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Prevalence & Risk Factors of Anxiety and Depression among Cases of Hyperemesis Gravidarum

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الملخص:

الخلفية: التقيؤ المفرط **(HG)** يحدث في الشهور الأولى من الحمل و يؤثر على صحة الام عامة و حالتها النفسية بصفة خاصة فقد لوحظ وجود علاقة بين حدوث القلق و الاكتئاب و التقيؤ المفرط اثناء الحمل. **هدف الدراسة**: هو التعرف على مدى انتشار القلق والاكتئاب في حالات التقيؤ المفرط أثناء الحمل (HG) ودراسة عوامل الخطورة المرتبطة بهما. **منهجية البحث:** استخدمت دراسة وصفية مقطعية أجريت في مركز بنغازي الطبي(BMC) للحالات التي تم تشخيصها على أنها HG وتم دخولها لقسم أمراض النساء في الفترة ما بين 1-10-2019 و 31-3-2021. تم جمع البيانات عن طريق مقابلة مباشرة مع النساء وباستخدام مقياس القلق والاكتئاب (HADS)، كما تم جمع بعض البيانات من سجلاتهن الطبية. تم تحليل البيانات باستخدام (SPSS) الإصدار 23-وكذلك استخدام الإحصاءات الوصفية. الترددات -متوسط -الانحراف المعياري -الوسيط. واستنتاجية؛ كاختبار chi-square، اختبار ANOVA أحادي الاتجاه واختبار t. استخدمت P <0.05 للدلالة على الأهمية الإحصائية. النتائج: اشتملت الدراسة على تسعة وثمانون حالة(HG) كان مستوى القلق المرتفع 76.4٪، ومستوى الاكتئاب المرتفع في 82٪ من الحالات. لوحظ أن الجنسية الليبية مرتبطة بشدة بقلق شديد (5، 95٪ CI: 1.021-1.284)، يليها الحالات التي عانت من التقيؤ المفرط في الحمول السابقة (3.375، 95٪ CI: 1.161-9.809) وتقدم عمر الأم (1.14، 95٪ CI: 1.021-1.284). بعد التعديل باستخدام الانحدار اللوجستي متعدد المتغيرات لوحظ فقط تاريخ التقيؤ المفرط في حالات الحمل السابقة كعوامل خطر مستقلة لارتفاع الاكتئاب بين حالات (HG) (AOR، 95 3.167٪ CI: 1.005-9.979). من بين الفحوصات المختبرية المدروسة مثل مستويات الصوديوم والبوتاسيوم بالدم ووظيفة الكلى والكبد وتحليل البول لمعرفة الكيتونات، وعلاقتها بالشدة السريرية لـ HG فقط ارتبط نقص بوتاسيوم الدم بشكل إيجابي مع القلق الشديد بينما لم تكن أي من العلامات المدروسة مرتبطة بحدوث اكتئاب مرتفع. **الاستنتاج:** تم تسجيل نسبة عالية من الاكتئاب والقلق بين حالات التقيؤ المفرط في مركز بنغازي الطبي ووجدنا أيضا أن هناك ارتباط قوي وتداخل بين حالات القلق والاكتئاب.

الكلمات المفتاحية: التقيؤ المفرط أثناء الحمل، القلق، الاكتئاب، مركز بنغازي الطبي.

Abstract

Background: Hyperemesis gravidarum (HG) is a sever nausea and vomiting before 22nd week of Gestation. Antenatal depression and anxiety become a common problem significantly affecting maternal and fetal health, there is a complex relation between anxiety and depression and hyperemesis gravidarum. **The aim:** is to identify and study the prevalence of anxiety and depression and their related risk factors for hyperemesis gravidarum(HG) cases. **Subject and methods:** A descriptive, cross-sectional study was conducted at the Benghazi Medical Center (BMC) on cases diagnosed with HG and admitted to the Gynecology Department in the period between 1-10-2019 and 31-3-2021. Data was collected through direct interviews with women and using the Hospital Anxiety and Depression Scale (HADS) with some data collected from their medical records. The data was analyzed using SPSS Ver. 23. The statistics used were descriptive; frequencies, mean, standard deviation and median as well as inferential; chi-square test, one-way ANOVA and t-test. P<0.05 is used to denote statistical significance. **Results:** High anxiety levels were found in 76.4% and high depression levels were noted in 82% of cases. From the value of the adjusted odd ratio, women with Libyan nationality are strongly associated with high anxiety (5, 95% CI: 1.021-1.284), followed by a positive history of hyperemesis in previous pregnancies (3.375, 95% CI: 1.161-9.809) and a higher maternal age (1.14, 95% CI: 1.021-1.284). Regarding maternal education and pregnancy planning, it has been found that these factors are protective against high anxiety. After adjustment by using multivariable logistic regression, only a history of hyperemesis in previous pregnancies was identified as an independent risk factor for high depression among the cases (AOR, 3.167 95% CI: 1.005-9.979). **Conclusion:** High levels of both depression and anxiety were recorded among cases of hyperemesis at the Benghazi Medical Centre.

Keywords: Anxiety, Benghazi Medical Centre, Depression, Hyperemesis gravidarum.

1. INTRODUCTION

Hyperemesis gravidarum (HG) is a severe and persistent nausea and vomiting disease during pregnancy which may cause more than 5% weight loss, dehydration and electrolyte imbalances.1 Its incidence is 0.3- 3 %.[2,3]

HG is one of the most common reasons for hospital admission in the first half of pregnancy.[4,5] The origin is unknown,[3] however it may be associated with younger age, primiparous, a previous history of HG, infection with H-pylori,[6] low body mass index,[7] increased HCG levels and increased placental mass as in molar or multiple gestations.[8] HG may result in nutritional deficiencies in vitamin B1, vitamin B6 and B12 causing anemia, hyponatremia, Wernicke's encephalopathy, central pontine myelinolysis, coagulopathy, Mallory-Weiss tears.[3] The effects of

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HG on the fetus are having a lower birth weight, being undersized for the gestational age and being born before term,[3,9,10,11] which are due to malnutrition & electrolyte imbalances caused by HG.[12]

Depression and anxiety disorders are frequently seen in the antepartum period and have obstetric and perinatal consequences.[13] Many risk factors of depression identified in pregnancy such as hormonal shifts, neuroendocrine changes, stress, a lack of social support, a history of depression prior to pregnancy, lower income, lower education levels, a history of antepartum and postpartum depression and a family history of depression during pregnancy or post-partum.[14.15] It is found that psychological disorders were higher in the first trimester while the second and third trimesters were protective factors,[15] which may be related to the occurrence of HG mainly in the first trimester which along with its physical effects, can also affect the quality of life and the psychological state of pregnant women.

It is stated that depression is a complication of HG and emotional support can be beneficial.[16] Patients with HG were reported with significantly more emotional distress than controlled cases:[17,18] it was found that 37% of HG pregnant women were depressed.[19] Previous reports evaluating psychological behavior in the etiology and pathogenesis of HG have been conflicting. While a psychiatric history prior to HG is reportedly uncommon, a psychiatric history may increase the risk of HG.[20] A familial history of psychiatric disorders was found significantly higher in HG cases.[21] In other studies, psychological distress associated with HG was a direct consequence rather than a cause of HG. Therefore, patients with HG during pregnancy should be evaluated for mood disorders as their medical conditions.[22] The predictors were a previous history of hyperemesis, increased gravidity and unwanted pregnancy.[19] Patients with HG were 5.5 and 6.7 times more prone to having depression and anxiety disorders compared with normal cases and the predictors of anxiety disorder were low educational levels, low income and poor social relationships.[23] It is also recorded that the employment status of pregnant women diagnosed with HG significantly predicted their anxiety. It is not known whether psychological distress adversely impacts the clinical severity of HG or whether the severe cases have high anxiety or depression in a study done by Tan et al.[24] Only a high hematocrit on hospitalization was positively associated with depression cases.[24]

As no studies have evaluated the prevalence and predictive factors or the cause-and-effect relation of these psychological disorders and pregnancy in our hospital, this study was conducted to find out the prevalence of anxiety and depression and identify their associated risk factors and the severity of HG as denoted by laboratory and clinical markers among women hospitalized with HG at the Benghazi Medical Center.

2. SUBJECTS AND METHOD:

A descriptive, cross-sectional study conducted at the Benghazi Medical Center (BMC) on women diagnosed with hyperemesis gravidarum and admitted to the Gynecology Department in the period between 1-10-2019 and 31-3-2021 was included in this study. The data was collected by the researcher by interviewing every patient with the aid of a data collection performa which was used to collect data regarding demographic characteristics, obstetric history, morbidity and some laboratory markers such as electrolyte levels, renal function and liver function tests and urine for ketones. The Hospital Depression and Anxiety Scale [HADS] was used to measure psychological distress and symptoms of anxiety and depression. The scale consists of 14 items, seven for anxiety (HADS Anxiety) and seven for depression (HADS Depression). Scoring for each item ranges from zero to three, with three denoting the highest anxiety or depression level.

A total subscale score of >8 points out of a possible 21 denotes considerable symptoms of anxiety or depression. Some data was collected from their medical records. The data was analyzed by using SPSS Ver. 23. The statistics used were descriptive; frequencies, mean, standard deviation and median as well as inferential; chi-square test, one-way ANOVA and t-test. P<0.05 is used to denote statistical significance.

Ethical Considerations

- A formal letter from the Department of Obstetrics and Gynecology, Faculty of Medicine at the University of Benghazi was sent to the Medical Affairs Office at the Benghazi Medical Center to obtain permission to conduct the study and verbal consent was obtained from the patients.

3. RESULTS

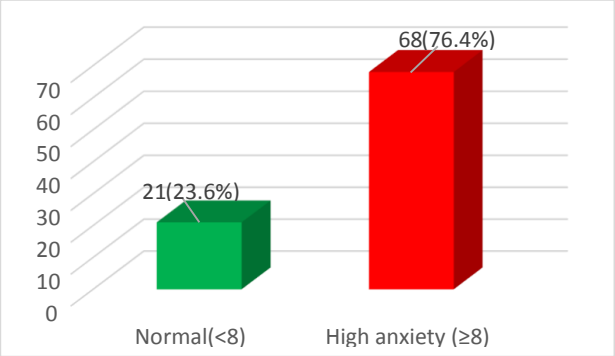


Figure 1: Distribution of women according to the level of anxiety

Anxiety was prevalent among HG cases. It was present in 76.4%, indicating a relation between HG and psychological disorders.

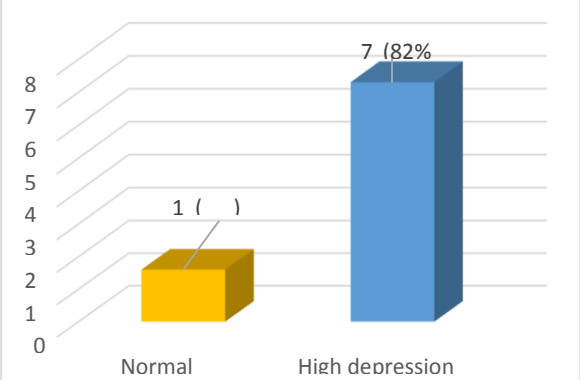


Figure 2: Distribution of women according to the level of depression.

High depression was also reported among the cases of hyperemesis gravidarum 82%.

- Sixty-four (71.9%) women had high levels of both depression and anxiety.
- There is a strong association and overlap between anxiety and depression cases (OR: 21.33, 95% CI 3.64- 30.615; P=0.001)

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Table (1): Risk factors of high anxiety (≥8) by using the Hospital Anxiety and Depression Scale in hyperemesis gravidarum

	High anxiety (≥8) n=68	Normal anxiety (<8) n=21	p-value	AOR (95% CI)	Adjusted P-value
Age	30.63 ±4.71	27.71 ±5.05	0.025*	1.14 (1.021-1.284)	0.021*
Nationality: Libyan Non-Libyan	64 (94.1%) 4 (5.9%)	16 (76.2%) 5 (23.8%)	0.017*	5 (1.021-1.284)	0.027*
Gravidity	3[3]	2[4]	0.149		
Parity	2[2]	1[2]	0.111		
Nulliparous	15 (22.1%)	7 (33.3%)	0.295		
Frequency of vomiting/day	9[4]	8[6]	0.883		
Duration of vomiting	21[16]	7[23]	0.996		
Previous miscarriage	26 (38.2%)	6 (28.6 %)	0.420		
Gestational age at admission	9.82 ±2.52	10.76 ±2.89	0.154		
Gestational age at the start of vomiting	6.61 ±2.05	7.38 (±2.10)	0.154		
Hyperemesis in a previous pregnancy	54 (81.8%)	12 (57.1%)	0.021*	3.375 (1.161-9.809)	0.025*
Planned pregnancy	34 (50.0%)	16 (76.2%)	0.034*	0.313 (0.103-0.949)	0.040*
Local family support	56 (86.2%)	18 (94.7%)	0.389		
Income Low (<500LD) Moderate (500-1000 LD) High (>1000 LD)	13 (19.1%) 34 (50.0%) 21 (30.9%)	8 (38.1%) 8 (38.1%) 5 (23.8%)	0.201		
Housing Owned Rented	58 (85.3%) 10 (14.7%)	14 (66.7%) 7 (33.3%)	0.058		0.064
Living in an extended family	40 (58.8%)	11 (52.4%)	0.602		
Educational level: Less than primary Primary /preparatory Secondary and above	2 (2.9%) 6 (8.8%) 60 (88.2%)	3 (14.3%) 5 (23.8%) 13 (61.9%)	0.019*	0.260 (0.069-0.983)	0.030*
Employment: Working Not working	17 (25.0%) 51 (75.0%)	3 (14.3%) 18 (85.7%)	0.304		

Values are expressed as mean ± standard deviation, number (%) or median [interquartile range]. Adjusted odds ratio AOR (95% Confidence Interval) is shown where adjusted P< 0.05.

By bivariate analysis for anxiety cases, the variables with crude P< 0.1 were age, nationality, history of hyperemesis in previous pregnancies, planned pregnancy, housing and educational level. After adjustment by using multivariable logistic regression, only age, nationality, history of hyperemesis in previous pregnancies, planned pregnancy and educational levels were identified as independent risk factors for high anxiety among the cases. From the value of the adjusted odd ratio, the Libyan nationality is strongly associated with the occurrence of anxiety (5, 95% CI:1.021-1.284) followed by a positive history of hyperemesis in previous pregnancies (3.375, 95% CI: 1.161-9.809) and a higher maternal age (1.14, 95% CI: 1.021-1.284).

Regarding maternal education and pregnancy planning, the AOR was less than one, which means that these factors are protective against high anxiety. Table (1)

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Table (2): Risk factors of high depression (≥8) by using the Hospital Anxiety and Depression Scale in hyperemesis gravidarum

	High depression (≥8) n=73	Normal depression (<8) n=16	p-value	AOR (95% CI)	Adjusted P-value
Age	30.41 ±4.72	27.81 ±5.39	0.055		0.060
Nationality: Libyan Non-Libyan	66 (90.4%) 7 (9.6%)	14 (78.5%) 2 (12.5%)	0.727		0.727
Gravidity	3[3]	2[3]	0.181		
Parity	2[2]	1[2]	0.269		
Nulliparous	17 (23.3%)	5 (31.2%)	0.504		
Frequency of vomiting/day	10[5]	6.5[4]	0.372		
Duration of vomiting	15[16]	18[23]	0.665		
Previous miscarriage	28 (38.4%)	4 (25.0 %)	0.313		
Gestational age at admission	9.90 ±2.62	10.68 ±2.62	0.283		
Gestational age at the start of vomiting	7.25 ±2.14	7.25 (±2.07)	0.341		
Hyperemesis in a previous pregnancy	57 (80.3%)	9 (56.2%)	0.042*	3.167 (1.005-9.979)	0.049*
Planned pregnancy	40 (54.8%)	10 (62.5%)	0.574		
Local family support	59 (86.8%)	15 (93.8%)	0.455		
Income Low (<500LD) Moderate (500-1000 LD) High (>1000 LD)	17 (23.3%) 36 (49.3%) 20 (27.4%)	4 (25.0%) 6 (37.5%) 6 (37.5%)	0.650		
Housing Owned Rented	59 (80.8%) 14 (19.2%)	13 (81.8%) 3 (18.8%)	0.969		
Living in an extended family	43 (58.9%)	8 (50.0%)	0.514		
Educational level: Less than primary Primary /preparatory Secondary and above	2 (2.7%) 9 (12.3%) 62 (84.9%)	3 (18.8%) 2 (12.5%) 11 (68.8%)	0.041*		0.089
Employment: Working Not working	18 (24.7%) 55 (75.3%)	2 (12.5%) 14 (87.5%)	0.219		

Values are expressed as mean ± standard deviation, number (%) or median [interquartile range]. Adjusted odds ratio AOR (95% Confidence Interval) is shown where adjusted P< 0.05.

By bivariate analysis for depression cases, the variables with crude P< 0.1 were age, nationality, history of hyperemesis in previous pregnancies and educational level. After adjustment by using multivariable logistic regression, only a history of hyperemesis in previous pregnancies was identified as an independent risk factor for high depression among the cases (AOR, 3.167 95% CI: 1.005-9.979). Table (2)

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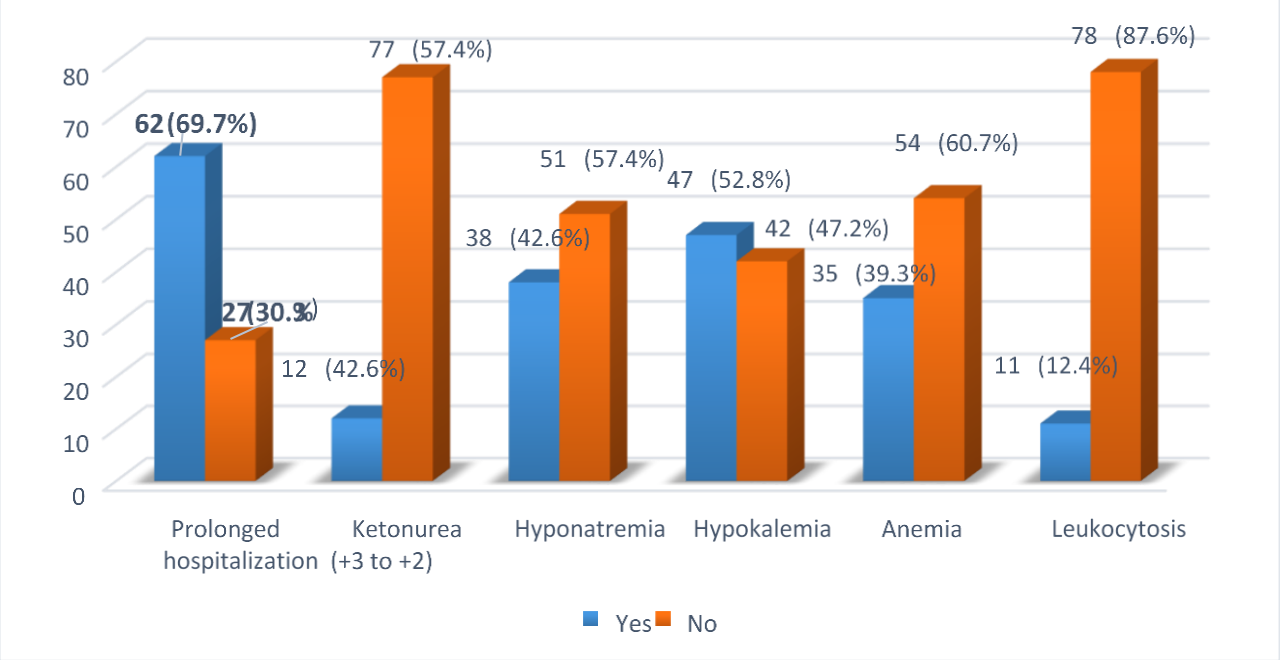


Figure 3: Distribution of the women according to clinical and laboratory data

Figure 3 shows that 62 (69.7%) women were admitted for 4 days or more at the time of the study, 77 (57.5%) women had ketonurea +3 to +4, 38 (42.6%) had hyponatremia, 47 (52.8%) had hypokalemia, 35 (39.3%) of the women were anaemic and 11 (12.4%) women had leukocytosis. No patient had a high creatinine level, one patient had high hematocrit and one patient had a high urea level.

Table (3): Distribution of the women according to the level of anxiety, level of depression and some laboratory and clinical data

	High anxiety (≥8) n=68	Normal anxiety (<8) n=21	p-value	High depression (≥8) n=73	Normal depression (<8) n=16	p-value
Prolonged hospitalization (≥ 4 days)	45(66.2%)	17 (81.5%)	0.184	51 (69.9%)	11 (86.8%)	0.930
Ketonurea: **+3 to +4** **+1 to +2**	8 (11.8%) 60 (88.2%)	4 (19.0%) 17 (81.0%)	0.409	9 (12.3%) 64 (87.7%)	3 (18.8%) 13 (81.3%)	0.510
Hyponatremia (≤ 135 mmol/l)	30 (44.1%)	8 (38.1%)	0.624	32 (43.8%)	6 (37.5%)	0.641
Hypokalemia ≤ 3.5 mmol/l)	32 (47.1%)	15 (71.4%)	0.047*	39 (53.4%)	8 (50.0%)	0.804
Anemia (≤11.5 g/dl)	28 (41.2%)	7 (33.3%)	0.517	29 (39.7%)	6 (37.5%)	0.869
Leukocytosis (≥ 11^{*10})	7 (10.5%)	4 (19.0%)	0.307	7 (9.6%)	4 (25%.0)	0.117

Values are expressed as numbers (%). Fisher's exact test (2 x2 datasets) was used for analysis.

Out of all the studied laboratory markers and clinical severity of HG, only hypokalemia was positively associated with high anxiety and this association was statistically significant (P<0.05). None of the studied markers was associated with the occurrence of high depression.

4. DISCUSSION:

Eighty-nine pregnant women were admitted to the hospital because of hyperemesis gravidarum during the data collection period. Both anxiety and depression were prevalent among HG cases. High anxiety levels were present in 76.4%, and depression in 82% of cases. This supports the relationship between HG and psychological disorders. Generally estimated, approximately 40% of pregnant women face symptoms of anxiety in developing nations. [25] In a study done by Peng Chiong Tan in 2010, anxiety was detected in 46.9% and depression was found in 47.8%.[24] Another study recorded that (11.5%, 9.9%,15.7%, 19.5% and 23%) of the participants suffered from extreme, severe, moderate, borderline clinical depression and mild mood disturbances respectively.[17] While in a study done in 2014, the levels of anxiety and depression among HG cases were 19%, and 69% respectively [11]. This study observed that there is a strong association and overlap between anxiety and depression cases (OR: 21.33, 95% CI 3.64- 30.615; P=0.000). Sixty-four (71.9%) women had high levels of both depression and anxiety.

It is not clear whether HG is a cause of these psychological disorders or whether some psychological factors before

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pregnancy predispose to hyperemesis. [26-28] Predictive factors for developing anxiety and depression in women with HG were investigated in some studies.[24,29,30] In this study, these factors were also evaluated where it was found by bivariate analysis for anxiety cases, the variables with crude P<0.1 were age, nationality, history of hyperemesis in previous pregnancies, planned pregnancy, housing and educational level. From the value of the adjusted odd ratio, the Libyan nationality is strongly associated with the occurrence of anxiety (5, 95% CI:1.021-1.284), followed by a positive history of hyperemesis in previous pregnancies (3.375, 95% CI: 1.161-9.809) and a higher maternal age (1.14, 95% CI:1.021-1.284). But maternal education and pregnancy planning were protective against high anxiety, Similar to what was stated by Kang et al. (2016), who found a connection between education levels lower than middle school and antenatal anxiety among pregnant women in China.[31] While Peng Chiong Tan's study (2010) found that only the employment status of respondents significantly predicted anxiety.[24]

By bivariate analysis for depression cases, the variables with crude P< 0.1 were age, nationality, history of hyperemesis in previous pregnancies, and educational levels. After adjustment by using multivariable logistic regression, only a history of hyperemesis in previous pregnancies was identified as an independent risk factor for high depression among our cases (AOR, 3.167 95% CI: 1.005-9.979. Similar to a study done in 2017 [22] where they found that low education levels, low income and poor social relationships were significant predictors for depression and HG. Tan et al found that the only independent protective factor for developing depression was the history of miscarriage.[23] In 2012, Hizli et al. evaluated the impact of HG and socio-demographic variables on depression. They reported the incidence of depression as 80% in the HG group and 5% in the control group. While a young maternal age and poor family interactions were weaker predictors of depression.[31]

More than half 69.7% of the women were admitted for more than 4 days at the time of the study, 77 (57.5%) women had ketonurea +3 to +4, 38 (42.6%) had hyponatremia, 47 (52.8%) had hypokalemia, 35 (39.3%) of the women were anaemic, one patient had a high level of hematocrit and 11 (12.4%) women had leukocytosis. None of the patients had high creatinine levels, but one patient had high urea levels. Out of all the studied laboratory markers and clinical severity of HG, only hypokalemia was positively associated with high anxiety. This association was statistically significant (P<0.05). None of the studied markers were associated with the occurrence of high depression. While in a study done by Tan et al. [24,] only a high hematocrit on hospitalization was positively associated with cases of depression. It is recommended that attention is paid to the psychological aspect of women with HG, who may improve with some behavioral therapy as presented in Iancu et al., a 1994 study which stated that psychotherapy, hypnotherapy and behavior therapy have been reported to contribute to the treatment of patients with HG.[29]

5. CONCLUSION

High levels of both depression and anxiety were recorded among cases of hyperemesis at the Benghazi Medical Center. There was a strong association and overlap between anxiety and depression cases. While Libyan nationality and a history of hyperemesis in previous pregnancies were associated with the occurrence of anxiety, out of all of the studied laboratory markers and clinical severity of HG, only hypokalemia was positively associated with a high occurrence of anxiety. In addition, maternal education and pregnancy planning were found to be protective against high anxiety.

Acknowledgement

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