microscopically, mild sinusoidal congestion was present in 50% (3/6) of victims with survival period of less than 24 hrs and moderate to severe in 85.7% (6/7) of victims who survived 2 to 3 days. Fatty changes of liver were present in various stages in victims with different survival periods [Tables 2 and 3]. Microvesicular steatosis were seen at focal places around centrilobular vein i.e., zone 3 in 42.8% (3/7) of cases that survived for 2 to 3 days; in victims with survival period of 4-7days although microvesicular steatosis was seen scattered all over the lobule in all cases, macrovesicular steatosis involved the major portion of the lobule in 77.8% (7/9) cases. Intrahepatic cholestasis was also found in 55.6% (5/9) victims. Thus as the survival period increased macrovesicular steatosis and fat cyst were observed; in victims with survival period of 8-15 days focal

/ confluent centrilobular hepatocyte degeneration/ necrosis is observed in 54.5% (6/11), while viable hepatocytes in periportal region showed macrovesicular steatosis in 100% (11/11) victims; in victims with survival period of 16- 30 days 50% victims (2/4) showed macrovesicular steatosis along with massive hepatocyte necrosis, the other two victims showed complete loss of lobular architecture, replaced by few fatty cyst and extensive necrosis. Special Reticulin staining was performed to examine the extent of loss of lobular architecture. Collapse of Reticulin fibers was even seen in liver of survival period of 3 days though at few places, indicating distortion of lobular architecture. Extensive necrosis was evident with Reticulin staining in cases with increasing survival period [Figures 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12]

### Photomicrograph: Liver of burn victim with survival period of less than 1 day(Figures 1 and 2)

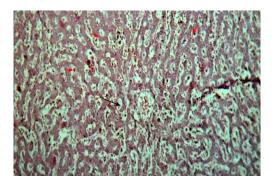


**Fig. 1:** H & E stained section of liver of burn victim with survival period of 1 day (100 x magnifications). It shows minimal sinusoidal congestion and central vein congestion (black arrow), while, the lobular architecture is intact.

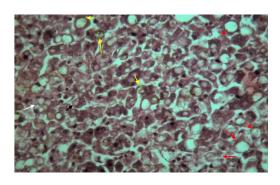


**Fig. 2:** H & E stained section of liver of burn victim with survival period of 1 day (400 x magnifications). It shows minimal sinusoidal congestion and central vein congestion, while, the lobular architecture is intact.

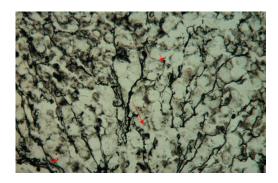
### Photomicrograph: Liver of burn victim with survival period of 2- 3 days(Figures 3 and 4)



**Fig. 3:** H & E stained section of liver of burn victim with survival period of 3 days (100 x magnifications). Shows extensive sinusoidal congestion (red arrow) and central vein congestion (black arrow) with lobular architecture disturbed at few places.



**Fig. 6:** H & E stained section of liver of burn victim with Survival Period of 7 days (400 x magnifications). Both microvesicular (black arrow) and macrovesicular (white arrow) type of steatosis and signet ring is seen (red arrow). Marked cholestasis within hepatocytes and kupffer cells (yellow arrow) is present.

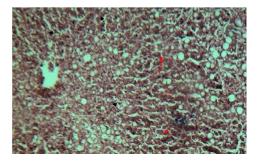


**Fig. 4:** Reticulin stained section of liver of burn victim with survival period of 3 days (400 x magnifications). Shows collapse of Reticulin strands (red arrow) at few places corresponding to an area of hepatocyte necrosis.

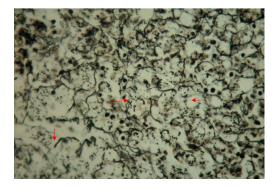


**Fig. 7:** Reticulin stained section of liver of burn victim with Survival Period of 7 days (100 x magnifications). Shows collapse of Reticulin strands (red arrow) around the central vein corresponding to an area of hepatocyte necrosis.

### Photomicrograph: Liver of burn victim with survival period of 4-7 days(Figures 5, 6, 7 and 8)

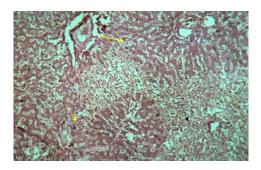


**Fig. 5:** H & E stained section of liver of burn victim with survival period of 7 days (100 x magnifications). Shows fatty infiltration of both microvesicular and macrovesicular type involving whole of the lobule. Focal necrotic areas are also seen in centrilobular region (black arrow). Few viable hepatocytes are seen in mid zonal region (red arrow).



**Fig. 8:** Reticulin stained section of liver of burn victim with Survival Period of 7 days (400 x magnifications). Shows collapse of Reticulin strands (red arrow)

### Photomicrograph: Liver of burn victim with survival period of 8- 15 days(Figures 9 and 10)

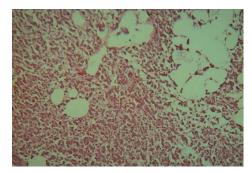


**Fig. 9:** H & E stained section of liver of burn victim with Survival Period of 10 days (100 x magnifications). Shows marked hepatocyte necrosis in centrilobular region (black arrow) with viable hepatocytes (yellow arrow) at periportal region and macrovesicular type of steatosis at places.

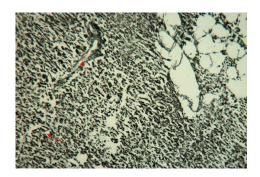


**Fig. 10:** Reticulin stained section of liver of burn victim with Survival Period of 10 days (100 x magnifications). Shows collapse of Reticulin strands (red arrow) around the central vein corresponding to an area of hepatocyte necrosis with viable hepatocytes at periportal region (yellow arrow).

### Photomicrograph: Liver of burn victim with survival period of 16-30 days (Figures 11 and 12)



**Fig. 11:** H & E stained section of liver of burn victim with Survival Period of 28 days (100 x magnifications). Shows extensive necrosis of hepatocytes with complete loss of lobular architecture (black arrow).



**Fig. 12:** Reticulin stained section of liver of burn victim with Survival Period of 28 days (100 x magnifications). Shows complete collapse of Reticulin strands (red arrow) corresponding to complete loss of lobular architecture.

#### 4. Discussion

Burn injuries occur universally and have plagued mankind since antiquity till the present day. In all societies including developed or developing countries, burns constitute not only medical and psychological problem, but also has severe economic and social consequences to the victims and also to their family and society in general.<sup>6</sup>

In this present study, fatty infiltration in the liver were present at various stages i.e. microvesicular steatosis to macrovesicular steatosis, followed by fatty cyst in victims with survival periods ranging from 2 days to 30 days. Thus as the survival period increased, the proportion of involvement of the hepatic lobule with macrovesicular steatosis and fat cyst markedly increased. Earlier studies conducted have also reported 80% of burn victims with fatty infiltration of the liver. 7 In victims with greater survival period (8-15 days), focal / confluent centrilobular hepatocyte necrosis was seen in 54.5% victims and massive hepatocyte necrosis to complete loss of lobular architecture was noted in cases belonging to the survival period of 16- 30 days. Bardeen<sup>8</sup> had described focal degeneration in the liver in autopsied cases of extensive burns, whereas many other studies have. 9,10 reported liver necrosis in 10% to 20% of the burn autopsies in their pathological studies. Jeschke et al. also reported Liver damage associated with increased hepatocyte necrosis in autopsied burn victims. 11 Histopathological findings of Liver in a study conducted on rats also showed inflammatory process in all periods investigated and hepatocyte degeneration added to increased amount of connective tissue 14 d post injury. <sup>12</sup> In our study, intrahepatic cholestasis was observed in 55.6% victims, while the study conducted by Linares et al. reported only 26% of the burn cases with intrahepatic cholestasis in. 10,13

### 5. Conclusion

So the present study reflects hepatic dysfunction in the form of hepatic steatosis, leading to hepatocyte necrosis and latter complete loss of liver architecture with increasing survival period of burn victims from 2- 30 days. Therefore, stress is laid upon re-evaluation of existing management protocol of burn victims, to give emphasis upon the maintenance of liver integrity and function, crucial for post burn survival.

### 6. Acknowledgements

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### 7. Conflicts of Interest

The authors have no conflict of interest to declare.

### 8. Source of Funding

None.

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