POST-MORTEM DIAGNOSIS OF ISCHAEMIC HEART DISEASE FROM GROSS MORPHOLOGICAL, HISTOPATHOLOGICAL AND BIOCHEMICAL CHANGES

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ABSTRACT

BACKGROUND

Among the unexpected and undiagnosed sudden deaths, incidence of Ischaemic Heart Disease (IHD) is very high. Appearance of characteristic morphological and histopathological changes in the myocardium due to IHD is often delayed. As such, opining as to the cause of death at autopsy also becomes very difficult. The objective of the present study is to evaluate the role of gross morphological, histopathological and biochemical (Cardiac Troponin I) parameters in ascertaining the cause of death to IHD.

MATERIALS AND METHODS

The present study was a prospective study carried out on a total of 63 consecutive bodies received for post-mortem examination with the history of sudden deaths. After opening the thoracic cavity, blood sample was collected from the cardiac chambers and used for cardiac Troponin I level estimation. A thorough gross examination was done in all the cases and tissue bits from representative sites were histopathologically evaluated.

RESULTS

Out of the total 63 cases, 38 had past history suggestive of IHD. Characteristic gross morphological changes were found only in 58% of cases whereas with the addition of histopathological findings 84% cases could be diagnosed. Cardiac Troponin I level was elevated i.e. tests positive in all the 38 cases with history suggestive of IHD whereas the remaining 25 cases without prior history of IHD were found to be negative.

CONCLUSION

Estimation of serum Cardiac Troponin I levels has been found to be a very useful and sensitive marker of early ischaemic damage to the heart particularly when there is lack of gross morphological and histopathological findings. This could be a significant diagnostic parameter coupled with gross morphological and histological changes in sudden deaths relating to IHD.

KEYWORDS

Histopathology, Ischaemia, Gross Morphology, Cardiac Troponin I, Post-mortem, Sudden Death.

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BACKGROUND

Sudden unexpected deaths have always raised suspicion of foul play, even when the case happens to be a natural one. Such sudden deaths i.e. where death takes place within a period of 24 hours from the onset of symptoms, with the subject being apparently alright prior to the onset of events is not uncommon. Therefore, a thorough autopsy in such cases is highly essential to avoid undue murder charge being brought against an innocent person.

Among the innumerable causes of sudden deaths, those due to Ischaemic Heart Disease (IHD) top the list and it is an ever-recurrent problem in Forensic Pathology to make an accurate diagnosis of IHD. This is especially because, the recognition of infarction by light microscopy using routine Haematoxylin-Eosin staining is possible only if death has occurred at least 6-12 hours after the onset of ischaemic injury.¹-³ Also, Myocardial Infarctions less than 6 hours old are usually not apparent either grossly or microscopically.¹-³ As such, demonstration of ischaemic damage to the heart can be a Herculean task particularly when the body is brought for autopsy within 12 hours of death, which most often is the case and thus gross & Histopathological changes in the Heart cannot solely be relied upon for the purpose of diagnosing early ischaemic damage. In addition to that the sensitivity and specificity of these modalities differ due to decompositional changes.⁴,⁵

However, several biochemical markers have been found to considerably reduce this lag and offer variable degree of sensitivity and specificity. Among them, cardiac troponins
have been analysed by various authors.\(^5\) The present study aims at evaluating the significance of one such biochemical marker, Cardiac Troponin I in diagnosing early myocardial ischaemia at autopsy.

The study was carried out on all the cases of sudden deaths brought for medicolegal autopsy to the mortuary of M. K. C. G. Medical College Hospital, Brahmapur, Odisha, India, over a period of two years from July 2015 to June 2017. A total of 72 consecutive cases of sudden deaths were subjected for autopsy within 12 hours of death during the period. 9 cases were discarded in whom there was history of hypertension/>30% burn/sepsis/CPR with cardiac contusion to avoid the interference in enzyme level due to cardiac stress. The remaining 63 cases constituted the study group. The study group was again divided into two groups (a) cardiac related death- 38 cases, in whom there was past history of cardiac pain and/or previous investigative findings suggesting myocardial ischaemia and (b) non-cardiac deaths – 25 cases and were considered as the control group.

At autopsy, after thorough external examination and opening of the body, first 5 mL of blood was collected from the chambers of the heart by using sterile syringe. Serum was separated out by centrifugation to prevent haemolysis. The serum thus separated was sent for Cardiac Troponin I estimation using the double sandwich paper immuno-chromatographic assay method. The results obtained were recorded in a semiquantitative manner based on the colour intensity. A thorough and careful gross examination of the heart was done and the following findings were recorded in each case such as size, weight, colour changes, presence of a whitish fibrotic patch or haemorrhagic areas, etc. before opening the heart. This was followed by dissection of the heart and study of features like Left Ventricular Hypertrophy (LVH), Atherosclerotic changes in the coronary vessels with the degree of narrowing of vessels (LVH), Atherosclerotic changes in the coronary vessels with the degree of narrowing of vessels, etc. Thereafter, 2 to 3 mm thick sections of the myocardial tissue from suspicious sites were collected and fixed in 10% neutral buffered formalin & were subjected to histopathological study using Haematoxylin-Eosin (H-E) staining technique. The histopathological changes were evaluated twice in each case in a blinded fashion to avoid biasing and recorded.

For convenience of study, the gross morphological and histopathological changes in the heart were categorised as No change, Mild changes, Moderate changes and Severe changes basing upon the following features:

For gross morphological Study:
- No Change: Size and weight normal (250 g - 350 g), no changes.
- Mild changes: Size increased, weight >350 g - 400 g, no LVH, Mild pallor.
- Moderate changes: Size increased, weight > 400 g - 450 g, LVH present, mild atherosclerotic changes in the vessels, 25%-50% narrowing of coronary artery, old fibrotic patch present, single or double vessel involvement.
- Severe Changes: Size grossly increased, weight >450 g, gross LVH, gross atherosclerotic changes in the vessels, >50% narrowing of coronary artery, fibrotic patch with haemorrhagic zone, triple vessel involvement.

For Histopathological Study:
- Earliest change, <½ hr. = Normal histopathology.
- Early changes, <24 hrs. = Coagulative necrosis/waviness of fibres at the borders, neutrophilic infiltration.
- Later changes, 1–7 days = Disintegration of myositis, phagocytosis, macrophages, and oedema.
- Late changes, >7 days = Granulation tissue with fibrosis.

RESULTS

In 62 (98.4%) cases of sudden death in the test & the control group, autopsy was conducted between 5-12 hours of death with 21 (33.33%) cases of these being subjected to autopsy within 8 hours following death. (\(P=0.91\)). (Table-1).

The gross morphological study of the myocardium in the Test group reveals no change in 16 (42.2%) cases. Gross evidence of ischaemic damage was noticed in 22 (57.8%) cases, of which majority 16 (42.2%) showed mild changes only. Mild morphological changes in 3 (12%) cases were found in the Control group as well. (\(P=0.003\)). (Table-2). A significant association was found between ischaemic damage to myocardium and gross morphological findings.

Histopathological study using H-E staining showed later changes in majority (23) (60.5%) of the cases among the Test group and no changes at all in 9 (23.68%) cases. Early and late histopathological changes were detected in 4 (10.5%) and 2 (5.2%) cases respectively. In the control group, histological change was not detected in all the 25 cases. (\(P<0.00001\)). (Table-3). There is a very strong association between the ischaemic damage to heart and the degree of histopathological findings.

As far as accuracy of post-mortem diagnosis of ischaemic heart disease in the test group is concerned, in 22 (57.8%) cases, ischaemic damage to heart was detectable with study of gross morphology of heart alone. Similarly, with histopathology study of heart, the accuracy of diagnosis increased to 29 (76.3%) cases. Morphology coupled with histopathology enhanced the possibility of accurate diagnosis to 32 (84.2%) cases. In the remaining 6 (15.8%) cases, the diagnosis was still doubtful. However, serum Cardiac Troponin I levels were elevated in all the 38 (100%) cases of test group whereas not a single case of Control group showed positivity. (Figure 1 & 2).

### Table 1. Distribution of Cases among Test & Control Groups according to Approximate time Interval between Death and Commencement of Autopsy

<table>
<thead>
<tr>
<th>Time interval between Death &amp; Commencement of Autopsy</th>
<th>Test Group</th>
<th>Control Group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4 Hours</td>
<td>1 (2.6%)</td>
<td>1 (4%)</td>
<td>2 (3.17%)</td>
</tr>
<tr>
<td>5-8 Hours</td>
<td>11 (28.9%)</td>
<td>8 (32.0%)</td>
<td>19 (30.15%)</td>
</tr>
<tr>
<td>9-12 Hours</td>
<td>26 (68.4%)</td>
<td>16 (64.0%)</td>
<td>42 (66.66%)</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>25</td>
<td>63</td>
</tr>
</tbody>
</table>

\(x^2 = 0.1798 \ df =2, \ p \ value = 0.914045\).
<table>
<thead>
<tr>
<th>Gross Morphological Changes</th>
<th>Test Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Earliest Change</td>
<td>16 (42.1%)</td>
<td>22 (88.0%)</td>
</tr>
<tr>
<td>Early Changes</td>
<td>16 (42.1%)</td>
<td>3 (12.0%)</td>
</tr>
<tr>
<td>Later Changes</td>
<td>4 (10.5%)</td>
<td>0</td>
</tr>
<tr>
<td>Late Changes</td>
<td>2 (5.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>25</td>
</tr>
</tbody>
</table>

Table 2. Distribution of Fatal Cases in the Test and Control Groups basing on Evidence of Ischaemic Damage in Gross Morphology

χ² = 13.74482, df = 3, p value = 0.003274.

<table>
<thead>
<tr>
<th>Histopathology</th>
<th>Test Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Change</td>
<td>9 (23.68%)</td>
<td>25 (100%)</td>
</tr>
<tr>
<td>Mild Change</td>
<td>4 (10.5%)</td>
<td>0</td>
</tr>
<tr>
<td>Moderate Change</td>
<td>23 (60.5%)</td>
<td>0</td>
</tr>
<tr>
<td>Severe Change</td>
<td>2 (5.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>25</td>
</tr>
</tbody>
</table>

Table 3. Distribution of Fatal Cases in the Test and Control Groups basing on Evidence of Ischaemic Damage in Histopathology

χ² = 45.254, df = 3, p value <0.00001.

Cardiac troponin I levels have been documented to be elevated within 3 hours of death and its level is very low or undetectable in non-cardiac causes of death. Therefore, we proceeded further with our study in an effort to measure the serum levels of the enzyme Cardiac Troponin I. Serum was preferred to other biological fluids owing to the fact that it is reasonably easy to collect, isolate, preserve & most often gives reliable results. But, some other authors prefer pericardial fluid for the purpose. Cardiac Troponin I was found to be elevated in all cases of the test group and was negative in all the cases of the control group making it the marker of choice to diagnose ischaemic heart disease. But, Burns J & co-authors in their study are in favour of the values of Creatinine Phosphokinase and its isoenzymes which are found to be raised in those who died of cardiac disease and were most discriminatory.

In the present study, when taken together both morphology and histopathology are diagnostic of IHD in 84.2% cases, whereas when taken alone they are helpful in 57.8% & 76.3% cases respectively. This finding is more or less in accordance with the study of others.

**CONCLUSION**

Diagnosis of IHD as the cause of sudden deaths at autopsy is always a challenging task. This becomes more apparent when autopsy is carried out in the early hours following...
death and at that time the gross and microscopic changes are not apparent. Cardiac Troponin I is a well-established enzyme marker that rises as early as 2 hours of myocardial injury. It was observed in the present study that the cardiac Troponin I was elevated in all cases of death with known prior cardiac ailment and the same was observed before definitive gross and histological changes appeared. And the enzyme level was not elevated even in a single case of death due to non-cardiac cause. Hence, the present study infers that detection of cardiac Troponin I levels in cases of sudden deaths will help either in confirming the cardiac cause of death or in ruling out the same.

REFERENCES


