Zagazig University Medical Journal

Volume 27
Issue 3 *May, 2021*

Article 12

April 2021

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Mai Nouh Ahmed Abd EL Hai
*Department of Pediatric, Faculty of Medicine, Zagazig University, Zagazig, Egypt*, mainouh@zu.edu.eg

Amal Mohamed Abdellatif
*Department of Pediatric, Faculty of Medicine, Zagazig University, Zagazig, Egypt*,
amalabdelatif49@gmail.com

AL Shaymaa Ahmed Ahmed
*Department of Pediatric, Faculty of Medicine, Zagazig University, Zagazig, Egypt*,
alshaymahmed@yahoo.com

Hanan Sameer
*Clinical Pathology Department, Faculty of Medicine, Zagazig University, Egypt*, hananclpath@yahoo.com

Zagazig University Medical Journal
www.zumj.journals.ekb.eg

**Manuscript ID** ZUMJ-1909-1560 (R1)
**DOI** **10.21608/zumj.2019.17593.1560**

**ORIGINAL ARTICLE**

# Assessment the Value of Serum Copeptin Level in Dilated Cardiomyopathy in Pediatrics

**Amal Mohamed Abd EL-Latef [1], AL Shaymaa Ahmed Ali [1], Hanan Samir Ahmed [2] and Mai Nouh Ahmed Abd El-Hai [1]**

[1]Pediateric Department, Faculty of Medicine, Zagazig University, Egypt.
[2]Clinical Pathology Department, Faculty of Medicine, Zagazig University, Egypt.

**Corresponding author:**
Mai Nouh Ahmed Abd EL-Hai
Neonatology resident at Menia El-Qamh Central Hospital
mainouh88@gmail.com

**Submit Date** 2019-10-03
**Revise Date** 2019-10-12
**Accept Date** 2019-10-19

## ABSTRACT

**Background:** Dilated cardiomyopathy (DCM) is considered a potential reason for heart failure in children. Serum copeptin level is utilized as a marker in different cardiovascular diseases, where copeptin level was observed to be increased with increasing severity of cardiovascular diseases. This study aims to assess the value of serum copeptin level in dilated cardiomyopathy in pediatrics. **Methods:** The present study was a case-control study involved 25 cases diagnosed as dilated cardiomyopathy and 25 patients diagnosed as control group. All children included in this study were subjected to full clinical examination and laboratory investigations which include CBC, CRP, Renal Function Tests and serum copeptin level by ELISA. **Results:** There was statistical significance increase in CRP and copeptin among the studied groups. Regarding heart failure, 60% had acute HF and 48% were stage II according to Ross classification. Copeptin level significantly correlate with severity and outcome of dilated cardiomyopathy, so it increased in cases with acute HF and dead cases and decrease among cases that had Ross II HF. The sensitivity of copeptin at cutoff value of 11.06 in diagnosis of dilated cardiomyopathy was 100%, specificity was 100% and the accuracy was 100%. Our results show that the sensitivity of copeptin at cut off 36.13 in prediction of death was 83.3%, specificity was 88.9% and the accuracy was 88%. **Conclusion:** Copeptin marker has a clinical use in HF and elevation of their levels is correlated with severity of heart failure.

**Keywords:** Copeptin, dilated cardiomyopathy, heart failure, pediatrics

## INTRODUCTION

Cardiomyopathy is redesigning in the structure and function of the myocardium, which weaken myocardial performance and it is viewed as one of the hazardous health problems which causes clinical heart failure. Cardiomyopathies might be clinically analyzed in heart only or they might be identified with other non-cardiovascular diseases, in either cases they influence cardiovascular system and cause cardiovascular death or progressive heart-failure related inability [1].

Cardiomyopathy Previously was divided into "hypertrophic, dilated, and restrictive cardiomyopathies", but recently researchers are more interested in dividing it into anatomic designations (hypertrophic and dilated) and functional one (restrictive) [1]. Dilated cardiomyopathy (DCM) is the most well-known type in children and a potential reason for heart failure [2].

AVP, copeptin, and other vasopressinergic neuropeptides levels are raised in acute stress caused by pathological conditions, like cardiomyopathy which increment vascular congestion. Clinical utilization of AVP levels has numerous weaknesses. Copeptin can act as a replacement because of its molecular stability,

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easier testing methods, and faster results [3]**.** Copeptin is a 39-amino acid glycopeptide that includes the C-terminal part of the Arginine Vasopressin Precursor (CT-proAVP), it has been demonstrated to be stable, dependable and sensitive surrogate marker for AVP release and it is one of the most important hormones in the human body [4]. Copeptin levels can be effectively determined in an hour, perfect for both HF and emergency setting.

Copeptin assessment has been demonstrated to be of interest in a variety of clinical indications. Copeptin level was useful in different, clinical indications, including the diagnosis of diabetes insipidus and the monitoring of sepsis and cardiovascular diseases such as cardiomyopathy, heart failure, myocardial infarction, stroke and congenital heart disease [5]. Serum copeptin level is recently utilized as a marker in different cardiovascular diseases, where copeptin level was observed to be increased with increasing severity of cardiovascular diseases [6]. **I.**

This study aims to assess the value of serum copeptin level in dilated cardiomyopathy in pediatrics and to find if any relation is present between copeptin level and severity of heart failure in children who have dilated cardiomyopathy.

## METHODS

A prospective case-control study was carried out at Pediatric Department and Clinical Pathology Department, Zagazig University Hospitals in the period from December 2017 to September 2018. Approval for the study was obtained from the Research Ethics Committee, Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. All subjects have agreed to participate in the study and written consent was taken from their parents.

Fifty infant and children patients were incorporated into this investigation after taking written consent. They were divided into two ages and sex matched groups: Group I: involved 25 infant and children patients who act as patients with dilated cardiomyopathy. This disease is diagnosed by its characteristic findings on clinical examination and laboratory tests. Group II: includes 25 infant and children patients who serve as healthy control group.

**Inclusion Criteria**: Patients with Age from one month to 18 years old and the patients with proven DCM by echocardiography.

**Exclusion Criteria:** Patients who had any of the following conditions: Below one month or above 18 years old, have diseases with elevated copeptin level (renal diseases, congenital heart diseases, heart failure without cardiomyopathy, acquired heart disease, or rheumatic heart disease), 2ry Cardiomyopathy due to chronic diseases (end stage renal disease, chronic hemolytic anemia, and iron over load), other types of cardiomyopathies (hypertrophic CM, restrictive CM, and others), and patients who refuse to participate in the study.

All patients incorporated into this investigation will be exposed to the following:

**Full history taking including:**

- Personal history: Name, Age, Sex, birth weight, and length of disease.
- Complaint: Symptoms of heart disappointment (hack, dyspnea, repetitive chest contamination, hemoptysis, chest wheeze …).
- History of present diseases: Incidence of disease, duration of illness and anti-failure drugs received (number, types, doses and duration).
- Past history of disease, medication operation.
- Family history.

**. Full clinical examination:**

1. General examination: Level of consciousness, complexion, built and decubitus with attention to dysmorphic features, mentality, neuromuscular system, GIT, endocrine and renal system affection to detect any evidence of metabolic cause.
2. Vital signs: including temperature, heart rate, respiratory rate, blood pressure, edema, cyanosis, pallor or congested pulsating neck veins.

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3. Anthropometric measurements (weight, length and body surface area).
4. Assessment of heart failure severity according to ROSS classification [7].

**III. Laboratory investigations:**

Complete blood count (CBC) by Sysmex XN-2000 (Siemens, Japan): Hemoglobin concentration. Total leucocyticcountneutophils lymphocytes platelets count capsular reactive protein (CRP) by Cobas 8000 **(**Roche Diagnostics, Germany**),** and serum copeptin levels by enzyme-linked immunosorbent assay (ELISA) [8].

**IV. Statistical Analysis**

The collected data were computerized and statistically analyzed using SPSS program (version 18.0.) Qualitative data were represented as frequencies and relative percentages. Chi square test was used to calculate difference between qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent T test was used to calculate difference between quantitative variables in two groups in normally distributed data. Mann Whitney (MW) test was used to calculate difference between quantitative variables in 2 groups in not normally distributed data. Pearson correlation coefficient used to calculate correlation between quantitative variables.

Receiver operating characteristic (ROC) curve analysis was used to identify optimal cut-off values of different parameters with maximum sensitivity and specificity for prediction of the outcome. Accuracy is measured by the area under the ROC curve. An area of 1 represents a perfect test; an area of 0.5 represents a worthless test. The significance Level for all above mentioned statistical tests done. The threshold of significance is fixed at 5% level **(**P-value).

## RESULTS

The present study was a case-control study designed to assess the value of serum copeptin level in children who have dilated cardiomyopathy (DCM). We took 25 cases diagnosed as DCM at Cardiology Unit, Paediatrics Department, Zagazig University Hospitals and compared them with 25 healthy children.

Our results show that there were no statistical significance differences between the studied groups (cases and control) as regard to age, sex but there was statistical significance decrease in weight & BMI among cases group compared to control group. Also, 32% of the studied group (cases only) had +ve family history (Table 1).

The results exhibited that there was statistical significance increase in temperature, heart rate (HR), respiratory rate (RR) and systolic blood pressure (SBP) and decrease in diastolic blood pressure (DBP) among the studied groups compared to control (Table 2).

Our results appeared that the most frequent symptoms among cases were dyspnea and cough (100% & 32%, respectively) (Table 3). Our results recorded that the disease duration ranged from 1 to 43 months with mean 9.08 months. Regarding heart failure, 60% had acute HF and according to Ross classification 48% were stage II, 28% were III and 24% were IV (Table 3). Also, the data recorded in Table 3 shows that the hospital stays ranged from 1 to 15 day with mean 6.52 day. For improvement, 16 cases (64%) had rapid improvement while 6 cases (24%) were died.

Table 4 shows that there was statistical significance increase in both Copeptin and inflammatory marker C-reactive protein (CRP) among cases group compared to control.

Our results show that there was statistical significance increase in Copeptin level among cases had acute HF and dead cases and decrease among cases had Ross II HF (Figure 1).

Our results show that the sensitivity of copeptin at cut off 11.06 in diagnosis of cardiomyopathy was 100%, specificity was 100% and the accuracy was 100% (Table 5).

The results show that the sensitivity of copeptin at cut off 11.06 in diagnosis of dilated cardiomyopathy was 100%, specificity was 100 % and the accuracy was 100 % (Table 5). Our results show that the sensitivity of Copeptin at cut off 36.13 in prediction of death was 83.3%, specificity was 88.9% and the accuracy was 88%.

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**Table 1:** Demographic data of studied groups.

| Variable | | Cases (n=25) | | Control (n=25) | | MW/t | p |
|---|---|---|---|---|---|---|---|
| **Age: (Months)** | | | | | | | |
| *Mean ± SD* | | 11.6 ± 12.04 | | 9.56 ± 7.04 | | 0.13 | 0.90 |
| *Median (Range)* | | 8 (2.5 – 48) | | 7 (2 – 24) | | | NS |
| **Weight: (Kg)** | | | | | | | |
| *Mean ± SD* | | 6.03 ± 3.53 | | 8.08 ± 2.62 | | 2.33 | **0.02** |
| *Median (Range)* | | 6 (3.85-16) | | 8 (4 – 13) | | | ***** |
| **Height: (cm)** | | | | | | | |
| *Mean ± SD* | | 71.52 ±10.91 | | 70.88 ± 8.67 | | 0.23 | 0.82 |
| *Median (Range)* | | 68 (60 -100) | | 69 (58 – 86) | | | NS |
| **BMI: (Kg/m$^2$)** | | | | | | | |
| *Mean ± SD* | | 4.67 ± 1.69 | | 5.59 ± 1.25 | | 2.19 | **0.03** |
| *Range* | | 4.7 (3.1-8.2) | | 5.8 (3.5 – 7.6) | | | ***** |
| **Variable** | | **No** | **%** | **No** | **%** | $\chi^2$ | **P** |
| **Sex:** | | | | | | | |
| *Female* | | 11 | 44 | 7 | 28 | 1.39 | 0.24 |
| *Male* | | 14 | 56 | 18 | 72 | | NS |
| **Family history** | *+ ve* | 8 | | --- | ---- | --- | --- |
| | *- ve* | 17 | | | | | |

SD: standard deviation t: Independent t test $\chi^2$: Chi square test NS: Non significant (P>0.05)

**Table 2:** Vital signs among studied groups.

| Variable | | Cases (n=25) | Control (n=25) | t | p |
|---|---|---|---|---|---|
| **Temperature ($C^0$)** | *Mean ± SD* | 36.82 ± 0.66 | 36.44 ± 0.54 | **2.23** | **0.03 *** |
| | *Range* | 36 - 38 | 35.3 – 37.1 | | |
| **HR (beat/min)** | *Mean ± SD* | 143.28 ± 25.28 | 122.44 ± 12.22 | **3.71** | **< 0.001 **** |
| | *Range* | 120 - 190 | 105 - 150 | | |
| **RR: (breath/min)** | *Mean ± SD* | 50.8 ± 10.11 | 38.24 ± 6.65 | **5.19** | **< 0.001 **** |
| | *Range* | 37 - 70 | 29 - 51 | | |
| **SBP (mmHg)** | *Mean ± SD* | 117.4 ± 8.59 | 89.76 ± 9.84 | **10.58** | **< 0.001 **** |
| | *Range* | 100 - 150 | 70 - 101 | | |
| **DBP (mmHg)** | *Mean ± SD* | 45.2 ± 9.61 | 59.32 ± 4.44 | **13.75** | **< 0.001 **** |
| | *Range* | 20 - 50 | 48 - 65 | | |

Sd: Standard deviation t: Independent t test *: Significant (P<0.05) **: Highly significant (P<0.01)

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**Table 3:** Clinical pictures, duration and progress of heart failure among cases.

| Variable | | Cases (*n*=25) | |
|---|---|---|---|
| | | **No** | **%** |
| **Dyspnea** | *Yes* | 25 | 100 |
| **Cough** | *No* | 17 | 68 |
| | *Yes* | 8 | 32 |
| **Expectoration** | *No* | 22 | 88 |
| | *Yes* | 3 | 12 |
| **Disease duration: (months)** | *Mean ± SD* | 9.08 ± 11 | |
| | *Median (Range)* | 4 (1-43) | |
| **Heart failure** | *Acute* | 15 | 60 |
| | *Chronic* | 10 | 40 |
| **Ross classification** | *II* | 12 | 48 |
| | *III* | 7 | 28 |
| | *IV* | 6 | 24 |
| **Hospital stay: (months)** | *Mean ± SD* | 6.52 ± 5.36 | |
| | *Range* | 7 (1 – 15) | |
| **Ventillation** | *No* | 17 | 68 |
| | *Yes* | 8 | 32 |
| **Improvement** | *Rapid* | 16 | 64 |
| | *Delayed* | 9 | 36 |
| **Death** | *No* | 19 | 76 |
| | *Yes* | 6 | 24 |

**Table 4:** Copeptin & CRP level among studied groups.

| Variable | | Cases (n=25) | Control (n=25) | MW | p |
|---|---|---|---|---|---|
| **Copeptin: (pmol/L)** | *Mean ± SD* | 32.26 ± 21.9 | 8.97 ± 1.04 | | |
| | *Median* | 17.66 | 8.81 | **6.07** | **< 0.001** |
| | *Range* | 11.13-79.14 | 7.21 -10.99 | | **** |
| **CRP: (mg/dl)** | *Mean ± SD* | 26.56 ± 9.01 | 3.5 ± 1.02 | | |
| | *Median* | 25.5 | 3.5 | **12.72** | **< 0.001** |
| | *Range* | 12 - 45 | 3 - 4 | | **** |

Sd: Standard deviation MW: Mann Whitney test **: Highly significant (P<0.01)

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**Table 5:** Validity of Copeptin in prediction of dilated cardiomyopathy and death, respectively.

| Cutoff | AUC | CI | Sens. | Spec. | +PV | -PV | Accuracy | p-value |
|---|---|---|---|---|---|---|---|---|
| ≥11.06 | 1 | 1 - 1 | 100 | 100 | 100 | 100 | 100 | < 0.001* |
| **Cutoff** | **AUC** | **CI** | **Sens.** | **Spec.** | **+PV** | **-PV** | **Accuracy** | **p-value** |
| ≥36.13 | 0.83 | 0.64 – 1 | 83.3 | 88.9 | 71.4 | 94.4 | 88 | 0.02* |

**Figure 1:** Relation between disease data, outcome and copeptin among cases.

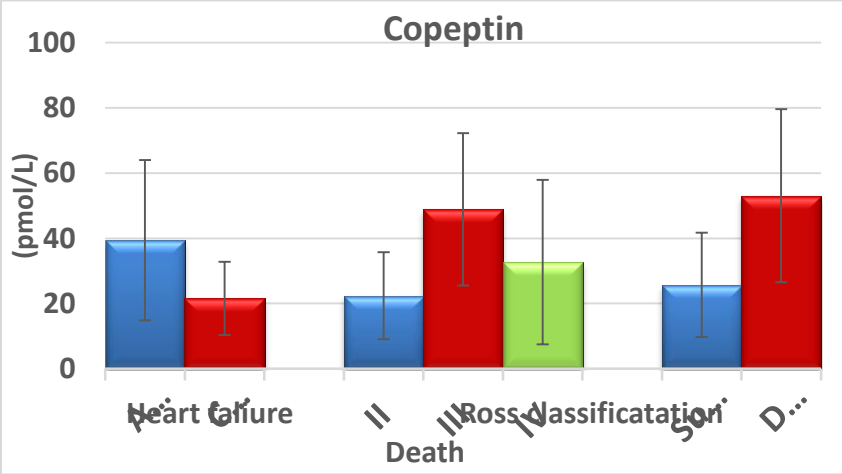


**Table 6:** Laboratory findings among studied groups.

| Variable | | Cases (*n*=25) | Control (n=25) | t | p |
|---|---|---|---|---|---|
| **Platelets: (x10$^3$/mm$^3$)** | *Mean ± SD* | 392.56±130.29 | 301.08 ± 56.79 | **3.22** | **0.002** |
| | *Range* | 190-595 | 221 - 385 | | ** |
| **Hb: (gm/dl)** | *Mean ± SD* | 10.93 ± 1.27 | 11.56 ± 0.84 | **2.07** | **0.04** |
| | *Range* | 8.2 – 12.4 | 10 - 13 | | * |
| **WBCs: (x10$^3$/mm$^3$)** | *Mean ± SD* | 10.82 ± 3.60 | 10.32 ± 1.09 | 0.65 | 0.52 |
| | *Range* | 6.6 – 20.8 | 9 – 12.5 | | NS |
| **HTC: (%)** | *Mean ± SD* | 31.65 ± 4.36 | 33.43 ± 4.37 | 1.44 | 0.16 |
| | *Range* | 25 – 38 | 25.6 – 39.3 | | NS |
| **Urea (mg/dl)** | *Mean ± SD* | 5.24 ± 1.23 | 5.32 ± 1.16 | 0.24 | 0.81 |
| | *Range* | 3.5 - 7 | 3.6 – 7.1 | | NS |
| **Creatinine: (mg/dl)** | *Mean ± SD* | 0.45 ± 0.16 | 0.43 ± 0.17 | 0.43 | 0.76 |
| | *Range* | 0.3 – 0.7 | 0.32 – 0.65 | | NS |
| **K: (mmol/L)** | *Mean ± SD* | 4.12 ± 0.75 | 4.24 ± 0.69 | 0.59 | 0.56 |
| | *Range* | 3.5 – 5.8 | 3.6 – 5.75 | | NS |
| **Na: (mmol/L)** | *Mean ± SD* | 140.65 ± 4.13 | 141.02 ± 5.34 | 0.27 | 0.79 |
| | *Range* | 135 – 148 | 138 - 146 | | NS |

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**Table 7:** Correlation between Copeptin and age, body measurements, disease duration, vital signs and laboratory findings among cases.

| Variable | Copeptin (*n*=25) | |
|---|---|---|
| | **r** | **P** |
| **Age (months)** | -0.35 | 0.09 NS |
| **Wight (Kg)** | -0.34 | 0.10 NS |
| **Height (cm)** | -0.27 | 0.20 NS |
| **BMI(kg/cm$_2$)** | -0.03 | 0.88 NS |
| **Disease duration (months)** | -0.34 | 0.10 NS |
| **HR: (beat/min)** | 0.20 | 0.33 NS |
| **RR: (breath/min)** | **0.44** | **0.03 *** |
| **SBP: (mmHg)** | -0.06 | 0.79 NS |
| **DBP: (mmHg)** | -0.30 | 0.15 NS |
| **Temperature: ($^0$)** | 0.20 | 035 NS |
| **Platelets: (x10$^3$/mm$^3$)** | 0.03 | 0.87 NS |
| **Hb: (gm/dl)** | **-0.43** | **0.03 *** |
| **WBCs: (x10$^3$/mm$^3$)** | 0.06 | 0.83 NS |
| **HTC: (%)** | -0.02 | 0.94 NS |
| **Urea (mg/dl)** | 0.35 | 0.09 NS |
| **Creatinine (mg/dl)** | 0.28 | 0.19 NS |
| **K (mmol/L)** | 0.03 | 0.97 NS |
| **Na (mmol/L)** | 0.13 | 0.54 NS |
| **CRP (mg/dl)** | 0.03 | 0.91 NS |

**Table 8:** Relation between disease data, outcome and copeptin among cases.

| Variable | | No | Copeptin | | MW | P |
|---|---|---|---|---|---|---|
| | | | **Mean** | **Sd** | | |
| **Heart failure** | *Acute* | 15 | 39.40 | 24.6 | **2.14** | **0.04** |
| | *Chronic* | 10 | 21.57 | 11.22 | | * |
| **Ross classification** | *II* | 12 | 22.38 | 13.35 | | |
| | *III* | 7 | 48.89 | 23.34 | **3.24** | **0.04** |
| | *IV* | 6 | 32.65 | 25.21 | | * |
| **Improvement** | *Rapid* | 16 | 31.84 | 24.22 | 0.45 | 0.65 |
| | *Delayed* | 9 | 33.02 | 18.39 | | NS |
| **Death** | *No* | 19 | 25.71 | 15.98 | **2.42** | **0.02** |
| | *Yes* | 6 | 53.01 | 26.54 | | * |

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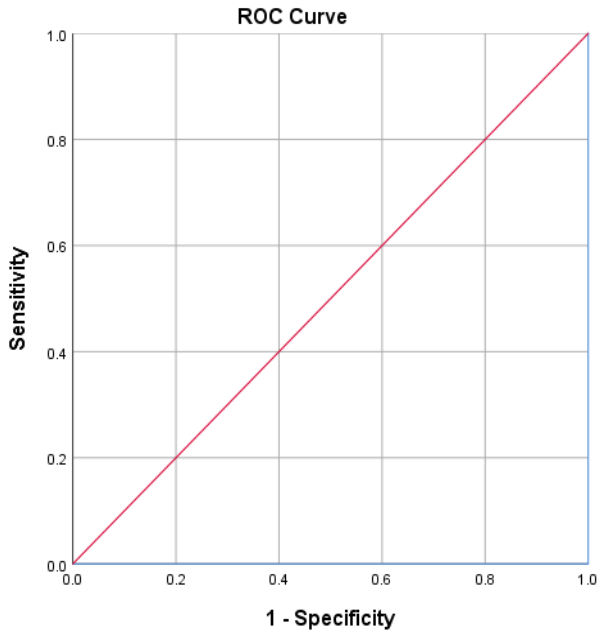


**Figure 2:** Roc curve for validity of Copeptin in prediction of cardiomyopathy.

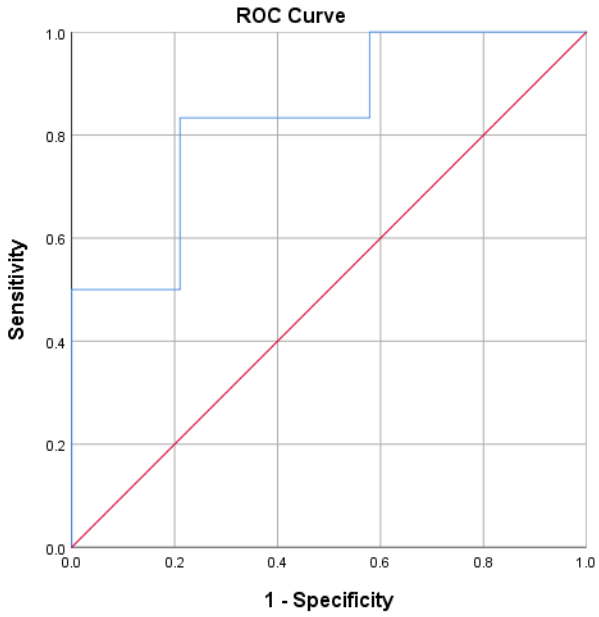


**Figure 3:** Roc curve for validity of Copeptin in prediction of death.

## DISCUSSION

Our results recorded that there were 11 female patients (44%) and 14 male patients (56%). There were no statistical significance differences between the studied groups as regard to age and sex. Also, 32% of the studied group (cases only) had +ve family history. Harmon et al [9] agreed with us where they reported that 51% males and 49% females were among their study. However, this ratio was not statistically significant (P>0.05). Cox et al [10], Towbin et al [11], Hershberger and

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Siegfried [12] also agree with our study who explained that boys have higher DCM incidence than girls,related to x-linked genetic causes.

Lipshultz et al [13] agreed with us and explaned that the differences in incidence between boys and girls among children who received a diagnosis after infancy, and the significant interaction between age and sex, were consistent with the male predominance and age-related expression of X-linked cardiomyopathies related to neuromuscular diseases. However, Diegoli et al [14] disagreed with our study as they concluded that the incidence of cardiomyopathy was similar in the two sexes.

Our study reported that there were stastical diffrence between studied groups as regard weight and body mass index which were lower among cases,weight ranged from 4 to 13 with mean of 8.08 ± 2.62, body mass index ranged from 3.5 to 7.6 with mean of 5.59 ± 1.25. Xu et al [15] disagreed with our study as they reported that two studied groups have no significant diffrence as regard weight and BMI.

Our study showed that two studied groups has significant difference as regard temperature, HR, RR and SBP which are higher in cases as follow temperature ranged from 36 to 38 with mean of 36.82 ± 0.66, HR ranged from 120 to 190 with mean of 143.28 ± 25.28, RR ranged from 37 to 70 with mean of 50.8 ± 10.11, SBP ranged from 100 to 150 with mean of 117.4 ± 8.59. Also, Shin et al [16] agreed with us as they found higher mean temperatures were recorded in patients with HF and infection (38.8°C ± 0.8 vs. 37.8°C ± 0.9, $P < 0.001$). Both heart failure and infection increase metabolic activity leading to increase temperature and heart rate.

Our study showed that the most frequent symptoms among cases were dyspnea and cough (100% and 32%, respectively). Also, Davis et al [17] agreed with our study as they stated that children in congestive heart failure will typically have a significant faster respiratory rate (RR) than their unaffected peers as heart failure patients often show a restrictive respiratory pattern secondary to heart enlargement, increase lung fluids & impairment of alveolar capillary gas diffusion. This lead to increase respiratory rate. Gebremariam and Moges [18] agreed with our study as they are reported that children with acute heart failure have increased work of breathing and increased cardiac activity to compensate for the low cardiac function and increase metabolic demands despite inadequate intake due to anorexia lead to weight loss.

In our study, the hospital stays ranged from 0 to 15 days with mean 6.52 days. Regarding improvement, 16 cases (64 %) had rapid improvement. Finally, 6 cases (24 %) were died.

Sahin et al [6] agreed with our study and found that during a follow-up period of 24 months, 16 (27%) patients had an episode of acute HF, 9 (15%) patients had ICD implantation, 19 (32%) patients were hospitalized due to cardiac diseases, and 7 (11.6%) patients died. The composite endpoint of hospitalization, ICD implantation, and death occurred in 20 HCM patients (33%).

Our study showed that copeptin level among cases is higher than control that is ranged from (11.13-79.14) with mean (32.26 ± 21.9). Sahin et al [6] agreed with our study and found that copeptin was significantly higher in the HCM group compared with the controls. Also, Morgenthaler et al [19] and Stoiser et al [20] agreed with us and found that the concentration of copeptin in the blood circulation ranges from 1 to 12 pmol/L in healthy individuals. Moreover, the data have shown that copeptin is a stronger predictor and the mean value was on average 19·7±19·1 pmol/L (8.8 ng/ml).

As regard platelets and inflammatory marker C-reactive protein (CRP), our study demonstrated that they are higher in cases as follow platelets range (190-595) with mean (392.56±130.29), CRP range from 12-45 with mean of (26.56±9.01). Huang et al [21] agreed with us and suggested that the levels of CRP are related to clinical outcomes and that measurement of CRP has the potential to play an important role

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as an adjunct for risk assessment in patients with chronic CHF.

Regarding heart failure, our study showed that copeptin level correlate with degree of heart failure as 60% of cases had AHF and higher copeptin level with mean of (39.40 ±24.6), but 40% of cases had CHF and lower copeptin level with mean of (21.57±11.22). Yan et al [22] and Bolignano et al [23] agreed with us and they demonstrated that the plasma copeptin levels in AHF group, pneumonia complicating AHF group and CHD complicating AHF group were significantly higher than those in the pneumonia control group and the healthy control group.They concluded that copeptin had important significance for the early diagnosis, condition evaluation, treatment guidance and prognosis in child AHF. Moreover, Bolignano et al [23] agreed with us and considered the observed plasma copeptin levels in patients with HF (21–32 pmol/l) were much higher than 4.2 pmol/l.

Also, Maisel et al [24] agreed with our study and found that in AHF with no knowledge of whether left ventricular function is depressed or not, copeptin has been shown to be prognostic predictor of HF hospitalization and mortality. Some studies also demonstrated significant positive correlation between elevated plasma copeptin level and incidence of HF that are agreed with us [25] [26] [27]. However, Mason et al [28] did not agree with our resultes and they were stated that in two diagnostic studies based on older residents, although plasma copeptin levels were elevated in patients with acute HF, using copeptin did not significantly improve the diagnosis of HF. At the same orintation, Bahrmann et al [29] also did not agree with our results and they are considered that HF is a dynamic syndrome characterized by dramatically increased neurohormonal activation and it should be better to use the combination of copeptin with other biomarkers to improve the predictive effect of adverse outcome in patients with HF.

According to Ross classification, copeptin level did not correlate with the ascending degree of classification where the highest degree was observed in class III with mean of (48.89±23.34) in 7 cases. For grading severity of CHF in infants, the Ross and modified Ross classifications incorporate feeding difficulties, growth problems and symptoms of exercise intolerance into a numeric score [30].

Kristyagita and Siswanto [3] strongly agreed with our results and he was demonstrated that HF still causes high rates of cardiovascular morbidity and mortality. Clinical symptoms alone could not accurately predict negative outcomes in HF patients, especially among those with elevated NT-proBNP. In unstable HF patients, copeptin can also accurately predict mortality, therefore copeptin is considered as a significant and independent predictor for mortality or negative outcome.

As regard relation of copeptin level to outcome of disease, our study revealed that copeptin level was higher in difficult 6 cases that are died with mean of (53.01±26.54). Bolignano et al [23] agreed with our study and they were found that increased copeptin levels have been described in several studies as a strong predictor of mortality in patients with chronic or acute HF.

Jink [31] also agreed with our study and he was investigated the relationship between serum copeptin level and the severity of dilated cardiomyopathy (DCM) with heart failure (HF). He concluded that the level of copeptin can be used as a parameter for the clinical diagnosis and patient's condition assessment in DCM patients with HF.

Our study showed that the sensitivity of copeptin at cut off value of 11.06 in diagnosis of dilated cardiomyopathy was 100 %, specificity was 100 % and the accuracy was 100 %. Also, we can use copeptin level in children who have been diagnosed as dilated cardiomyopathy patients to follow up and predict outcome of their cases as regard degree of heart failure, ross stage, hospital stay and other complication that may occur like chest infection. Our study found that the sensitivity of copeptin at cutoff value of 36.13 in prediction of death was 83.3%, specificity was 88.9% and the accuracy was 88%. Sahin et al

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[6] agreed with us and they were found that copeptin levels >10.1 pmol/L (sensitivity 80%, specificity 94.4%, AUC: 0.895, *P* = 0.01) predicted HCM in the study population. When AUCs were compared, the discriminative properties of copeptin measurements were not statistically different.

## CONCLUSION

This study highlights that dilated cardiomyopathy is a relatively common cause of acquired heart disease related to heart failure (HF), so the treatment of dilated cardiomyopathy means treatment of heart failure. Copeptin is a novel biochemical marker that has clinical use in HF. Our findings indicate that copeptin levels are elevated in children with dilated cardiomyopathy more than control group and patients with higher copeptin levels may have a higher risk for poor outcome and complications. Copeptin elevated levels correlate with severity of heart failure.

**Conflict of interest:** - No Conflict of interest
**Financial disclosure:** - No funding or grants

## REFERENCES

**[1] Maron BJ, Towbin JA, Thiene G, Antzelevitch C, Corrado D, Arnett D, et al.** Contemporary Definitions and Classification of the Cardiomyopathies: An American Heart Association Scientific Statement from the Council on Clinical Cardiology, Heart Failure and Transplantation Committee; Quality of Care and Outcomes Research and Functional Genomics and Translational Biology Interdisciplinary Working Groups; and Council on Epidemiology and Prevention. Circulation 2006;113 (14): 1807-1816. doi:10.1161/CIRCULATIONAHA.106.174287

**[2] Caforio AL, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, et al.** Current state of knowledge on etiology, diagnosis, management, and therapy of myocarditis: A position statement of the European Society of Cardiology. Working Group on Myocardial and Pericardial Diseases. Eur Heart J 2013; 34 (33): 2636–2648. doi: 10.1093/eurheartj/eht210

**[3] Kristyagita A and Siswanto B.** The role of copeptin as a novel cardiovascular biomarker. Med J Indones 2015; 24 (1): 59-66. doi: https://doi.org/10.13181/mji.v24i1.1208

**[4] Giannopoulos G, Deftereos S, Panagopoulou V, Kossyvakis C, Kaoukis A, Bouras G, et al.** Copeptin as a biomarker in cardiac disease. Curr Top Med Chem 2013; 13(2):231-240. doi: 10.2174/1568026613139990088

**[5] Balling L and Gustafsson F.** Copeptin as a biomarker in heart failure. Biomark Med. 2014; 8 (6):841-854. doi: 10.2217/bmm.14.50

**[6] Sahin I, Gungor B, Ozkaynak B, Uzun F, Küçük SH, Avci I I, et al.** Higher copeptin levels are associated with worse outcome in patients with hypertrophic cardiomyopathy. Clin cardiol 2017; 40(1): 32-37. doi: 10.1002/clc.22602

**[7] Läer S, Mir TS, Behn F, Eiselt M, Scholz H, Venzke A, et al.** Carvedilol therapy in pediatric patients with congestive heart failure: A study investigating clinical and pharmacokinetic parameters. Am Heart J 2002; 143 (5)**:** 916-922. doi:10.1067/mhj.2002.121265

**[8]** Human CPP (Copeptin) ELISA Kit. Kit. Catalog #:C6064. Science Co., Ltd. Gloray. www.glorybioscience.com.

**[9] Harmon WG, Sleeper LA, Cuniberti L, Messere J, Colan SD, Orav EJ, et al.** Treating children with idiopathic dilated cardiomyopathy (from the Pediatric Cardiomyopathy Registry). Am J Cardiol 2009; 104 (2):281-286. doi: 10.1016/j.amjcard.2009.03.033

**[10] Cox GF, Sleeper LA, Lowe AM, Towbin JA, Colan SD, Orav EJ, et al.** Factors associated with establishing a causal diagnosis for children with cardiomyopathy. Pediatrics 2006; 118 (4): 1519-1531. doi:10.1542/peds.2006-0163

**[11] Towbin JA, Lowe AM, Colan SD, Sleeper LA, Orav EJ, Clunie S, et al.** Incidence, causes, and outcomes of dilated cardiomyopathy in children. JAMA 2006; 296 (15): 1867-1876. doi:10.1001/jama.296.15.1867

**[12] Hershberger RE and Siegfried JD.** Update 2011: clinical and genetic issues in familial dilated cardiomyopathy. J Am Coll Cardiol 2011; 57 (16): 1641-1649. doi: 10.1016/j.jacc.2011.01.015

**[13] Lipshultz SE, Sleeper LA, Towbin JA, Lowe AM, Orav EJ, Cox GF, et al.** The Incidence of Pediatric Cardiomyopathy in Two Regions of the United States. N Engl J Med 2003; 348 (17):1647-1655. doi:10.1056/NEJMoa021715

**[14] Diegoli M, Grasso M, Favalli V, Serio A, Gambarin FI, Klersy C, et al.** Diagnostic Work-Up and Risk Stratification in X-Linked Dilated Cardiomyopathies Caused by Dystrophin Defects. J Am Coll Cardiol 2011; 58(9): 925-934. doi: 10.1016/j.jacc.2011.01.072

**[15] Xu L, Liu X and Wu S.** The clinical application value of the plasma copeptin level in the assessment of heart failure with reduced left ventricular ejection fraction. Medicine (Baltimore) 2018;

**May. 2021 Volume 27 Issue 3** **Doi: 10.21608/zumj.2019.17593.1560**

97(39):e12610. doi: 10.1097/MD.0000000000012610

**[16] Shin AY, Jin B, Hao S, Hu Z, Sutherland S, McCammond A, et al.** Utility of Clinical Biomarkers to Predict Central Line-associated Bloodstream Infections after Congenital Heart Surgery. Pediatr Infect Dis 2015; 34 (3): 251–254. doi: 10.1097/INF.0000000000000553

**[17] Davis EQ, Permutt Z, Permutt S, Naureckas ET, Bilderback AL, Rand CS, et al.** Perception of air flow obstruction in patients hospitalized for acute asthma. Ann Allergy Asthma Immunol 2009; 102 (6):455-461. doi: 10.1016/S1081-1206(10)60117-2

**[18] Gebremariam S and Moges T.** Pediatric Heart Failure, Lagging, and Sagging of Care in Low Income Settings: A Hospital Based Review of Cases in Ethiopia. Cardiol Res Pract 2016; Article ID 71477234, 7 pages. doi: 10.1155/2016/7147234

**[19] Morgenthaler NG, Struck J, Jochberger S and Dünser MW.** Copeptin: clinical use of a new biomarker. Trends Endocrinol Metab 2008; 19 (2): 43–49. doi: 10.1016/j.tem.2007.11.001

**[20] Stoiser B, Mörtl D, Hülsmann M, Berger R, Struck J, Morgenthaler NG, et al.** A fragment of the vasopressin precursor, as a novel predictor of outcome in heart failure. Eur J Clin Invest. 2006; 36(11):771-778. doi:10.1111/j.1365-2362.2006.01724.x

**[21] Huang J, Trinkaus K, Huddleston CB, Mendeloff EN, Spray TL and Canter CE.** Risk factors for primary graft failure after pediatric cardiac transplantation: importance of recipient and donor characteristics. J Heart Lung Transplant 2004;23(6): 716-722. doi:10.1016/j.healun.2003.08.001

**[22] Yan JJ, Lu Y, Kuai ZP and Yong YH.** Predictive value of plasma copeptin level for the risk and mortality of heart failure: a meta-analysis. J Cell Mol Med 2017; 21 (9):1815-1825. doi: 10.1111/jcmm.13102

**[23] Bolignano D, Basile G, Parisi P, Coppolino G, Nicocia G and Buemi M.** Increased plasma neutrophil gelatinase-associated lipocalin levels predict mortality in elderly patients with chronic heart failure. Rejuvenation Res. 2009; 12 (1): 7–14. doi: 10.1089/rej.2008.0803

**[24] Maisel A, Xue Y, Shah K, Mueller C, Nowak R, Peacock WF, et al.** Increased 90-day mortality in patients with acute heart failure with elevated copeptin: secondary results from the Biomarkers in Acute Heart Failure (BACH) study. Circ. Heart Fail. 2011; 4 (5): 613–620. doi: 10.1161/CIRCHEARTFAILURE.110.960096

**[25] Khan SQ, Dhillon OS, O'Brien RJ, Struck J, Quinn PA, Morgenthaler NG, et al.** C-terminal provasopressin (copeptin) as a novel and prognostic marker in acute myocardial infarction: Leicester Acute Myocardial Infarction Peptide (LAMP) study. Circulation 2007; 115 (16): 2103–2110. doi:10.1161/CIRCULATIONAHA.106.685503

**[26] Dieplinger B, Gegenhuber A, Haltmayer M and Mueller T.** Evaluation of novel biomarkers for the diagnosis of acute destabilized heart failure in patients with shortness of breath. Heart 2009; 95 (18):1508-1513. doi: 10.1136/hrt.2009.170696

**[27] Reinstadler SJ, Klug G, Feistritzer HJ, Metzler B and Mair J.** Copeptin Testing in Acute Myocardial Infarction: Ready for Routine Use? Disease Markers 2015; Article ID 614145: 9 pages. doi.org/10.1155/2015/614145

**[28] Mason JM, Hancock HC, Close H, Murphy JJ, Fuat A, de Belder M, et al.** Utility of biomarkers in the differential diagnosis of heart failure in older people: findings from the heart failure in care homes (HFinCH) diagnostic accuracy study. PLoS One 2013; 8 (1): e53560. doi: 10.1371/journal.pone.0053560

**[29] Bahrmann P, Bahrmann A, Hofner B, Christ M, Achenbach S, Sieber CC, et al.** Multiple biomarker strategy for improved diagnosis of acute heart failure in older patients presenting to the emergency department. Eur. Heart J. Acute Cardiovasc 2015; 4 (2): 137–147. doi: 10.1177/2048872614541904

**[30] Ross RD.** The Ross Classification for Heart Failure in Children After 25 Years: A Review and an Age-Stratified Revision. Pediatr Cardiol 2012; 33 (8)**:** 1295-1300. doi: 10.1007/s00246-012-0306-8

**[31] Jinke Y.** The role of serum copeptin in the diagnosis and treatment of dilated cardiomyopathy patients with heart failure. Department of Cardiology, Farming Nada Hospital of Hainan Province, Hainan Danzhou 2013; 571700, China. Laboratory Medicine, 2013-07, R541.6. www.cnki.com.cn.

How to Cite

Ahmed Abd EL Hai, M., abdellatif, A., Ahmed Ali, A., Sameer, H. Assessment the Value of Serum Copeptin Level in Dilated Cardiomyopathy in Pediatrics. Zagazig University Medical Journal, 2021; (516-527): -. doi: 10.21608/zumj.2019.17593.1560