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ORIGINAL ARTICLE

Anatomical and Clinical Study of Liver Steatosis Severity as a Predictor of Sudden Unexpected Death in Metabolic Syndrome

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ABSTRACT

Background: Metabolic syndrome is a disorder that impacts on several organ systems and liver steatosis has risen as a possible marker of more profound metabolic damage. Knowledge on whether the severity of steatosis is a predictor of sudden unexpected death could help to elucidate the relationship between the liver and the heart in a case of advanced metabolic disease. The paper has analyzed the clinical and anatomical value of steatosis severity in postmortem cases, whose findings can be used in preventive medicine and in autopsies.

Methodology: The analytical clinico-anatomy research was carried out between January 2022 and January 2023 in Khairpur Medical College, Khairpur Mir's. Eighty two consecutive cases of medico-legal autopsies that met diagnostic criteria of metabolic syndrome were included. Demographic data, microscopic liver and cardiac, and comprehensive histopathological were noted. They were statistically compared, correlated and odds ratios to determine the relationship between the severity of steatosis and sudden unexpected death.

Results: Severe steatosis was much more prevalent with sudden death cases and was characterized by increased grades of inflammation, advanced stages of fibrosis, and increased chances of steatohepatitis. The same pattern was observed in cardiac abnormalities which included increased heart weight, left ventricular hypertrophy and myocardial fibrosis where there was a close association with the severity of hepatic injury. Severe steatosis was a predictive factor of sudden unexpected death ($p < 0.001$), and there was also evidence that showed that liver pathology and cardiac remodelling were connected through a common metabolic pathway.

Conclusion: The severity of liver steatosis is a valuable anatomical predictor of people with metabolic syndrome that could be prone to sudden unexpected death. These results underscore the importance of steatosis assessment in clinical prevention and forensic studies in which early detection of severe hepatic involvement can be used to emphasize individuals with high risk.

Keywords: Liver steatosis, metabolic syndrome, sudden unexpected death, myocardial fibrosis, preventive medicine, forensic autopsy, cardiac remodeling.

INTRODUCTION

Metabolic syndrome has become a significant health issue in the world today, and its prevalence is on the increase in both developed and developing societies. The disease unites a group of metabolism abnormalities centrally located obesity, dyslipidemia, hypertension, and insulin resistance that affect multiple organ systems at the same time. Hepatic steatosis is one of its presentations and has received specific interest due to its frequent occurrence as well as the possibility of being used as an indicator of systemic dysfunction. Towards the end of 2022, the relationship between metabolic liver disease and cardiac structure started to gain more and more research interest, indicating that the impact of steatosis might be even greater than on the liver itself[1-3].

Sudden unexpected death is one of the most difficult medico-legal and clinical situations, which may happen any moment, and in people who did not have previous cases of severe cardiac disease. Within the framework of the metabolic syndrome, minor anatomical and pathologic alterations can be piled up over the years, leaving environments conducive to life-threatening arrhythmias or cardiovascular failure. Knowledge of the most appropriate markers that most effectively indicate this vulnerability may be valuable as it relates to the clinic, as well as forensic experts[4-7].

Liver steatosis provides such possibility. The metabolic strain is manifested by structural and functional changes in the liver as fat accumulation occurs in hepatocytes. It seems that this burden is closely related to the cardiac remodeling processes, such as the hypertrophy and fibrosis, which can precondition the sudden death. Although the relationship has been increasingly of interest, there has been little evidence of the relationship using autopsy methods to quantify the relationship between the severity of steatosis and outcomes in terms of death[8-10].

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This research was thus intended to explore the possibility of the extent of hepatic steatosis as a significant predictor of sudden unexpected death in people with metabolic syndrome. Clinical data, gross anatomical observations, and detailed histopathological evaluation were combined to clear up the anatomical links on which this risk was based and to advance to a more detailed understanding of how metabolic diseases develop.

METHODOLOGY

This is an analytical clinico-anatomical investigation using the autopsy data and histopathology and clinical data to determine whether the severity of liver steatosis could be used to predict sudden unexpected death in patients with metabolic syndrome. The tests were conducted in Khairpur Medical College, Khairpur Mir's, between January 2022 and January 2023. However, in spite of the fact the study was carried out on postmortem material, the anatomical indicators of assessment, especially liver and heart changes, are also applicable to preventive medicine, as such abnormalities can be identified in the abdomen of people at risk.

All study period medico-legal autopsy cases of individuals aged ≥18 years meeting accepted criteria of metabolic syndrome (ATP III/IDF definitions up to December 2022) who were deceased were considered. There were 82 successive cases that met these requirements. This was done to exclude cases which had advanced decomposition, chronic liver disease, which did not cause steatosis, surgery on the liver before, poisoning or incomplete records in order to maintain accuracy.

The medico-legal documentation, the hospital/family record of the patient, where present, provided demographic information, metabolic risk factors (hypertension, diabetes, dyslipidemia, BMI, waist circumference), and circumstances of death.

A standard forensic autopsy procedure was undertaken. The liver was evaluated in terms of weight, size, and appearance whereas, the heart was evaluated in terms of weight, left ventricular thickness, coronary narrowing, and myocardial fibrosis.

These operations were in line with accepted forensic and pathology standards issued until December 2022.

The liver and cardiac tissue samples were fixed and processed and analyzed under a microscope. as mild (<33%), moderate (33–66%), or severe (>66%) were used to rate steatosis. There was inflammation, fibrosis (0–4), and steatohepatitis. Myocardial fibrosis and arrhythmogenic substrates cardiac slides were examined. All the slides were assessed by two independent histopathologists with any disagreements settled by consensus. Sudden unexpected death was also referred to as a natural death that happened during one hour of the onset of symptoms of a natural death or an unwitnessed death of a person that was last seen alive and well within a 24-hour period, which is in line with the forensic standards.

Continuous variables were represented as mean SD, and the categorical variables as frequencies. Group comparisons were done using independent t-tests and chi-square. Pearson coefficient was used to test correlations and odds ratios with 95% confidence interval to test predictive strength. The p-value below0.05 was taken as significant.

RESULTS

No significant age or gender variations were found in the sudden and non-sudden death groups in the demographic profile and this depicts similar baseline factors. But metabolic pointers including BMI, waist circumference, diabetes, hypertension, and dyslipidemia were found to be much more prevalent among the people who died suddenly. This trend indicates that a greater metabolic load can force the subject to an even more unstable physiological condition, which makes them clinically significant in prevention and forensic interpretation.

Gross examination demonstrated how among sudden deaths, the livers were considerably heavier and fatter. Markedly higher were hepatomegaly and greasy, pale surfaces common to this group which is indicative of a significant amount of lipid storage. These results highlight that progressive hepatic steatosis cannot simply be regarded as an incident, but it could indicate a greater physiological risk that is in tandem with lethal metabolic instability.

Microscopic evaluation revealed that there was a clear trend of which more severe steatosis, increased inflammation, and advanced fibrosis was closely linked with sudden death. There was also more prevalence of steatohepatitis, which implies that the liver was still being damaged but not just accumulating fat. These are some of the microscopic observations confirming the notion that progressive hepatic microscopic is a contributor of systemic susceptibility and could be an attractive alarm signal in preventive clinical assessment.

The changes in the structure of the heart were highly congruent with hepatic pathology. Cases of the sudden deaths showed increased weight of the heart, left ventricular thickening and myocardial fibrosis that was significantly more. Such discoveries indicate a consistent pattern of liver-heart injury, and they go in line with the new evidence that cardiac remodeling is accelerated by extreme metabolic stresses and leads to the high probability of fatal arrhythmias.

Table 1. Demographic and Metabolic Characteristics (n = 82)

Variable	Sudden Death (n=41)	Non-Sudden Death (n=41)	p-value
Age (years), Mean ± SD	46.2 ± 11.4	45.1 ± 10.8	0.62
Gender (Male), n (%)	29 (70.7%)	27 (65.8%)	0.64
BMI (kg/m²), Mean ± SD	33.8 ± 4.6	30.1 ± 4.1	0.001
Waist Circumference (cm)	108.4 ± 11.2	101.2 ± 10.7	0.003
Hypertension, n (%)	30 (73.1%)	22 (53.6%)	0.048
Diabetes Mellitus, n (%)	27 (65.8%)	18 (43.9%)	0.039
Dyslipidemia, n (%)	32 (78.0%)	21 (51.2%)	0.007

The severity of steatosis was found to be a good predictor of sudden unexpected death, and severe steatosis was found to contribute to sudden unusual death by close to five times. Correlations revealed that liver pathology deterioration was associated with cardiac fibrosis, which proved that there is a common metabolic pathway leading to sudden collapse. These correlations reinforce the clinical case that it may be possible to determine those at a higher risk in order to assess the severity of steatosis at the time of autopsy or in living patients.

Table 2. Liver Gross Anatomical Findings

Variable	Sudden Death	Non-Sudden Death	p-value
Liver Weight (grams), Mean ± SD	1760 ± 340	1505 ± 310	0.002
Hepatomegaly (yes), n (%)	31 (75.6%)	19 (46.3%)	0.006
Pale/Yellow Fatty Appearance	35 (85.3%)	22 (53.6%)	0.001

Table 3. Histopathology (Steatosis Severity and Injury Markers)

Variable	Sudden Death	Non-Sudden Death	p-value
Severe Steatosis (>66%)	28 (68.3%)	11 (26.8%)	<0.001
Moderate Steatosis	10 (24.4%)	17 (41.5%)	0.09
Mild Steatosis	3 (7.3%)	13 (31.7%)	0.004
Inflammation Grade (0–3)	2.1 ± 0.7	1.4 ± 0.6	<0.001
Fibrosis Stage (0–4)	2.3 ± 1.0	1.5 ± 0.9	0.002
Steatohepatitis (yes)	21 (51.2%)	10 (24.3%)	0.01

Table 4. Cardiac Anatomical Findings

Variable	Sudden Death	Non-Sudden Death	p-value
Heart Weight (grams)	455 ± 72	392 ± 65	<0.001
LV Wall Thickness (mm)	15.4 ± 2.1	13.2 ± 1.9	<0.001
Coronary Stenosis ≥50%	26 (63.4%)	18 (43.9%)	0.07
Myocardial Fibrosis (%)	12.3 ± 4.2	8.1 ± 3.9	<0.001
Arrhythmogenic Substrate	18 (43.9%)	9 (22.0%)	0.03

Table 5. Predictive Indicators of Sudden Death

Variable	Sudden Death	Non-Sudden Death	p-value
Severe Steatosis as Predictor (Odds Ratio)	OR = 4.75		<0.001
Correlation: Steatosis vs Myocardial Fibrosis	r = 0.52		<0.001
Correlation: Liver Weight vs Sudden Death	r = 0.41		0.002

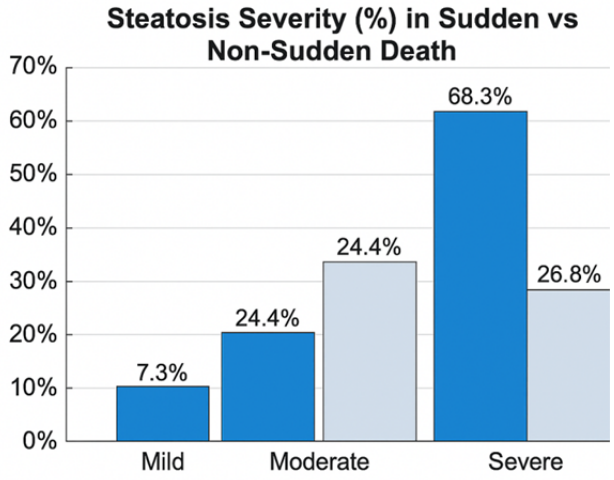

Figure 1. Comparison of steatosis severity between sudden and non-sudden death groups. The sudden death group showed a markedly higher proportion of severe steatosis (68.3%) compared with the non-sudden group (26.8%), while mild steatosis was notably more common in non-sudden deaths. The pattern suggests that increasing steatosis severity is strongly associated with sudden unexpected death in individuals with metabolic syndrome.

DISCUSSION

The present study examined the anatomical and clinical association between the severity of liver steatosis and sudden unexpected death in patients with metabolic syndrome. The results revealed one distinct and homogenous trend, namely, severe hepatic steatosis levels, more advanced inflammation, and higher levels of fibrosis were significantly higher in individuals who died suddenly than those who died non-suddenly. The findings indicated that fatty liver disease is not just a coincidental metabolic feature, but it can be regarded as a quantifiable pathological determinant of increased susceptibility to unfortunate death situations[11-13].

There are a number of mechanisms that can be used to explain this association. Severe steatosis has been associated with being indicative of high levels of metabolic dysregulation associated with insulin resistance, low-grade-inflammatory chronicity, and lipid toxicity. Such pathways are capable of elevating myocardial structural alterations like fibrosis and myocardial hypertrophy, which was also more evident in the sudden death group. Similar results of increased myocardial fibrosis and thickening of the left ventricle helps prove that myocardial metabolic load is a contributor of downstream cardiac remodeling to establish an arrhythmogenic substrate and predisposes to sudden cardiac arrest. The correlations that were observed during the research support an increasing body of evidence concerning the fact that metabolic syndrome is a multisystem stressor, with the liver-heart axis being in the center stage[14-16].

The autopsy findings of the gross anatomy further give more clinical information. Markedly enlarged, fatty livers were greatly more prevalent in sudden death cases, and is consistent with previous imaging-based studies, and autopsy studies. Likewise, the observed rise in weight of the heart as well as the left ventricular thickness is similar to patterns of metabolic cardiomyopathy. These findings combined underscore the fact that the hepatic and cardiac anatomic markers add to risk prediction. In practice, the extent of fatty liver infiltration (measured either by imaging or biopsy) can be a convenient measure that clinicians use to determine the high-risk population of people with the metabolic syndrome[17-19].

Even though the findings reinforce the investigation of systemic metabolic injury, the research is limited. Incomplete clinical histories also may influence the autopsy-based studies and a part of the confounding factors, including lifestyle exposures, are impossible to fully regulate. However, the same statistical correlations and correspondence with the previous literature give credibility to the results. Future studies that would use prospective clinical cohorts and biomarker mapping would be useful in verifying the predictive value of steatosis severity and elucidate its mechanistic associations with sudden cardiac death[20].

CONCLUSION

Severe steatosis of liver proved to be a strong anatomical and clinical indicator of abrupt demise in people with metabolic syndrome. Advanced hepatic fat buildup combined with increased levels of inflammation and higher stages of fibrosis were very well correlated with major cardiac defects including higher heart weight, left ventricular hypertrophy, and myocardial fibrosis. The findings indicate the need to estimate the severity of liver steatosis as an extension of routine assessment of high-risk metabolic patients. Early detection of severe fatty liver disease can also provide an opportunity as it is a valuable idea to detect people at high risk and preventative measures, which could avoid sudden deaths.

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