Postmortem clots (PMC) of the heart; is it merely an artifact or a predictor of cause of death?

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Abstract

Background: Post Mortem Clots (PMC) are considered as artifacts observed during forensic autopsies; hence, their medico legal importance has not been evaluated at length in the past. This study was designed with the intent of finding the association of age, gender, cause of death (COD) and postmortem interval (PI) with PMC formation.

Methods: Secondary data of all postmortems performed by the 1st author from June, 2015 to June, 2018 at Teaching Hospital Anuradhapura were extracted. Eligible autopsies were evaluated for the presence of PMCs in the heart. Length of the PMCs present was quantified as a percentage of the length of the cardiac chambers. Presence of PMCs varied according to the COD which were clustered based on their mechanism of death.

Results: The study evaluated 1259 autopsies with a median age of 56 years (IQR 40-67). PMCs were found in 46% of the subjects and showed a female predominance. The percentage of length of PMCs ranged from 20% to 100%. A higher rate of PMC formation was observed in natural and infectious causes, especially in the elderly. Traumatic causes with multiple injuries, heavy bleeding and a short agonal period showed less tendency of PMC formation. A higher duration of hospital stay/injury to death (>90 h) was associated with formation of PMC. PMC is not associated with PI while it's associated with increased age.

Conclusions: PMC is not a mere artifact but has significant medicolegal importance with regards to COD and time from injury to death.

Introduction

Postmortem clots (PMC) are frequently found during postmortem examinations and are easily recognized due to non-adherence to endothelial surface and their soft, gelatinous consistency [1]. Absence of lines of Zahn as seen in an ante mortem thrombi is also characteristic since PMCs are layered into two parts; as a surface layer of yellow plasma and a lower sediment layer of red cellular part [1]. This is an important feature that distinguishes a PMC from ante mortem clot (thrombus). Apart from this pathological identification, virtual autopsy techniques such as Computed Tomography (CT) combined with Magnetic Resonance Imaging (MRI) are also used in differentiating between arterial, venous ante mortem thrombi from postmortem clots [2, 3]. In the past, PMC were considered as mere artifacts in forensic studies and had no value in establishing the cause of death or mechanism of death [4]. But late researches indicate that PMC has a certain value in that they are not postmortem clots, but agonal thrombi which point toward prolong agony against sudden death [4]. It was also a known fact that asphyxia related deaths did not show any postmortem clots [5]. In another instance, some researchers have used this artifact to their advantage as an investigation medium. For example, the yellow plasma portion of PMCs has been used to detect antibodies for infective diseases such as Leptospirosis and also to measure ferrous concentration in cases of drowning [6, 7].

Current forensic practices in Sri Lanka may aid from using presence of PMC as a diagnostic tool to establish doubtful causes and mechanisms of death. Research on this area is scanty. Therefore, through this study, we aimed to find if age, gender, cause of death (COD) and postmortem interval (PI) had an association with PMC formation in postmortem subjects.

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Methods

This descriptive cross-sectional study was conducted at Teaching Hospital Anuradhapura, the Provincial General Hospital in the North Central Province of Sri Lanka. Approximately 1000 postmortem examinations are conducted annually in the hospital. The study was conducted for a period of three years from June 2015 to June 2018. All the medico legal autopsies performed by the 1st author were considered. Unascertained cause of death and unascertained time of death were excluded.

Data collection

Ethical approval to conduct the study was obtained from the Ethics Review Committee of Faculty of Medicine, Rajarata University of Sri Lanka. The consultant Judicial Medical Officer (first author) carried out data collection during each postmortem examination using data extraction sheets. All the autopsies performed by the 1st author during these three years were observed for the presence of PMC, postmortem interval and cause of death. If PMCs were present, its length was quantified as a percentage of the longitudinal length of the heart chambers (both atria and ventricles). Calculation of time since death was a major limitation as bodies were refrigerated after about 12 hours. Therefore, the cases were classified as refrigerated and non-refrigerated. Non-refrigerated postmortem interval is the time since death of fresh bodies. Refrigerated postmortem interval is the sum of duration before refrigeration of the body and the duration it was kept in the refrigerator.

For the purpose of analysis and presentation, cases were grouped according to causes of death which showed similar/ related underlying cause of death or mechanism of deaths. Deaths due to road traffic trauma were grouped as 'mainly head injuries' and 'mainly multiple bodily injuries'. All complications of chronic kidney diseases were placed in one group. When the cause of death was mainly due to bleeding, cases were grouped together. Drowning, hanging, traumatic asphyxia and strangulation were included in the "Asphyxia group" due to common mechanism of death. The majority of heart diseases were sectioned into three groups as myocardial infarction, ischemic heart diseases and heart diseases excluding myocardial infarction and ischemic heart diseases. All the bacterial infections were placed in a single group. When underlying COD is related to liver and the immediate COD was liver failure, they were grouped together. Poisoning related deaths were divided into three clusters depending on the substances such as Thevetia peruviana (Kaneru), organophosphate and other agrochemical poisoning. Owing to the nature of rapid deaths and crushed/stamping injuries seen in elephant attacks, they were grouped in to one. Train accidents were also placed in a single group due to rapid deaths, multiple severe injuries and minimum bleeding.

In data evaluation, all continuous variables PMC present and PMC absent groups were compared using t-test and categorical variables were tested using chi-square test.

Results

A total of 1259 autopsies were eligible for the study after applying the exclusion criteria. Table 1 shows the basic characteristics of the study sample including the postmortem interval and number of autopsies with postmortem clots. The majority of the autopsies were male and age ranged from 1 day to 95 years. Postmortem interval (PI) ranged from 3 to 5760 hours (240 days). Nearly half of the autopsies consisted with postmortem clots. The mean size of the PMC was 78.5% of right ventricular length (SD 35.4) and the minimum and maximum values were 20% and 100% respectively.

The presence and the absence of Postmortem clots were compared with postmortem interval (PI), sex and age of the participants. Table 2 and 3 summarizes the associations of PMC with PI, age and sex. Table 2 depicts that autopsies with lower PI and higher age have PMCs. Table 3 shows predominance among females to have PMCs.

Table 1. Basic characteristics of the sample

Characteristic	*Value*
Total autopsies	1259 (100%)
Sex	
Male	923 (73.3%)
Female	336 (26.7%)
Age	
<20	67 (5.4%)
21-40	243 (19.6%)
41-60	450 (36.3%)
60-80	427 (34.4%)
81<	53 (4.3%)
Post mortem interval (Non refrigerated)	
Median	7.2 hours
IQR*	6-10 hours
Post mortem interval (Refrigerated)	
Median	19 hours
IQR	17-23 hours
Post mortem clots	
Present	579 (45.9%)
Absent	680 (54.1%

** IQR-Interquartile Range*

Table 2. Association of PMC with PI, age

Category	*Mean (SD)*		*T value*	*P value*
	With PMC	*Without PMC*		
PI (Refrigerated)	7.6 (2.5) hr	7.7 (2.7) hr	0.46	0.64
PI (Non refrigerated)	66.7 (198.5) hr	103.5 (427.8) hr	1.39	0.16
Age (Refrigerated)	55.7 (18.6) Y	52.8 (18.3) Y	1.7	0.07
Age (Non refrigerated)	55.2 (19.1) Y	48.5 (20.7) Y	4.4	<0.000
H-hours, Y-years				

Table 3. Association of PMC with Sex

Gender	*Number*	*Chi-square*	*P value*
Male		8.2	0.004
With PMC	402 (43.6%)		
Without PMC	521 (56.4%)		
Female			
With PMC	177 (52.7%)		
Without PMC	159 (47.3%)		

Table 4 summarizes the association between COD and the presence of PMC. This explains that PMCs are higher in infectious causes and are less in other causes of deaths.

Table 4. Group of disease and presence of PMC

Group of diseases	*Number of Cases*	*% of PMC*
Road traffic trauma mainly to body	102	44.4
Road traffic trauma mainly to head	99	47.0
Burn	6	50.0
Malignant tumor	39	61.5
Chronic kidney diseases	44	56.8
Anaphylaxis	4	75
Bleeding	32	21.8
Shock lungs due to viral infection	3	33.3
Asphyxia	141	5.6
Hanging	75	5.3
Traumatic asphyxia	3	0
Manual strangulation	5	0
Drowning	45	4.4
Compression of neck	2	0

(Continued)

Group of diseases	*Number of Cases*	*% of PMC*
Asthma	13	46.1
Ischemic heart diseases	116	44.5
Bacterial infections	264	86.3
Liver diseases	26	23.0
Heart diseases excluding ischemic heart diseases and myocardial infraction	10	60
Agrochemical poisoning other than organophosphate and Kaneru (*Thevetia peruviana*)	19	52.6
Electrocution	5	0
Multiple injuries due to elephant attack	4	0
Epilepsy	6	66.6
Influenza	1	100
Kaneru (*Thevetia peruviana*) poisoning	9	0
Myocardial infarction	202	38.1
Organophosphate poisoning	50	26
Pancreatitis	3	66.6
Pulmonary embolism	6	16.6
Snake bite	9	55.5
Multiple injuries due to train accident	11	27.2
Spontaneous intracerebral hemorrhages	35	54.2

The database of road traffic accidents was analyzed for the duration of injury to death (agonal period). Table 5 summarizes the association of injury to death with presence of PMC. This shows that the higher duration of hospital stay/injury to death is associated with formation of PMC.

Table 5. Association of time since injury to death, with presence of PMC in road traffic accidents

Group	*Number*	*Median duration from injury to death (h)*	*P value*
With PMC	57	90	<0.000
Without PMC	101	2	

Discussion

This study was tailored to observe if age, sex and PI affected the tendency to develop PMCs in postmortem subjects and several key findings were demonstrated as follows. A variable tendency to develop PMCs was found among different groups of subjects depending on their CODs. Non- refrigerated autopsies with lower PI and a higher age showed presence of PMCs and there was predominance among females to have PMCs. In case of road traffic accidents, a higher duration of hospital stay/ injury until death was also associated with formation of PMC.

COD groups where PMCs were 100% absent included elephant attacks, electrocution, Kaneru (Thevetia Peruviana) poisoning, traumatic asphyxia and manual strangulation. Factors such as heavy bleeding, very short agonal period, chemicals or changes of the blood that inhibit or delay PMC formation could be some underlying causes for this observation even if they were not identified specifically in this study. Prior research had also shown that Alcohol has a negative effect on postmortem clot formation [8]. Therefore this could be a possibility. Yet, more research on PMC is necessary to identify the underlying mechanism of PMC formation, its promoting and inhibitory factors.

Another possible explanation suggested by previous research could be the short agonal interval seen in the causes of deaths. A longer dying process is known to cause a higher rate of PMC formation [9]. As evidenced by the research of Ross et al, few or no PMCs were found in postmortem CT angiography of deaths with a fast dying

process; and deaths with a longer, slower dying process were found to have PMCs in plenty[9]. In our study, only three out of eleven train accident cases showed PMCs and they each had a prolonged agonal period due to treatment at intensive care units or a ward setting. Therefore, it seemed that people who lived for a substantial period immediately after trauma, had some but not 100% filling cardiac chambers with PMC formation. Other CODs with a longer dying process, such as malignancy, anaphylaxis, infections, heart diseases (excluding ischemic heart diseases), epilepsy, pancreatitis, poisoning and envenomation, showed PMC in more than 50% of the cases. It is possible that other cofactors which predisposed to thrombosis even before death (Virchow's triad) were acting in the above circumstances and further studies are necessary to identify them in particular.

In medico legal practice, underlying COD is the important finding but one can have several mechanisms (immediate COD) of death. Therefore, in research purposes, major mechanism of death such as renal failure, heart failure, liver failure, exsanguination, and septicemia should be mainly considered with sub sections of underlying COD such as heart failure due to myocardial infarction, heart failure due to myocarditis or heart failure due to ischemic heart diseases. When closely related COD groups were analyzed, some showed a lower tendency for presence of PMC. Here, medico-legally important asphyxia group had the lowest percentage of presence of PMC (5.6%). Hanging, the most common COD showed PMC in 5.3% cases. This observation, however was contradictory to the general accepted concept "hanging deaths have no PMC" among medico-legal practitioners. The reason for the formation of PMC in these cases could be due to various mechanisms (immediate COD) of death operated in hanging cases such as vagal inhibition, arterial or venous compression and tracheal obstruction or the presence of comorbidities. Out of 75 hanging cases, only four cases had PMCs. As a result, according to this study, even if the data suggested that PMC formation was a possibility, it was a rare finding. Therefore it is safe to consider that PMC is unlikely to develop in hanging cases. However, not many evidence exists in published literature. Thus future research could solidify the explanation further.

Other COD groups which rarely showed PMC were bleeding, multiple injuries of body, Organophosphate poisoning and pulmonary embolism. However, when considering each case, they seemed to have other comorbidities which may have predisposed to PMC clot formation. For example, out of 45 cases of drowning, only 2 had PMC. One was complicated with fatty liver disease and the other was treated at the ICU before demise.

All the drowning cases were associated with a fresh water source and their respective postmortem studies revealed fresh water aspiration. Thus, a common factor inhibiting PMC can be suggested. Accumulation of water in lungs could lead to diffusion of water in to blood resulting in hemodilution. This in turn could result in an osmotic imbalance leading to bursting of red blood cells. Therefore, a reason for not observing PMCs could be because either hemodilution or bursting of red cells with releasing of chemicals was acting as inhibitory factors for PMC formation. Nevertheless, the 2 exceptions had other comorbid reasons promoting PMC which could have led to forming PMCs only in drowning cases with comorbidities. It should be noted that dry drowning or sea water drowning were not observed in this study. So, this could be a limitation to arrive at the above hypothesis and further observation is needed.

It should be emphasized that none of the COD groups showed 100% presence of PMC. Nevertheless, bacterial infection group contained some specific diseases which showed PMC in 100% of cases. All cases of meningitis, peritonitis, pyelonephritis and leptospirosis were among these. Additionally, most cases of septicaemia and pneumonia also showed presence of PMCs. This observation suggested not only the causative bacteria, but some other factors such as duration of agonal period or inhibitory factors such as medication in blood might also have some effect on formation of PMC.

As depicted in Table 1, Female subjects showed a significant predominance over males to develop PMCs. Previous literature lacks evidence regarding the exact cause. But our data suggested that most female subjects as well as the elderly have passed away due to natural causes as opposed to the younger and the males who mostly died of unnatural traumatic causes. Unnatural CODs such as fatal injuries, poisoning and asphyxia seemed to have a lower chance of developing PMCs. Previous studies conducted in vitro to test the effects of synthetic female sex hormones; progesterone and estrogen on blood coagulation, have identified an association with pathophysiological clot formation due to aberrant erythrocyte and clotting factors interaction [10]. It was found that progestins had influenced the rate of clot formation in whole blood samples but the influence of female sex hormones on postmortem blood was never investigated [10]. If such a relationship was observed, this could also be another plausible explanation as to why females had a higher tendency to develop PMCs.

As for future extension of this research, the causes of deaths that resulted in higher percentages of PMC need to be explored more extensively for its possible diagnostic value. All things considered, the mechanism of formation of postmortem clots is not yet fully understood. Prior research has come up with possible associations of longer agonal period, association of comorbidities and inhibitory factors such as alcohol, and the cessation of the fibrinolytic system. Few studies have hypothesized that existence of PMC is rare in cases of sudden deaths and have attempted to understand the underlying mechanism of fibrinolysis by means of immunoelectrophoresis[11]. But PMC promoting factors or the associated comorbidities that could promote or inhibit PMCs have not been studied as of yet and no satisfactory evidence were published.

Conclusion

This study depicted that non-refrigerated autopsies with lower PI and a higher age showed presence of PMCs and there was predominance among females to have PMCs. A higher agonal period was also associated with formation of PMC. When considering the COD, some showed PMC always and some never, suggesting that there may be underlying PMC promoting or inhibiting factors associated with the COD. If further research could be conducted to determine these factors, the presence or absence of PMC can be used as supportive evidence in establishing COD in future forensics studies.

Limitations

One significant limitation to the study was the prolonged and variable times the subjects were kept in a refrigerator under colder temperatures. Even if the raw data showed a significant relationship between PMC formation and PI, when refrigeration time was factored in, the data did not to show any association. Even in previous research, it has been shown that colder temperatures appeared to slow the process of postmortem blood coagulation. As evidenced by a study done to show effects of caffeine on post mortem coagulation, Leo et al showed that refrigerated blood, regardless of caffeine addition, had very little coagulation after 24 hours [12].

Conflict of Interests

All Authors declare that there are no conflicts of interest.

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