ECG delineation techniques and applications in Cobra venom interacted patients

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Abstract-ECG signal provides a dynamic assessment of the cardiac activities. To analyze the ECG signal, some innovative ECG delineation techniques along with a few known techniques were used to provide the optimum strategy for marking of events. The techniques were applied on 125 records of CSE DS-3 database for calibration and subsequently, on the data acquired from no known-cardiac Cobra bitten patients under strict ethical protocol and medical supervision.

Cobra bite cases are commonly observed in India. The ECG morphology changes due to Cobra venom interaction may be attributed to the cardio-toxins present in the venom and their synergistic effect with other venom constituents. A study was conducted to observe relationship between cobra venom interaction and the ECG wave parameters changes. The study included patients, accidentally interacted with Cobra venom and with no known cardiac disease history.

This study provided significant visible effects of Cobra venom in the ECG waves and manifested some specific morphological changes.

I. INTRODUCTION

The ECG signal is susceptible to any change in physiology or psychology of the subject. Since the exploration of ECG, it has become a common tool for cardiac disease diagnosis. Because of its well-defined features, restricted frequency band and its affinity to the imaginary iso-electric zero potential reference, the ECG remained an apt signal for application of analog and digital signal processing tools for nearly fifty years [1].

The digitized ECG provides a facility to extract features automatically and help objectively in classification. Clinically, a number of morphological parameters have been standardized and disease specific groups of parameters have been identified [2]. Quest is still on for more applications of ECG in diverse areas. A number of studies have been undertaken amongst different races, populations, cardiac disease classes and non cardiac disease classes which may affect the ECG signal [3, 4].

However, venom interacted cases have yet not been considered for this type of study anywhere else. Probably, either because of rarity of accidental venom interacted cases or because of the emergent seriousness of the victims, which leaves little place for such studies. Reports of venom interaction have been published but with lesser interest on ECG morphology/processing and more on physiological manifestations [5, 6, 7, 8].

Cobra (Naja Naja, Linne, 1750) venom interaction is a common occupational hazard in India, due to widespread availability of Cobras in the rainy and harvesting seasons and their hazardous encounters with human beings often resulting in snakebite. A study has been undertaken with the objective of identifying the ECG changes observed in victims of Cobra venom accidental interaction. It was observed that certain morphological features in the victim’s ECG were beyond the textbook normal range, prior to any medication. However, with the course of medical management, these features indicated a return to normal trend.

II. DATA ACQUISITION

The CSE standards suggest simultaneous acquisition of all the leads for multiple point of view representation of cardiac events. A 16 bit commercially available ECG data acquisition system was employed for ECG recording of 10 second duration. The ECG signal was recorded at a sampling frequency of 500 Hz as per the CSE guidelines [9].

The system was kept ready as the arrivals of the victims of venom interaction were often sudden. Following a strict ethical protocol, in order to not to disturb or bias the medical management, ECG signal were obtained at the time of admission, during the course of treatment and at the time of discharge from the hospital. The supporting information of age and sex were obtained.

In the course of medical management, the condition of the victim is classified in one of the four severity grades of ‘mild’, ‘moderate’, ‘severe’ and ‘very severe’ envenomation. The severity grading of the patients depends on manifested symptoms, age and the delay in reaching the medical assistance [10]. From a large number of cases admitted for treatment, one from each grade, are being presented here, who

1. accompanied the remains of the biting species for confirm identification,
2. interacted venom accidentally and had no previous episode of snakebites,
3. had not received any medication which could also induce changes in ECG,
4. and had not been suffering with any cardiac disease or had no history of cardiac ailments.

ECG records of a “very severe” envenomation are shown at admission in Figure 1 and the Figure 2 at discharge.
The ECG signals were cleaned from the power-frequency interference using an adaptive notch filter, to preserve and divulge the diagnostic features. Subsequently, a syntactic wave detection and feature extraction methodology was applied. The wave detection methods were tested on Database DS-3 of CSE library for accessing their performance within the CSE tolerance limits.

III. QRS DETECTION

The QRS complex is the first event to be detected in the ECG signal. The QRS complex has the highest frequencies in the entire ECG biosignal with distinctively tall R wave preceded by a small q wave and often followed by S wave. A number of methods have been used for QRS detection with high degree of success, including amplitude slope criteria, ANN (99.3%), Wavelet (99.6%) and Spatial Velocity method [11, 12, 13]. The Spatial Velocity method was chosen due to its simplicity, apathetic response to noise and baseline wander. The Spatial Velocity was given as

$$SV_i = \sqrt{\frac{1}{12} \sum_{j=1}^{12} [2(x_{i,j+2} - x_{i,j-2}) + 6(x_{i,j+1} - x_{i,j-1})]^2}$$  (1)

Where,

\[ x_{i,j} \] is amplitude of \( i^{th} \) instance in \( i^{th} \) lead.

The Spatial Velocity method exploits the simultaneity of the 12 leads and suppresses all other but the high frequency components of the QRS complex [1]. So, the QRS complex remains the only visible activity in the entire ECG cycle. This method was applied on CSE Database DS-3 with 100% true detection rates.

The crisp QRS onset and offsets were detected with first and second derivative criteria in each lead. In a simultaneous twelve channel record, the onsets and offsets across all the leads in every beat were supposed to coincide. In order to find the most probable onset and offset, median QRS onsets and offsets, across all twelve channels, were detected for each complete beat in the entire length of 5000 sampling instants.

IV. T WAVE DETECTION

From the QRS offset, a T peak is searched and then its offset and onsets are identified. A non-horizontal ST segment often makes identification of T-wave onsets tricky. Clinically, T-onset may not be significant but the end of T-wave has to be identified carefully. A new method of Fiducial Segment averaging was used for T wave parameters identification assuming that the ST-T morphology would not change in the limited acquisition period of 10 seconds. This method averages serially all the post QRS wave segments to result in an average T wave [14]. This averaged wave contains less noise than the individual wave segments as the random noise signals are averaged out. This method was further improved with averaging the correlated parts of the segment.
The points, between the first QRS offset and second QRS onset, were selected as the initial fiducial segment in each lead. Correlation coefficient between the fiducial segment and the second corresponding wave segment, starting from nth sample was identified as under

\[ C_{i,n} = \frac{\sum_{i=1}^{M} Fid_{i,i}x_{i,i+n}}{\sqrt{\sum_{i=1}^{M} (Fid_{i,i})^2} \sqrt{\sum_{i=1}^{M} (x_{i,i+n})^2}} \]  

Where,

- \( C_{i,n} \) is the correlation coefficient at nth instant in ith lead,
- \( Fid_{i,i} \) is amplitude of ith instance in fiducial segment of ith lead
- \( x_{i,i+n} \) is amplitude of (i+n)th instance in ith lead, and
- \( M \) is the length of fiducial segment

The process was repeated till the segment with highest correlation was identified. An average of the two segments resulted in new fiducial segment. In subsequent segments, weighted averages were taken and a representative T wave was formed.

The onset and offset of this fiducial segment T wave were obtained with comparative ease and the fiducial T-wave segment was used as a wavelet for detection of T wave onset and offset in each individual beat.

The QRS onset and T offset were tried as the reference point for T wave measurement, but they were error prone due to baseline shift and possible presence of overlapping U wave, respectively. So, the T wave amplitudes were measured from the J point. The T wave amplitude was reported more in cases with depressed J point and resulted in reported reduction of T wave amplitude in some of the leads with recovery of J point.

V. P WAVE DETECTION

P wave precedes the QRS complex and has very low amplitude. Since the beginning of applications of computer techniques in ECG, P wave detection is a challenge [15]. Being prone to noise, its onset and offset identification is also complicated. It was observed that the P waves were more susceptible to noise than QRS complex and T wave, particularly in the chest leads. It was identified quantitatively that the noise content in QRS complex and T wave was less than the average noise level in the signal.

Probably, it is due to the fact that at the generation of QRS complex and T waves, a very large number of ventricular myocardial cells are involved and they make the biological ECG signal very strong compared to the distant muscle tremor signal from the apexes of the body. The resultant signal at the electrode input has a dominant fraction of ECG signal and a suppressed tremor noise. However, in case of P wave, the number of atrial myocardial cells is comparatively less and so the output ECG signal is very weak compared to the previously discussed ventricular ECG wave, and hence the suppression of the muscle tremor noise may not be so effective.

A comparatively higher noise level, smaller magnitude and varied onset and offsets of P wave in different leads make them more difficult to identify and locate correctly. The severity is enhanced when the subjects make shakier movements due to pain or neuromuscular complications.

Hence a number of methods were used to correctly identify the P-wave. These methods are

1. The Amplitude slope method [11]: The amplitude slope criterion is the oldest and a very reliable method, however, this method fails in the presence of baseline wonder and high frequency noise. This method had a true detection rate of 64.8% in CSE dataset-3.

2. Quiescent zone search method: The P wave has a preceding isoelectric zone. This zone should be flat and should have minimum deflection, if it is not a part of any wave. This can be ascertained by taking standard deviation in a window of 11 points at each instant in the entire wave as under.

\[ \sigma_{i,n} = \frac{1}{11} \sum_{i=n-5}^{n+5} (x_{i,i} - \bar{x})^2 \]  

Where,

- \( \sigma_{i,n} \) is standard deviation of nth instant in ith lead
- \( x_{i,i} \) is amplitude of nth instant in ith lead
- \( \bar{x} \) is the mean of amplitudes in the lead from n-5 to n+5 sample locations.

With the onset of the P wave, the deviation would be more than a specified adaptive threshold. This method is unaffected by evenly distributed power frequency noise but fails if the baseline wonder is extraordinary. This method yielded a true detection in 71.2% cases of CSE dataset-3.

3. Tendon method: Classical ECG strips present hemispherical P wave with x axis having 1 cm representing 0.4 seconds and on y axis 1 cm is equal to 1 mV. To match these proportions, the amplitude, on y axis, was scaled by dividing by 5 and sample number was taken on x axis. With these proportions, tendons (T) were drawn symmetrically around each instant and average tendon-length for each instance was calculated as under.

\[ T_{i,n} = \frac{1}{M} \sum_{i=1}^{M} (y_{i,m} - y_{i,me})^2 + (x_{i,m} - x_{i,me})^2 / 2i \]
4. Kurtosis method: Kurtosis is a measure of the peakedness of any distribution [16]. If any new instant does not contribute to the peaked shape of distribution, the Kurtosis of the instant would not be different than the previous one. This philosophy was employed to identify the P wave offset. When P wave onset was established with the above three methods, Kurtosis coefficient (K) at nth sample was given as

$$K_{l,n} = \frac{\sum_{i=P\text{-}onset}^{P\text{-}onset+n} (y_{l,i} - \bar{y}_{l,n})^4}{(n-1)\sigma_{l,n}^4} - 3$$

Where,

- $y_{l,i}$ is the amplitude at ith instant, lying between P wave onset and nth instant
- $\bar{y}_{l,n}$ is the mean of amplitudes between P wave onset and nth instant
- $\sigma_{l,n}$ is the standard deviation of amplitudes between P wave onset and nth instant.

With the onset of P wave firmly established, the kurtosis was used to find out the P wave offset. The sharp decline in Kurtosis coefficient was an indicator of the P wave offset with a true detection rate of 65.6% in CSE Dataset-3.

Because of the heterogeneity in advantages and disadvantages of each method, no single method was found suitable for P wave identification. Hence, all the methods were applied independently in all the twelve leads of each record. Median across all leads and methods were taken to minimize the detection error in onset and offset.

VI. U WAVE DETECTION

The U waves have been given the least importance amongst all the ECG wave features, till sometime ago. Probably it was due to its mystic appearance and amorphous origin [17]. A recent publication has tried to yield some more insights about the origins of U wave [18]. Validation of U wave presence/P-wave overlaps may call for revamping of automated ECG analysis systems. Identification of U wave may be error-prone if the baseline is assumed straight. In the presence of baseline wonder with frequency components around one Hertz, the iso-electric baseline may look curved and a false U wave would be identified.

A simpler technique was employed for U wave detection. A cubic Spline baseline estimation was made from the end of T wave to the next P wave onset. In the absence of U wave, the TP segment should match the cubic spline estimate uniformly, but the presence of a U wave would result in a non-uniform difference between the cubic spline estimate and the TP segment. The difference would gradually reduce on both sides. The U wave was indicated in cases where it had a distinguished appearance with the amplitude at least 33% of that of the T wave in the same beat.

VII. WAVE PARAMETERS OF COBRA BITE PATIENTS

The duration, segment, interval and amplitude parameters in all 12 leads of each beat were identified using the flowchart described above. Combination parameters like q/R or Corrected QT interval (The software was programmed to use Bazett’s formula except if the HR was less than 60 BPM [19]; it was programmed to report if corrected QT was more than 0.40 seconds) were also calculated for each beat. Median across beats was obtained for each parameter. The amplitudes, onsets and offsets of all the waves and the derived parameters made a large feature vector.

In order to identify the susceptible parameters, only those parameters were chosen that departed from the normal range either alone or in combination. It reduced the size of the feature vector. Out of twelve Cobra bite cases, only four cases, one representative of each severity grade, are being tabulated here. There was a marked similarity in a number of parameters in the representative cases, which departed from the normal range. These parameters with patient statistical data are reported in Table I.

VIII. RESULTS AND DISCUSSION

The morphological abnormalities in all the ECG waves indicated an enhancement of QTc and changes in ST-T patterns in all the four patients, uniformly. Some parameters with marked abnormalities, exhibited a return to normal tendency with treatment; but the presence of venom for longer duration in the body may lead to some permanent cardiac ailment due to the cardiotoxins present in the venom.

The same phenomena was observed in other Cobra bite cases as well, where ST-T depression and QTc interval elongation was observed initially, but in due course of medical management, they exhibited a return to normal tendency.

It was observed that

1. The QTc interval prolonged in almost all the cases,

2. Tachycardia was observed in severe and very severe envenomation case. It could have been oxygenation responsive, because Sp02 level was less than 95% in these cases.
### TABLE I

**PATIENT DETAILS AND THE ABNORMALITIES IDENTIFIED**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex/ Age</th>
<th>Delay after bite</th>
<th>Severity grade*</th>
<th>Lead</th>
<th>Abnormal parameters at Admission</th>
<th>Abnormal parameters at discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>F/25</td>
<td>2 Hrs</td>
<td>mild</td>
<td>All</td>
<td>QTc interval ^ 0.44Sec</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>V2</td>
<td>Q/R ^ 0.71</td>
<td>ST Shift -7.06µV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>V3</td>
<td>ST Shift -41.9µV</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>M/60</td>
<td>9 Hrs</td>
<td>moderate</td>
<td>All</td>
<td>QTc interval ^ 0.43Sec</td>
<td>QTc interval ^ 0.41Sec</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>V3</td>
<td>ST Shift -41.08µV</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>M/10</td>
<td>7 ½ Hrs</td>
<td>severe</td>
<td>All</td>
<td>QTc interval ^ 0.44 Sec</td>
<td>QTc interval ^ 0.43Sec</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>II</td>
<td>Q/R ^ 0.4</td>
<td>ST Shift -8.04µV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>III</td>
<td>Q/R ^ 0.79</td>
<td>ST Shift -64.71µV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T wave -124.54µV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>aVF</td>
<td>Q/R ^ 0.42</td>
<td>T wave -59.84µV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>V1</td>
<td>T wave -325.54µV</td>
<td>T wave -292.26µV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>V2</td>
<td>Q/R ^ 0.37</td>
<td>ST Shift -112.71µV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T wave -384.98µV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>V3</td>
<td>Q/R ^ 0.02Sec</td>
<td>ST Shift -227.63µV</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td>T wave -637.88µV</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>V4</td>
<td>ST Shift -106.06µV</td>
<td>T wave -104.2µV</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>V5</td>
<td>Q/R ^ 0.36</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>V6</td>
<td>Q/R ^ 0.46</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>F/33</td>
<td>17 ½ Hrs</td>
<td>very severe</td>
<td>All</td>
<td>QTc interval ^ 0.44Sec</td>
<td>PR interval 0.11Sec</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>II</td>
<td>ST Shift -99.4µV</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>III</td>
<td>ST Shift -65.17µV</td>
<td>T wave -28.8µV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>V1</td>
<td>ST Shift -82.6µV</td>
<td>ST Shift -17.03µV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T wave -78.93µV</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>V2</td>
<td>ST Shift -110.86µV</td>
<td>ST Shift -30.12µV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>V3</td>
<td>ST Shift -155.55µV</td>
<td>ST Shift -47.15µV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>V4</td>
<td>ST Shift -138.72µV</td>
<td></td>
</tr>
</tbody>
</table>

* (As adjudged by attending physician, based on victim's age, sex, delay and other symptoms)

3. ST segment depression in chest leads was more pronounced, compared to limb leads. The ST segment depression was more significant in the right side chest leads. Probably because of larger contact area in right ventricle than in the left for the circulating toxins.

4. In severe and very severe envenomation cases, PR interval shortened.

5. Q waves were observed in a few leads in chest leads (in the right side), mimicking infarction patterns but were reduced within their normal range following medication.
It was also observed that the patients were not given any specific medication for the cardiac abnormalities but the standard polyvalent ASV, corticosteroids, antihistaminic drugs and NSAID as per the attending physician’s prescription during the course of treatment.

IX. CONCLUSION

Venom interaction cases are very common in India with mortalities and morbidities. The Cobra venom affects the cardiovascular system and the heart. There are marked ECG morphological changes which are reversible, subject to a timely and proper medical management. The ST segment variations and Q waves are also observed in a number of leads and their reversal is indicative of non-stationary cardiac ailment.

This study is an attempt to attract attention towards a more detailed cardiovascular study of the venom interacted cases from medical point of view. It is anticipated that a study of effects of species specific venom on different biosignals would be highly useful for proper medical management of the victims, with the objective of assessment of quantitative variations.

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REFERENCES


