Original Article
Analysis of outcomes in hospitalized pregnant patients with acute myeloid leukemia

Sunny J Patel, Germame Ajebo, Vamsi Kota, Achuta K Guddati

Division of Hematology/Oncology, Georgia Cancer Center, Augusta University, Augusta, GA 30909, USA

Abstract: Background: There have been significant advances in the management of acute myeloid leukemia (AML) in the past decade. However, management of AML in the pregnant patient has been challenging as most interventions are contraindicated in pregnancy. Medical termination of pregnancy is advocated over chemotherapy in the first trimester as delaying chemotherapy could often be fatal. Chemotherapy during second and third trimesters may be provided with close surveillance of fetal abnormalities. The outcomes in these patients have not been systematically studied and have been limited to case reports and case series in medical literature. Methods: Patients hospitalized with a diagnosis of AML were identified using the International Classification of Disease (ICD-9) codes in the National Inpatient Sample database. This database is maintained by the Agency of Healthcare Research Quality under the United States Department of Health and Human Services. It represents 20% of all hospitalizations occurring in the United States every year. Amongst these AML patients, all patients who were pregnant were identified and their demographic information was extracted. Other details related to their hospitalization, hospital size, location, region and teaching status were also determined. The association of outcomes with common medical comorbidities was studied. Pregnancy related outcomes, mode of delivery and mortality rates were calculated for the 15 year time period. Results: During the time period of 2000 to 2014, 678942 hospitalizations involved AML patients of which 5076 were noted to be from pregnant women. The hospitalization trend gradually increased over these years and was noted to be the highest in the age group of 18-34 years. The highest hospitalization rates were noted in African American and Native American patient populations. Hypertension, hyperlipidemia, chronic kidney disease and smoking were noted to be more prevalent in pregnant women with AML. A majority of these patients had a Charlson's comorbidity index of 1-3. 3.5% of patients underwent medical termination of pregnancy, 16.25% suffered from pregnancy related complications, 0.6% suffered from puerperal infection, 4% of patients had normal vaginal delivery, 2.8% of patients had caesarian section and 5.7% of patient died. The rate of mortality was the highest in Native Americans followed by Caucasians. Multiple regression showed that odds of mortality have decreased from 2000 to 2015 and that a higher Charlson's comorbidity score was an independent predictor of mortality. Conclusions: This is the first nationwide study to document the outcomes of pregnancy in hospitalized AML patients. AML in pregnancy is rare and this study shows that the mortality has been improving over the past 15 years. Notably, vaginal delivery has been more common than caesarian section in pregnant AML patients. Native Americans have high prevalence and high mortality rates, a likely result of healthcare disparity. Pregnant AML patients with high Charlson's comorbidity score may benefit from aggressive management of their comorbidities. Further studies are required to better characterize outcomes in pregnant women with AML.

Keywords: Acute myeloid leukemia, pregnancy, outcome, treatment

Introduction

Acute myeloid leukemia (AML) is a hematologic malignancy characterized by the rapid growth and immature differentiation of abnormal myeloid cells within the bone marrow, blood, and surrounding tissues. AML is the most common form of leukemia occurring in adults, generally affecting older patients with a median age of approximately 68 years. While it has a predisposition for older patients, hematologic malignancies like AML are the third most common form of cancer found in pregnant women behind breast and cervical cancer [1]. AML accounts for approximately two-thirds of all acute leukemia cases in pregnancy. Its incidence is estimated to be 1/75000-1/100000 pregnancies [1, 2].

Although virtually incurable 50 years ago, improvements in the prognosis of patients with AML have been noted even though therapeutic management has not changed significantly in >30 years [3]. Very minimal progress has been made in the development of new drugs for this particular type of leukemia. Adjusting for age and other prognostic factors, intensive induction therapy with an anthracycline (i.e. daunorubicin) and the anti-metabolite cytarabine continues to be the most common standard treatment for complete remission. Additional treatments such as high-dose cytarabine or hematopoietic stem cell transplants can be incorporated to reduce tumor burden and maintain remission as well [3, 4]. Enhancements in timely diagnosis and initiation of therapy along with more supportive management involving prophylaxis and treatment of infections during therapy have contributed to an improved outlook for patients suffering from this deadly cancer [4]. However, the management of AML during pregnancy imposes a unique challenge. Leukemia in a pregnant woman can have devastating consequences on not only the pregnant patient but also the fetus. AML can cause leukocytosis, thrombosis, and coagulopathy [5], all of which increase mortality significantly. In addition to potential complications in the mother, leukemia in a pregnant woman increases fetal risk for abortion, intrauterine growth restriction, and perinatal mortality due to a higher likelihood of infections from a pancytopenic state and possible placental ischemia [3, 6, 7]. Treatment of AML in early pregnancy particularly around gestation and the first trimester is almost just as harmful. Chemotherapy administered within the first trimester is associated with the greatest risk of miscarriage, fetal death and congenital malformation [8, 9]. Yet, given the aggressive nature of the disease, AML diagnosed during early pregnancy requires an immediate therapeutic intervention to prevent rapid morbidity and mortality [10]. Unfortunately, both the therapeutic and side effects of cytotoxic agents can cause unwanted fetal damage as chemotherapy can cross the placenta. Drugs like cytarabine and anthracyclines are specifically known to cause fetal abnormalities [11-13]. Cytarabine in particular is extremely teratogenic and is associated with limb malformations [12, 14]. Evidence also exists that chemotherapy may cause neonatal low birth weight as well but the data is based on limited

retrospective studies and case reports [12]. Given these potential teratogenic consequences of chemotherapy administration, it is better to provide chemotherapy during the second and third trimester of pregnancy, during which time administration with close surveillance is most safe although risks for stillbirths and low birthweight are present [3, 10, 15, 16]. An option for therapeutic termination should also be presented to patients given the inherent risks associated with treatment and possible likelihood of fetal anomalies [3]. Thus, the management of AML in pregnant patients is challenging as multiple factors have to be taken into account.

While the potential issues of AML in pregnancy have been well-explored from a therapeutic management standpoint that assesses the effects of chemotherapy on the mother and fetus, very little evidence exists regarding overall outcomes in this patient population. Several authors have attempted to clarify outcomes in pregnant women with AML tumors, but population-based studies addressing this scenario are lacking. It has been reported that pregnant patients with AML have worse outcomes compared to non-pregnant age-matched female patients with AML. One meta-analysis evaluated a cohort of 138 pregnant females with AML and found that overall survival in the group was 30% lower [17]. Yet, while such outcomes in these patients are reported, they have not been systematically studied likely due to the general rarity of hematologic malignancy in pregnancy. This in turn provides a narrow understanding of AML and its management in pregnancy. Previous estimates, demographics, clinical manifestations and outcomes regarding AML in this patient population have been limited to retrospective series and case reports and thus lacked the power to draw statistically significant conclusions [5, 6, 10, 15, 17].

The primary goal of this study is to document the outcomes of pregnancy in hospitalized AML patients. We hope to assess the prevalence of AML in pregnant patients across the United States as well as identify any statistically significant trends and associations between AML in pregnancy and mortality with respect to patients' gender, race, modes of delivery, pregnancy outcomes, and common comorbidities like hypertension, hyperlipidemia, diabetes,

and chronic kidney disease, atrial fibrillation, and smoking. Recognition and awareness of such contributing factors along with an improved understanding of mortality rates may help us more appropriately risk stratify patients in the hopes of providing better management of this patient population.

Methods

Data source

The current study is a cross-sectional analysis of in-hospital data from the years 2000-2014 obtained from the National Inpatient Sample (NIS) database. NIS is a database maintained by the Agency for Healthcare Research and Quality as part of the Healthcare Cost and Utilization Project. It represents the largest publicly available collection of longitudinal inpatient hospital care data in the United States. The NIS consists of data from approximately 20% sampling of inpatient admissions to acute care hospitals in the United States. It is stratified by geographic region, urban/rural location, teaching status, and hospital bed size to minimize sampling bias. Each admission is weighted to make NIS representative of nationwide hospital systems. Patient's demographics, primary and secondary diagnoses, Clinical Modification (ICD-9-CM) diagnosis and procedure codes, resource utilization and clinical outcomes are reported in the database. The data within the NIS is publicly available and does not contain any identifying information, making this retrospective study exempt from review by the Institutional Review Board. The retrospective nature of studying de-identified patient data, lack of direct patient contact or intervention also makes this study exempt for ethics committee and from the requirement of patient consent.

Data extraction

Records of any admissions with a principal diagnosis of AML were obtained. The current procedural terminology code (CPT) for AML were utilized to ensure inclusion of all patients with AML. Amongst these AML patients, all patients who were pregnant were identified. Pregnant women were defined as those women who had not yet delivered prior to admission. Demographic information consisting of age, gender, race, comorbidities was extracted from patients that met this criterion. Other details

related to their hospitalization, hospital size, location, region and teaching status were also determined. The extent of common medical comorbidities such as hypertension, hyperlipidemia, diabetes, chronic kidney disease atrial fibrillation, and smoking was studied in this patient population. Comorbidities were itemized and assessed using the Charlson Comorbidity Index (CCI) [18, 19]. CCI is a composite measure of the patient's health status based on chronic conditions. Pregnancy-related outcomes, mode of delivery and mortality rates were calculated for the 15-year period as well.

Statistical analysis

Descriptive statistics were used to estimate the national rate of AML among pregnant women. We assessed the distribution of socio-demographic, behavioral, hospital characteristics, selected clinical conditions, and pregnancy outcomes to explore differences in baseline characteristics. We categorized maternal age in years into five clinically consequential categories: 18-34, 35-49, 50-64, 65-79, ≥80. Race was determined by self-reported ethnicity. The primary payer for each hospitalization was classified into private (commercial carriers and private HMOs and PPOs), Medicare, Medicaid, self-pay, and other. Hospital characteristics assessed included US geographic region (Northeast, Midwest, South, or West) and size dependent on hospital occupancy. Categorical group comparisons were made using Pearson χ^2 tests. Survey logistic regression analyses were used to estimate odds ratios and 95% confidence intervals for the association between pregnant patients with AML and each outcome of interest. This was used to determine independent predictors of mortality. Covariates were picked based on a review of the literature and included year, age, race, sex, comorbidities, CCI, hospital characteristics, insurance, and pregnancy outcomes and complications. Statistical significance was defined as a *P* value of <0.05. All statistical analysis was performed using STATA software version 14.2 (College Station, TX).

Results

Patient demographics

In the 15-year period from 2000 to 2014, there were 678,942 hospitalizations involving AML patients of which 5076 (0.75%) were noted to
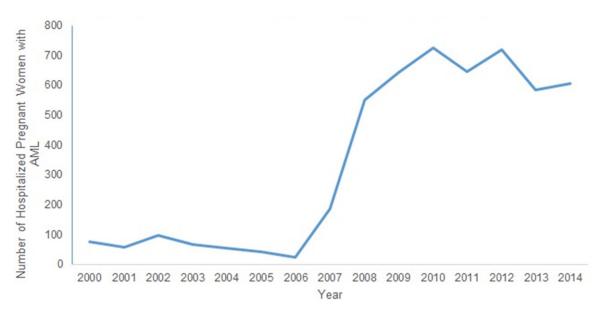
Figure 1. Hospitalization trend in pregnant women with AML.

be of pregnant women. The trend of hospitalizations for AML and specifically pregnant women with AML gradually increased over these years (**Figure 1**). Hospitalizations were noted to be the highest in the age group of 18-34 years. The prevalence of AML was highest amongst Caucasians, African American and Native Americans with a statistically significant difference (P=0.001). There was no significant difference in rate of hospitalizations between different hospital sizes (small vs. medium vs. large) and geographical location (Northeast vs. Midwest vs. South vs. West). Hypertension, hyperlipidemia, chronic kidney disease and smoking were noted to be more prevalent in pregnant women with AML. A majority of these patients had a burden of medical comorbidities as measured by the Charlson comorbidity index of 1-3. 3.5% of patients underwent medical termination of pregnancy, 16.25% suffered from pregnancy related complications, 0.6% suffered from puerperal infection, 4% of patients had normal vaginal delivery, 2.9% of patients had cesarean section and 5.7% of patient died. **Table 1** illustrates the summary statistics for demographic, clinical, hospital, and pregnancy factors.

Multivariate analysis

We assessed whether certain demographic, behavioral, hospital, and clinical conditions were associated with an increased odds of mortality using multivariable logistic regression. The rate of mortality was the highest in Native Americans followed by Caucasians. Mortality in these patients was also not related to hospital size or geographical location. Multiple regression showed that odds of mortality have decreased from 2000 to 2015 and that a higher Charlson comorbidity score was an independent predictor of mortality (OR=1.65). These data are summarized in **Table 2**.

Discussion

AML is an aggressive hematologic cancer of the bone marrow and blood characterized by uncontrolled proliferation of immature blood cells. Although AML mostly occurs in older patients, it can be seen in women of childbearing age. The objective of our study was to evaluate the outcomes of pregnant women with AML utilizing a nationwide population-based study. In the present study, we investigated pregnancy outcomes in more than 5,000 hospitalizations in pregnant women with AML. To date, there are no such large population-based studies of outcomes in hospitalized patients with AML. Our results indicate that AML is rare in pregnant patients, but cases of hospitalization have increased over the 15-year period. This may be the direct result of increased surveillance of patients not only during pregnancy but also prior to pregnancy through regular doctor's visits and checkups. Diseases like AML may inad-

Table 1. Characteristics of pregnant patients with active AML

Characteristic	Patients, No. (%)	P value
Sex		<.0001
Male	3494 (52.9%)	
Female	3114 (47.1%)	
Age, years		<.0001
18-34	1070 (21.1%)	
35-49	453 (8.9%)	
50-64	973 (19.2%)	
65-79	1717 (33.8%)	
>80	864 (17.0%)	
Race		<.0001
White	3440 (67.8%)	
African American	465 (9.2%)	
Hispanic	344 (6.8%)	
Asian/Pacific Islander/other	135 (2.7%)	
Native American	165 (3.3%)	
Unknown	527 (10.4%)	
Primary expected payer		<.0001
Medicare	2636 (52.0%)	
Medicaid	655 (12.9%)	
Private insurance	1602 (31.6%)	
Self-pay	63 (1.2%)	
Other	116 (2.3%)	
Comorbidity		
Atrial fibrillation	479 (9.4%)	
Hypertension	1963 (38.7%)	
Diabetes	712 (14.0%)	
Hyperlipidemia	894 (17.6%)	
Chronic renal failure	433 (8.5%)	
Smoking	794 (15.6%)	
CCI		<.0001
0	269 (5.3%)	
1-3	3772 (74.3%)	
4-6	884 (17.4%)	
>6	152 (3.0%)	
Hospital characteristics		
Region		0.29
Northeast	1159 (22.8%)	
South	1841 (36.3%)	
Midwest	1254 (24.7%)	
West	823 (16.2%)	
Bed Size		0.67
Small	527 (10.5%)	
Medium	817 (16.2)	
Large	3684 (73.3%)	
Pregnancy outcomes		

vertently be screened for by basic lab tests like CBC done in medical offices. Yet, although hospitalizations have increased, mortality from AML has improved over years. This general trend in survival can be attributed to supportive care, including better blood transfusion support and improved infection prophylaxis, and better success in detecting cancer earlier in its disease course and providing the necessary treatment resulting in more favorable prognoses [3, 20].

AML was also found to be more prevalent in Caucasians, African Americans, and Native Americans. In general, whites have a higher age-adjusted incidence of disease compared to other ethnic groups [21]. Taking this into account along with the improved therapeutic management of AML in recent years, this may contribute to the increased prevalence that was noted in our study. However, our study also found that rates of mortality were higher in Native Americans and Caucasians. This is consistent with a study that looked at over one million patients and noted rising trends in maternal morbidity among Native Americans. The study concluded that this may be due to healthcare disparities resulting in maternal comorbidities that severely impact mortality [22]. While it is plausible to understand the increased risk in Native Americans, it is surprising that African Americans were not found to have a higher rate of mortality, especially given the fact that multiple studies evidence minorities to have worse clinical outcomes [21, 23]. Being African American and having certain healthcare disparities such as residing in an area with a high poverty level and being covered only by Medicaid, have been found to be independent predictors of worse survival in AML [21, 24].

In addition to increased prevalence in certain demographics, our study also illustrated that common medical comorbidities like hypertension, hyperlipidemia, chronic kidney disease and smoking were more prevalent in pregnant

Abortion	181 (3.6%)	<.0001
Pregnancy complications	825 (16.3%)	<.0001
Labor	216 (4.3%)	<.0001
Puerperal infection/sepsis	29 (0.6%)	<.0001
Puerperium	125 (2.5%)	<.0001
Delivery by normal vaginal delivery	204 (4.0%)	<.0001
Delivery by caeserian section	145 (2.9%)	<.0001
Died during hospitalization	288 (5.8%)	<.0001

Table 2. Independent predictors of in-hospital mortality in pregnant patients with AML

Predictor	Odds ratio (95% confidence interval)	P Value
Year		
2001	1.04 (0.93-1.16)	0.52
2002	0.94 (0.82-1.08)	0.37
2003	0.90 (0.78-1.03)	0.12
2004	0.95 (0.84-1.08)	0.46
2005	0.87 (0.75-1.00)	0.06
2007	0.76 (0.67-0.86)	0.05
2008	0.79 (0.70-0.88)	0.048
2009	0.72 (0.64-0.82)	0.045
2010	0.64 (0.56-0.72)	0.04
2011	0.66 (0.59-0.75)	0.04
2012	0.63 (0.56-0.70)	0.04
2013	0.62 (0.55-0.69)	0.04
2014	0.64 (0.57-0.71)	0.04
Comorbidity		
Atrial fibrillation	1.62 (1.53-1.72)	0.05
Hypertension	0.73 (0.67-0.80)	0.01
Diabetes	0.77 (0.73-0.81)	0.02
Hyperlipidemia	0.67 (0.64-0.71)	0.02
Chronic renal failure	0.73 (0.67-0.80)	0.03
Smoking	0.57 (0.53-0.61)	0.2

women with AML. Comorbidity burden has been shown to be an important predictor of outcome in cancers like AML, particularly in older patients [25-27]. However, literature is scant on comorbidities in young pregnant patients with cancer. A few studies investigated medical comorbidities in pregnant women and revealed that pregnant women with medical comorbidities are more likely to have adverse medical outcomes and higher mortality rates due to increased chances of complications [23, 28, 29]. Our research supports these studies and further suggests that a higher CCI in pregnant women is an independent predictor of mortality. It is evident that the presence of comorbidities in cancer patients can signifi-

cantly impact their outcome. Investigating and managing individual comorbidities in pregnant patients with AML can improve risk stratification and provide better strategies to help diminish treatment complications.

AML in a pregnant patient is also noted to exacerbate the risk of abortion, fetal wastage, and perinatal mortality along with increasing the chances for general pregnancy complications for the mother and fetus [6]. In this study, 16.25% of patients with AML had complications, much lower than the anticipated risk of 40-50% acknowledged by other studies [10]. Only 3.5% of patients decided to undergo medical termination, possibly indicating that more patients are willing to pursue treatment given advancements in therapeutic management of the disease. Mortality rates also remained congruent with past data. Survival rates of both mother and fetus following delivery at ≥28 weeks gestation are >90% in most large medical centers and even higher, around >95%, if the delivery occurs at ≥32 weeks gestation [5, 30]. In terms of mode of delivery in the hospital, patients with AML were more likely to undergo vaginal delivery compared to caesarean section. This is preferable regardless of a history of malignancy given the lower risks of infection and quicker recovery [30].

As recommended by recent guidelines [30], pregnant patients with AML should be educated about their diagnosis, the treatment and its implications, and the possible complications during pregnancy and must be managed by a multidisciplinary team consisting of hematologists, obstetricians, neonatologists and anesthetists to optimize a successful pregnancy outcome. The results of this study elucidate associated risks that affect the general outcomes of hospitalized pregnant patients battling AML in the hopes of improving outcomes in this patient population.

Strengths & limitations

The observational retrospective study design and use of the NIS database have several important strengths and limitations in this study. A major strength of this study is the utilization of a large nationwide sample size, which is representative of most hospitalizations across the US. Limitations include the possible erroneous entry of ICD-9-CM diagnostic and procedural

codes by hospital systems and clinicians, insufficient coding of medical conditions, and the inability to assess follow-up data after a patient is discharged from her respective hospital. The NIS unfortunately limits the amount of detailed clinical data that can be obtained about outcomes and increases the likelihood of potential coding errors that can skew data results [31]. Moreover, there is also the possibility that the same patients may have been counted multiple times in this study since the database only provides data based on admissions, not individuals. Thus, some women may have had multiple admissions during their pregnancy.

Conclusions

The study uses a large, nationally representative cohort to describe outcomes and trends in all hospitalized pregnant patients with AML. To our knowledge, this is the first nationwide study to document such data in hospitalized AML patients in the Unites States. Our study found that AML in pregnancy is rare. Certain ethnic groups like Caucasians and Native Americans are more likely to suffer from this disease with higher rates of mortality, likely due to healthcare disparities. Pregnant AML patients were more likely noted to have medical comorbidities and thus a higher Charlson comorbidity score, which was also found to be an independent predictor of mortality in this patient population. Vaginal delivery was also noted to be more common than cesarean section in pregnant AML patients. The results of this investigation may lead to further research into significant predictors of mortality and assist in creating a more specific and accurate personalized risk stratification for pregnant patients with AML.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Achuta K Guddati, Division of Hematology/Oncology, Georgia Cancer Center, Augusta University, 1411 Laney Walker Blvd, Augusta, GA 30909, USA. Tel: 312-404-8928; E-mail: aguddati@augusta.edu

References

[1] Pavlidis NA. Coexistence of pregnancy and malignancy. Oncologist 2002; 7: 279-87.

[2] Ferrara F and Schiffer CA. Acute myeloid leukaemia in adults. Lancet 2013; 381: 484-495.

[3] Döhner H, Estey EH, Amadori S, Appelbaum FR, Büchner T, Burnett AK, Dombret H, Fenaux P, Grimwade D and Larson RA. Diagnosis and management of acute myeloid leukemia in adults: recommendations from an international expert panel, on behalf of the European LeukemiaNet. Blood 2010; 115: 453-474.

[4] Döhner H, Estey E, Grimwade D, Amadori S, Appelbaum FR, Büchner T, Dombret H, Ebert BL, Fenaux P and Larson RA. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. Blood 2017; 129: 424-447.

[5] Fracchiolla NS, Sciumè M, Dambrosi F, Guidotti F, Ossola MW, Chidini G, Gianelli U, Merlo D and Cortelezzi A. Acute myeloid leukemia and pregnancy: clinical experience from a single center and a review of the literature. BMC Cancer 2017; 17: 442.

[6] Avivi I and Brenner B. Management of acute myeloid leukemia during pregnancy. Future Oncol 2014; 10: 1407-1415.

[7] Sheikh SS, Khalifa MA, Marley EF, Bagg A and Lage JM. Acute monocytic leukemia (FAB M5) involving the placenta associated with delivery of a healthy infant: case report and discussion. Int J Gynecol Pathol 1996; 15: 363-366.

[8] Thomas X. Acute myeloid leukemia in the pregnant patient. Eur J Haematol 2015; 95: 124-136.

[9] Vandenbroucke T, Verheecke M, Fumagalli M, Lok C and Amant F. Effects of cancer treatment during pregnancy on fetal and child development. Lancet Child Adolesc Health 2017; 1: 302-310.

[10] Chelghoum Y, Vey N, Raffoux E, Huguet F, Pigneux A, Witz B, Pautas C, de Botton S, Guyotat D and Lioure B. Acute leukemia during pregnancy: a report on 37 patients and a review of the literature. Cancer 2005; 104: 110-117.

[11] Germann N, Goffinet F and Goldwasser F. Anthracyclines during pregnancy: embryo-fetal outcome in 160 patients. Ann Oncol 2004; 15: 146-150.

[12] Milojkovic D and Apperley JF. How I treat leukemia during pregnancy. Blood 2014; 123: 974-984.

[13] Wagner V, Hill J, Weaver D and Baehner R. Congenital abnormalities in baby born to cytarabine treated mother. Lancet 1980; 316: 98-99.

[14] Cardonick E and Iacobucci A. Use of chemotherapy during human pregnancy. Lancet Oncol 2004; 5: 283-291.

[15] Greenlund LJ, Letendre L and Tefferi A. Acute leukemia during pregnancy: a single institu-

tional experience with 17 cases. Leuk Lymphoma 2001; 41: 571-577.

[16] Zuazu J, Julia A, Sierra J, Valentin MG, Coma A, Sanz MA, Batlle J and Flores A. Pregnancy outcome in hematologic malignancies. Cancer 1991; 67: 703-709.

[17] Horowitz NA, Henig I, Henig O, Benyamini N, Vidal L and Avivi I. Acute myeloid leukemia during pregnancy: a systematic review and meta-analysis. Leuk Lymphoma 2018; 59: 610-616.

[18] Charlson ME, Pompei P, Ales KL and MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987; 40: 373-383.

[19] Deyo RA, Cherkin DC and Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 1992; 45: 613-619.

[20] Zawam H, Salama R, Alsirafy S and Bishr M. Treatment outcome of acute myeloid leukemia in Egypt: a developing country perspective. Int J Cancer Tremnt 2018; 1: 53-59.

[21] Kirtane K and Lee SJ. Racial and ethnic disparities in hematologic malignancies. Blood 2017; 130: 1699-1705.

[22] Fridman M, Korst LM, Chow J, Lawton E, Mitchell C and Gregory KD. Trends in maternal morbidity before and during pregnancy in California. Am J Public Health 2014; 104 Suppl 1: S49-S57.

[23] Master S, Mansour R, Devarakonda SS, Shi Z, Mills G and Shi R. Predictors of survival in acute myeloid leukemia by treatment modality. Anticancer Res 2016; 36: 1719-1727.

[24] Byrne MM, Halman LJ, Koniaris LG, Cassileth PA, Rosenblatt JD and Cheung MC. Effects of poverty and race on outcomes in acute myeloid leukemia. Am J Clin Oncol 2011; 34: 297-304.

[25] Etienne A, Esterni B, Charbonnier A, Mozziconacci MJ, Arnoulet C, Coso D, Puig B, Gastaut JA, Maraninchi D and Vey N. Comorbidity is an independent predictor of complete remission in elderly patients receiving induction chemotherapy for acute myeloid leukemia. Cancer 2007; 109: 1376-1383.

[26] Salako O, Okediji PT, Habeebu MY, Fatiregun OA, Awofeso OM, Okunade KS, Odeniyi IA, Salawu KO and Oboh EO. The pattern of comorbidities in cancer patients in Lagos, South-Western Nigeria. Ecancermedicalscience 2018; 12: 843.

[27] Tawfik B, Pardee TS, Isom S, Sliesoraitis S, Winter A, Lawrence J, Powell BL and Klepin HD. Comorbidity, age, and mortality among adults treated intensively for acute myeloid leukemia (AML). J Geriatr Oncol 2016; 7: 24-31.

[28] Adeoye IA, Onayade AA and Fatusi AO. Incidence, determinants and perinatal outcomes of near miss maternal morbidity in Ile-Ife Nigeria: a prospective case control study. BMC Pregnancy Childbirth 2013; 13: 93.

[29] Nair M, Kurinczuk J, Brocklehurst P, Sellers S, Lewis G and Knight M. Factors associated with maternal death from direct pregnancy complications: a UK national case-control study. BJOG 2015; 122: 653-662.

[30] Ali S, Jones GL, Culligan DJ, Marsden PJ, Russell N, Embleton ND and Craddock C; British Committee for Standards in Haematology. Guidelines for the diagnosis and management of acute myeloid leukaemia in pregnancy. Br J Haematol 2015; 170: 487-495.

[31] Foley SM, Daley J, Hughes J, Fisher ES and Heeren T. Comorbidities, complications, and coding bias: does the number of diagnosis codes matter in predicting in-hospital mortality? JAMA 1992; 267: 2197-2203.