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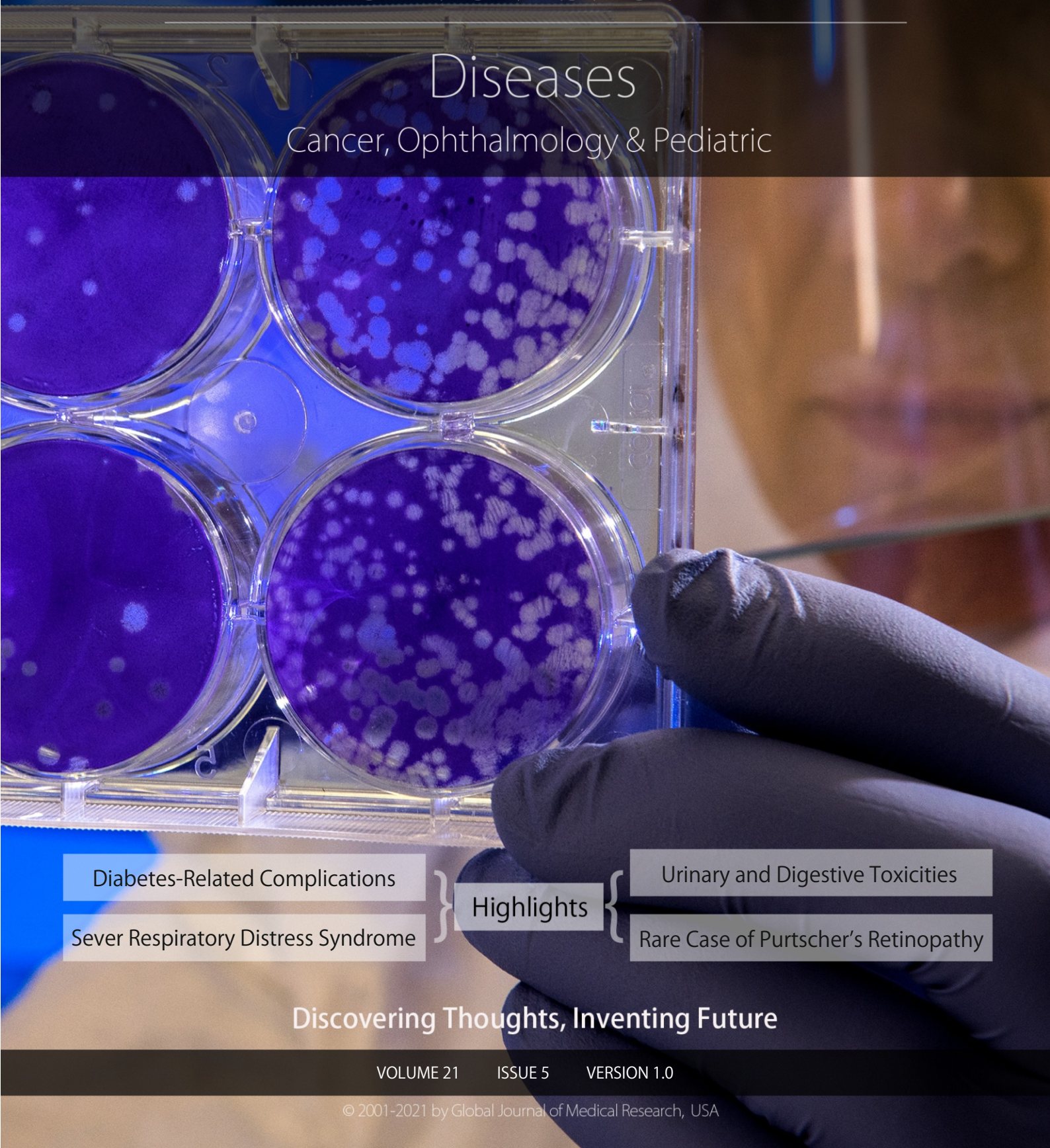

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Discovering Thoughts, Inventing Future

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Hospitalizations for Diabetes-Related Complications by Race, Gender, and Age in Maryland

By Samuel L. Brown, Ph.D., Fatou Diouf, Ph.D, Tiffany Henley, Ph.D. & Tracy Rone, Ph.D.

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Keywords: *diabetes, quality of care, hospitalizations, adverse outcomes.*

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Results: Our analysis of a statewide hospital discharge dataset uncovered differences in hospitalization rates along demographic, disease specific conditions, and insurance lines. Among Maryland hospital discharges, African Americans had significantly higher diabetes-related adverse outcomes. The racial disparity was more pronounced for African American males. The hospitalization ratio of African American males to White males ranged from 1.55 for lower limb amputation to 3.77 for uncontrolled diabetes.

Conclusion: Over twenty-five years ago, the Diabetes Control and Complications Trial demonstrated that preventive diabetes care leads to reductions in health complications and better long-term outcomes. This study uncovered significant racial disparities in potentially-avoidable hospitalizations for diabetes complications. These findings highlight the need for better primary care and for more evidence-based preventive programs for African Americans with diabetes to improve quality of care while averting costly hospitalizations.

Keywords: diabetes, quality of care, hospitalizations, adverse outcomes.

I. Introduction

Diabetes is the seventh-leading cause of death in the United States.[1] It presents a major public health problem because it affects an estimated 29.1 million people.[1] People who are diagnosed with diabetes are 1.8 times more likely to die from all causes and are more likely to experience heart attacks, kidney failure, lower limb amputation, and adult-onset blindness.[1,2] According to the Centers for Disease Control (CDC), in 2012 the estimated financial cost of diabetes in the United States was $245 billion.[1] Over $176 billion of diabetes-related expenses were spent on direct medical expenditures and $69 billion was spent on indirect costs (disability, work loss, premature death).[3]

For at least two decades the health community has known that preventive diabetes care leads to improvements in health complications and better long-term outcomes.[4] The American Diabetes Association (ADA), has established clinical guidelines directed at improving preventive care for patients with diabetes, including glycosylated hemoglobin (HbA1c) testing at least twice per year, foot examinations, and dilated eye examinations annually.[5] Despite the clinical advances in the prevention, diagnosis and treatment of diabetes, the underprivileged communities and racial minorities tend to have higher prevalence rates of diabetes and are more likely to experience diabetes-related complications.[6,7,8,9,10] As a result, federal agencies including the CDC and the NIH have delineated national goals related to diabetes in the Healthy People 2020 Objectives. Included in these objectives are reducing the number of new cases of diagnosed diabetes in the population and improving glycemic control among people with diabetes.[11] The Healthy People 2020 Objectives also established a set of goals related to diabetes incidence, mortality, and lower-extremity amputations.

While the goals of Healthy People 2020 are national in scope, local solutions are needed to address the wide variations in diabetes incidence and prevalence rates by state. In Maryland, diabetes is the sixth-leading cause of death, higher than the national figure.[12]In the first decade of the 21st century, Maryland's age-adjusted diabetes mortality rate was also higher than the national rate.[12] From 2006 to 2008, the diabetic mortality rate was 81 per 100,000 in Maryland and 74.4 per 100,000 nationwide.[12] African American females in Maryland were nearly twice as likely as White females to be diabetic (12.5% vs. 6.8%).[12]

The Behavioral Risk Factor Screening System (BRFSS) for Maryland estimated that as Maryland's population ages, residents are more likely to be diagnosed with diabetes, with the older working age population (50-64) experiencing the fastest rate of

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growth in the state.[12] According to this data, income, education, race and ethnicity are closely associated with diabetes prevalence in Maryland. The percentage of adults 18 years and older diagnosed with diabetes was higher for African Americans (12.3%) than for Whites (7.5%).[12] Income was inversely related to a diabetes diagnosis among people 18 years and older, with the highest prevalence occurring among people with an annual household income below $15,000.[12] In 2009-2010, the lowest prevalence of diabetes was among college and technical school graduates and the highest was among people without a high school diploma.[13]

In the past 20 years, the United States has seen a decline in the rates of major complications among adults diagnosed with diabetes due to prevention efforts.[13] This trend does not reflect Maryland, where from 2004 to 2008, the number of hospital discharges for coronary heart disease (CHD), a potential complication from diabetes, increased with CHD morbidity and mortality.[13] The percentage of CHD hospitalizations related to diabetes is also on the rise. We analyzed a state-level hospital discharge dataset to identify the relationship between race, age and sex and rates of diabetes-related hospitalizations to examine how changes in social determinants could alter the course of the public health problem of diabetes.

II. Methods

This study uses Maryland's hospital inpatient discharge data for 2012 from the Health Services Cost Review Commission and U.S. Census Data for Maryland. We conducted a retrospective analysis and it is limited to patients who lived in Maryland at the time of admission in 2012 with a principal diagnosis of uncontrolled diabetes (ICD-9-CM code 250.02 or 250.03); short-term complications of diabetes (ICD-9-CM codes 250.10-250.13, 250.20-250.23, or 250.30-250.33); long-term complications of diabetes (ICD-9-CM codes 250.40-250.43, 250.50-250.53, 250.60-250.63, 250.70-250.73, 250.80-250.83, or 250.90-250.93); and lower limb amputations defined as one of the following procedures based on the primary procedure code and up to 14 secondary procedure codes(ICD-9-CM codes 84.10–84.19). The focus of this study is to determine whether there are any differences in avoidable hospitalization rates of diabetes patients based on sociodemographic characteristics.

The Health Services Cost Review Commission is an independent state agency responsible for collecting and maintaining patient-level case mix data, such as hospital inpatient discharge information containing medical record abstracts of clinical demographic and billing data in Maryland. Since 1977, the agency has also set rates for hospital services. Maryland is now the only state in the nation to retain an all-payer hospital system through a federal waiver with approval from the Centers for Medicare and Medicaid Services. This unique system has led to substantial cost savings by reimbursing all payers at the same rate for hospital services, including Medicare, Medicaid, and private insurers.

The patients chosen for the study were at least 18 years of age and were categorized into five cohorts: 18–29, 30–39, 40–49, 50-50, and 60+. In terms of race, patients who were not listed as White or African American were excluded because they comprised a small percentage of patients. Since African Americans constitute 70% of the minority population in Maryland, this allowed for a more statistically significant dichotomous comparison between African Americans and Whites.[14] There were four insurance groups based on the patient's primary payer: Medicare, Medicaid, private (Blue Cross and other Commercial Insurance) and the uninsured.

The results are provided in crude data and data adjusted for the Maryland population. Standardized rates (SRs) per 10,000 persons, standardized rate ratios (SRRs), and standardized rates are reported on the adjusted hospital data. The first analysis examines diabetes-related hospitalizations and discharges to assess the effects of gender, while controlling for age and race/ethnicity. The reference groups are White, male, and patients with Medicare. The subsequent analyses explore the same effects for each of the four avoidable kinds of hospitalization: short-term complications, long-term complications, uncontrolled diabetes, and lower-limb amputation. The reference groups are White, male, Medicare for the avoidable types of hospitalization as well.

III. Results

We used four adverse outcome measures to assess avoidable hospitalizations among Marylanders with diabetes because the Agency for Healthcare Research and Quality (AHRQ) has selected them as Prevention Quality Indicators (PQI) related to diabetes care.[15] These outcome measures include (1) hospital admission for uncontrolled diabetes (PQI1), (2) hospital admission for short-term complications of diabetes (PQI2), (3) hospital admission for long-term complications of diabetes (PQI3), and (4) lower limb amputation (PQI4). A patient whose blood glucose level falls within an unacceptable range is diagnosed with "uncontrolled" diabetes. A diagnosis of short-term complications is made when a patient's complications include diabetic ketoacidosis, hyperosmolarity, and coma. Alternately, a diagnosis of long-term complications is assigned when a patient develops renal, eye, neurological, and circulatory disorders. A lower limb amputation can be below the knee, above the knee, or through the foot.

In 2012, there were more than 694,000 reported hospital discharges in Maryland. Of these, more than 139,000 (20%) were diabetes-related; 10,136 listed one of the four AHRQ Quality Indicators as the first diagnosis. When compared to the total number of hospital admissions where patients were coded as having any diagnosis of diabetes (142,000), the number of those with a principal diagnosis of diabetes was relatively small (10,136). There were, however, significant differences by race, insurance status and sex. In 2012, African Americans had higher hospital admission rates for preventable adverse outcomes than Whites.

In 2012, 7 percent of all diabetes-related hospital admissions were for an adverse but preventable condition. Of those admitted with an adverse event, 6.4 percent had uncontrolled diabetes (such as severe hyperglycemia); 17.5 percent had a lower-limb amputation; 31.6 percent had short-term complications, such as ketoacidosis; and 55.7 percent had long-term complications of diabetes—such as cardiovascular or renal complications—as the most frequent diagnosis (11.2 percent had a combination of lower-limb amputation procedure and a primary diagnosis of a complication of diabetes).

For the discharges with a principal diagnosis of diabetes considered preventable by AHRQ, the mean patient age was 55 years, the average stay was 5.1 days, and the mean inpatient charge was $13,882. Table 1 summarizes the sociodemographic characteristics for these patients by age, sex, race/ethnicity and insurance status. There is a clear dichotomy between White and African American patients with diabetes-related hospitalizations for analyzing other sociodemographic characteristics and their effects on preventable admissions.

By race, 45 percent of patients were White, and 55 percent were African American. By gender, 46.6 percent were female, and 53.4 percent were male. Combining race and gender, more White males were admitted for diabetes-related conditions than White females, and more African American males were admitted than African American females. By age, most were 64 and under; however, African American patients tended to be younger than White patients. The mean age of White patients was 57; that of African American patients was 53. In terms of insurance status, the majority of patients had Medicare. However, African Americans were more likely to be covered by Medicaid.

a) Diabetes-related Hospitalizations by Age, Sex, Race and Insurance

Diabetes-related hospital discharge rates increased with age (Table 1). Patients over 60 years of age with diabetes had more than 2.65 times the rate of preventable hospital admissions for diabetes-related conditions than did patients in the 18-to-29-year-old age group (SRD 27.02, SRR 2.67). Women had fewer diabetes-related hospitalizations and a lower rate of hospitalizations than men (SRD -6.04, SRR 0.80).

When adjustments for age and sex were computed (Table 1), African Americans were more than twice as likely as Whites to be admitted to a Maryland hospital for a preventable diabetes-related condition (SRD 25.99, SRR 2.37). The racial differences were more pronounced when examined in combination with gender. African American men had a higher rate of preventable hospitalizations than any other race/sex category (Table 1).

After adjustments for race and gender, African American males with diabetes had more than three times as many hospital admissions for adverse conditions (SRD 34.13 SRR 3.11) than White males. These race and gender differences were noted in each sex category. African American females had a higher rate of hospital admissions for adverse conditions than White females (Table 1).

A very similar pattern emerged among dually eligible patients admitted with insurance coverage under Medicare and Medicaid (because of their low-income status), and among those with no insurance coverage. African American males with no insurance were more likely to be admitted to a Maryland hospital in 2012 for potentially preventable adverse events (SRD 6.42, SRR 9.92); dually eligible African American females also were most likely to be admitted for one of these conditions (SRD 5.17, SRR 4.02).

b) Outcomes for Prevention Quality Indicator 1: Uncontrolled Diabetes

Hospital admissions for uncontrolled diabetes (PQI1) were greater among older people with diabetes. Differences in admission rates per 10,000 people statewide were greatest (SRD 1.94) and four times higher among patients 60 and over than among discharges among patients in the 18-to-29-year-old age group (Table 2). Admissions were higher among men than women (SRD 0.34, SRR 1.22). Differences in PQI1 hospital admission rates by race were similar to the patterns observed in the overall hospitalization rates. African Americans had rates of potentially avoidable hospitalizations for uncontrolled diabetes that were nearly four times those of Whites (Table 2). The racial differences persisted along gender lines: African American males had higher admission rates for PQI1 than all other race/gender categories. African American females had a higher rate than White females (Table 2). Medicare patients had higher rates than all other insurance categories.

c) Outcomes for Prevention Quality Indicator 2: Short-term Complications of Diabetes

With the exception of the risk-factor of age, similar differences were observed for preventable hospitalization rates for short-term complications of

diabetes (PQI2). Patients in the 18-to-29-year-old category had the highest admission rate (SRD 5.97, SRR 1.99), and men had a higher rate than women (SRD 1.38, SRR 1.18). The rate of hospitalizations for short-term complications of diabetes among African Americans was almost three times that of Whites (SRD 8.79, SRR 2.68). African American females had more admissions for PQI2 than White females, and African American males had the highest rate (SRD 11.56, SRR 3.21). Given the large number of younger patients admitted for short-term complication of diabetes, Medicaid was the largest provider of insurance coverage for these admissions (SRD 1.02, SRR 1.83).

d) Outcomes for Prevention Quality Indicator 3: Long-term Complications of Diabetes

Hospital admissions for the long-term complications of diabetes (PQI3) had similar differences as those for PQI1 (uncontrolled diabetes). Patients over 60 years of age had the highest rate of preventable hospitalizations (SRD 25.08, SRR8.06), and men had a higher rate than women (SRD 2.62, SRR 1.19). African Americans with diabetes experienced more preventable hospitalizations than Whites with diabetes (SRD 13.46, SRR 2.24). African American females experienced more preventable hospital admissions than White females (SRD 14.82, SRR 2.68). Medicare covered the cost of more preventable hospitalizations for PQI3 than all other insurers (Table 4).

e) Outcomes for Prevention Quality Indicator 4: Uncontrolled Diabetes (PQI1)

The patterns observed for uncontrolled diabetes (PQI4) were consistent with those of most previous PQIs (Table 4). Patients over 60 years of age experienced the highest rate of preventable hospitalizations for lower-limb amputations (SRD 10.6, SRR 54), and men had a higher rate than women (SRD 3.56, SRR 2.12). African Americans had a higher rate of amputations than Whites (SRD 2.28, SRR 1.55), although this difference was largely driven by the large disparity between African American and White men; White men had a higher rate of preventable hospitalization for lower-limb amputations than African American women. Medicare was most often the insurance provide for hospital admission for PQI4.

IV. Discussion

From 1980 through 2014, there was a fourfold increase in the number of Americans with diagnosed diabetes.[1] This increased prevalence has resulted in corresponding adverse impacts on clinical outcomes and the cost of diabetes care.[16,17] Significantly higher health care utilization and costs have been associated with people with diabetes because of the related comorbidities.[17,18] Between 2007 and 2011, researchers noted that type 2 diabetics on insulin had more comorbidities, higher hospitalization rates[19] because poor glycemic control is associated with more neurological complications, renal complications and peripheral vascular disease.[20]

Diabetes has been associated with increased morbidity and mortality.[21] It is a risk factor for cognitive changes,[22] and is often linked with patients who experience concomitant heart failure (HF).[23] Among patients with chronic HF, diabetes has been associated with worsening conditions.[23] Another risk factor of diabetes is its impact on the incidence of hospital admissions for foot ulcers. From 2005 to 2010, hospital costs increased tenfold because of the association of hospital admissions for foot ulcers and lower limb amputations.[24] People with diabetes are nearly twice as likely to experience premature death than people in the same age groups but without diabetes.[25] These factors result in higher levels of poor health outcomes, more health care utilization, and higher health care costs for patients with diabetes. For these reasons, they demand the attention of policymakers and providers.

For the past 30 years at least, African Americans have had a higher prevalence of diabetes and more complications than Whites with diabetes.[26] Racial differences have been consistently reported for diabetes-related hospitalizations. Our analysis of a statewide hospital discharge dataset uncovered differences in hospitalization rates along demographic and insurance lines. Among Maryland hospital discharges, African Americans had significantly higher diabetes-related adverse outcomes. The racial disparity was more pronounced for African American males. The hospitalization ratio of African Americans to Whites ranged from 1.55 for lower limb amputation to 3.77 for uncontrolled diabetes. There were also significant differences in hospitalization rates across jurisdictions. Baltimore City and Prince George's County, jurisdictions with large African American population, and several rural counties, had higher hospitalization rates for diabetes-related conditions. These results indicate that race is a strong predictor of preventable hospitalizations among Marylanders with diabetes. Adjustments in the analysis were made for demographic and socioeconomic factors and the racial disparities persisted.

The social determinants of the health model could explain the observed racial differences in our data. Diabetes-related preventive services could prevent hospitalizations for adverse events by delaying or preventing the onset of diabetes complications.[27] For diabetics, continuous medical care and patient self-management are needed to prevent short-term complications and reduce the risk of long-term complications that often result in substantial increases in the economic burden of diabetes.[28] Short-term complications include hypoglycemic or hyperglycemic episodes, foot ulcers, or hospital admissions. Long-term complications include kidney disease (nephropathy), nervous system damage (neuropathy), amputation or

end-stage renal disease. Preventive services such as the annual hemoglobin A1c test have been associated with fewer adverse cardiovascular outcomes in Medicare populations.[29] Hospital admission rates are also related to periodic hemoglobin A1c testing. When diabetics adhere to the recommended guidelines for HbA1c, low-density lipoprotein cholesterol, and retinal eye exam, they are less likely to have diabetes-related hospital admissions.[30] The differences we observed in our hospital discharge data may be a consequence of disparities in the utilization of preventive services.

Since we examined discharge data from the State of Maryland, there are limits to the generalizability of the study. Our findings could be confirmed with broader national sampling of discharge data, and examination of longitudinal data to overcome the limitations of this cross-sectional study. The lack of individual patient identifiers in the Maryland discharge data could have affected the results because the data are at the diagnosis and procedure levels of discharge and could reflect multiple admissions for the same patient. The observed racial differences might be biased downward because some patients are less likely to respond to questions about race and ethnicity. The lack of a racial designation has been found to be biased toward White patients.[31]

In light of the disproportionate burden of diabetes and its complications for African Americans who have higher rates of diabetes, experience more adverse outcomes, and receive fewer preventive services, it seems appropriate to develop interventions to increase the provision of preventive services and reduce diabetes prevalence among high-risk groups.

Implications for Policy & Practice

- Our findings suggest that racial disparities exist in the treatment of diabetes-related illnesses and hospitalizations can be avoided by self-management by patients and routine medical care services.
- The implementation of evidence-based preventative care programs can be a worthwhile effort to close the gap in the management of short-term and long-term complications in diabetes among gender, race, and insurance status.

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Table 1: Diabetes-Related Hospitalizations in Maryland by Age, Sex and Race, 2012

Characteristic	Frequency	SR	SRD	SRR
All	10,136			
Age Group (years)				
18-29	1,045	16.76	Reference	Reference
30-39	958	58.32	0.288	1.02
40-49	1,617	71.8	6.38	1.4
50-59	2,437	75.76	16.03	1.99
60 & over	4,075	94.41	27.03	2.67
Sex				
Male	5,408	30.9	6.02	1.24
Female	4,728	24.88	Reference	Reference
Race				
White	4565	18.94	Reference	Reference
Black	5571	44.93	25.99	2.37
Race/Gender				
White Male	2590	21.74	5.58	1.34
Black Male	2818	50.32	34.13	3.11
White female	1975	16.19	Reference	Reference
Black Female	2753	40.49	24.3	2.5

**Each category adjusted for other variables in the table.*
SR=standardized rate; SD=standardized rate difference; SRR=standardized rate ratio.

Table 2: Hospital Admissions for Uncontrolled Diabetes in Maryland by Age, Sex, Race, and Insurance 2012

Characteristic	Frequency	SR	SRD	SRR
All	618	1.69		
Age Group (years)				
18-29	38	0.58	Reference	Reference
30-39	65	1.11	0.53	1.91
40-49	125	1.74	1.16	3
50-59	152	2	1.42	3.45
60 & over	238	2.52	1.94	4.34
Sex				
Male	175	1.87	0.34	1.22
Female	290	1.53	Reference	Reference
Race				
White	211	0.88	Reference	Reference
Black	407	3.28	2.4	3.73

Race/Gender				
White Male	108	0.91	0.07	1.08
Black Male	220	3.93	3.09	4.67
White female	103	0.84	**Reference**	**Reference**
Black Female	187	2.75	1.91	3.27
Insurance				
Medicare	248	0.68	0.44	2.83
Medicaid	112	0.31	0.07	1.29
Private	130	0.36	0.12	1.5
Uninsured	86	0.24	**Reference**	**Reference**

**Each category adjusted for other variables in the table.*
SR=standardized rate; SD=standardized rate difference; SRR=standardized rate ratio.

Table 3: Hospital Admissions for Short-Term Complications of Diabetes in Maryland by Age, Sex, Race and Insurance 2012

Characteristic	Frequency	SR	SRD	SRR
All	3,004	8.2		
Age Group (years)				
18-29	776	11.98	**5.97**	**1.99**
30-39	451	7.73	1.72	1.29
40-49	586	8.16	2.15	1.36
50-59	621	8.2	2.19	1.36
60 & over	570	6.01	**Reference**	**Reference**
Sex				
Male	1,566	8.95	1.38	1.18
Female	1,438	7.57	**Reference**	**Reference**
Race				
White	1264	5.24	**Reference**	**Reference**
Black	1740	14.03	8.79	2.68
Race/Gender				
White Male	626	5.26	0.03	1.01
Black Male	940	16.79	11.56	3.21
White female	638	5.23	**Reference**	**Reference**
Black Female	800	11.76	6.53	2.25
Insurance				
Medicare	730	2	0.77	1.63
Medicaid	823	2.25	1.02	1.83
Private	760	2.08	0.85	1.69
Uninsured	450	1.23	**Reference**	**Reference**

**Each category adjusted for other variables in the table.*
SR=standardized rate; SD=standardized rate difference; SRR=standardized rate ratio.

Table 4: Hospital Admissions for Long-Term Complications of Diabetes in Maryland by Age, Sex, Race and Insurance 2012

Characteristic	Frequency	SR	SRD	SRR
All	5,622	15.4		
Age Group (years)				
18-29	230	3.55	Reference	Reference
30-39	419	7.18	3.63	2.02
40-49	814	11.33	7.78	3.19
50-59	1,456	19.22	15.67	5.41
60 & over	2,703	28.63	25.08	8.06
Sex				
Male	2,934	16.77	2.62	1.19
Female	2,688	14.15	Reference	Reference
Race				
White	2610	10.83	Reference	Reference
Black	3012	24.29	13.46	2.24
Race/Gender				
White Male	1531	12.87	4.03	1.46
Black Male	1403	25.05	16.21	2.83
White female	1079	8.84	Reference	Reference
Black Female	1609	23.66	14.82	2.68
Insurance				
Medicare	3002	8.22	7.33	9.24
Medicaid	908	2.49	1.6	2.8
Private	1038	2.84	1.95	3.19
Uninsured	326	0.89	Reference	Reference

**Each category adjusted for other variables in the table.*

SR=standardized rate; SD=standardized rate difference; SRR=standardized rate ratio.

Table 5: Lower Limb Amputations in Maryland by Age, Sex, Race, and Insurance 2012

Characteristic	Frequency	SR	SRD	SRR
All	1,783	4.88		
Age Group (years)				
18-29	13	0.2	Reference	Reference
30-39	58	0.99	0.79	4.95
40-49	207	2.88	2.68	14.4
50-59	485	6.4	6.2	32
60 & over	1,020	10.8	10.6	54
Sex				
Male	1,179	6.74	3.56	2.12
Female	604	3.18	Reference	Reference
Race				
White	991	4.11	Reference	Reference
Black	792	6.39	2.28	1.55
Race/Gender				
White Male	677	5.69	3.12	2.21
Black Male	502	8.96	6.39	3.49
White female	314	2.57	Reference	Reference
Black Female	290	4.26	1.69	1.66
Insurance				
Medicare	1046	2.87	2.63	11.96
Medicaid	249	0.68	0.44	2.83
Private	307	0.84	0.6	3.5
Uninsured	86	0.24	Reference	Reference

**Each category adjusted for other variables in the table.*

SR=standardized rate; SD=standardized rate difference; SRR=standardized rate ratio.

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Urinary and Digestive Toxicities of 3D Conformal Radiotherapy of Localized Prostate Cancer at the Pointe a Pitre University Hospital in Guadeloupe

By Ibrahima Thiam, Kanta Ka, Boucar Ndong, El Hadj Amadou Sall, Ousseynou Sarr, Mahomed Yessoufou, Awa Sadikh Badiane & Papa Macoumba Gaye

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Abstract- *Introduction:* At present, despite the advent of innovative methods such as IMRT, which improves therapeutic performance while reducing toxicity, RC3D is still widely used, especially in developing countries. The objective of this work was to evaluate the urinary and digestive toxicities of RC3D on prostate cancers located at the Pointe à Pitre University Hospital in Guadeloupe in order to position this technique in the therapeutic arsenal.

Materials and methods: We conducted a retrospective study of 29 patients with localized prostate cancer treated with RC3D. The endpoint was urinary and digestive toxicities.

Keywords: *toxicities, radiotherapy, cancer, prostate.*

GJMR-F Classification: *NLMC Code: WJ 752*

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Materials and methods: We conducted a retrospective study of 29 patients with localized prostate cancer treated with RC3D. The endpoint was urinary and digestive toxicities.

Results: Twenty-nine patients were enrolled. Their median age was 75 years. All patients were treated with RC3D +/- hormone therapy. Toxicities were assessed according to RTOG criteria. Acute toxicity was defined as all toxicities occurring during treatment and even 3 months after the end of treatment. Toxicities occurring beyond 3 months after treatment were considered late. Grade 1 acute bladder toxicity was found in 7 patients (24.14%), grade 2 in 1 patient (3.45%). Grade 1 acute rectal toxicity was found in 7 patients (24.14%). As for late bladder toxicity, it was found for grade 1 in 5 patients (17.24%), grade 2 in 3 patients (10.34%) and finally for grade 3 in 1 patient (3.45%). As for late rectal toxicity, grade 2 was found in 3 patients (10.34%) and grade 3 in 1 patient.

Conclusion: RC3D offers acceptable toxicities. However, for dose escalation with minimisation of toxicities, IMRT is better than 3D-CRT.

Keywords: toxicities, radiotherapy, cancer, prostate.

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I. Introduction

Prostate cancer is the second most diagnosed cancer in men after lung cancer with 13.7% of cases [1]. Its incidence is high in Guadeloupe [2]. The treatment of prostate cancer is multidisciplinary, with radiotherapy and surgery as the main curative methods.

Radiotherapy is said to be conformal when the dose of ionising radiation used is delivered homogeneously to a precisely defined tumor volume while sparing healthy tissue and surrounding organs as much as possible. This is achieved through initial three-dimensional imaging for location and repositioning. The precise calculation of the dose to be delivered is achieved through computer-controlled multi-blade collimators.

Thanks to the progress made by conformal radiotherapy, the results obtained are becoming similar in terms of disease control to those of surgery, as shown by several comparative series. Radiotherapy has therefore become an essential technique in the treatment of prostate cancer despite its complications, notably urinary and digestive [3]. In this paper, we evaluate these complications that arise during the management of localised prostate cancer treated with 3D conformal radiotherapy.

II. Patients and Method

a) Patients

This was a descriptive, retrospective study that took place at the Radiotherapy Department of the Pointe à Pitre University Hospital in Guadeloupe, carried out over a period of one year (January 2015 to December 2015).

A total of 29 patients consulting for localized prostate cancer with a negative distant extension assessment were treated with 3D radiotherapy plus or minus hormone therapy. These patients had not received any previous specific treatment and their characteristics are summarised in Table I.

b) Method

Data were collected using archived medical records, from the Varian Aria software and Easily from the CHU Guadeloupe. A data collection form was drawn up for this purpose.

The data were entered and analysed on Epi info 7 on Microsoft Excel 2007. Histograms and other figures were produced with Microsoft Excel 2007.

III. Results

The median age of the patients was 75 years. The most common comorbidity was hypertension, which was found in 23 patients (79.31%). The diagnosis was made on the basis of urinary symptoms in 10 patients (34%). They were generally in good general condition. The median PSA level was 12 ng/ml with extremes of 3.05 and 79 ng/ml. Histological examination revealed adenocarcinoma in all patients. The Gleason score was heterogeneous with a score of 6 (3+3) in 6 patients (20, 69%), a score of 7 (3+4) in 12 patients (41, 38%) and another score of 7 (4+3) in 11 patients (37, 93%).

A loco-regional extension assessment by MRI was performed in 26 patients (89, 66%) and contraindicated in 3 patients. On imaging, we found T3a in 5 patients (19, 23%), T3b in 4 patients (15, 38%) and lymph node involvement in 1 patient (3, 8%). Thoracoabdomino-pelvic CT was performed in 9 patients (31.03%) and scintigraphy in 25 patients (86.21%).

The D'AMICO classification was established for all patients. It is a major criterion in the therapeutic decision.

Thus, 3 patients (10.34%) were classified as low risk, 12 patients (41.38%) as intermediate risk and 14 patients (48.28%) as high risk

Among the patients classified as intermediate risk, 7 were of favourable intermediate risk and 5 unfavourable intermediate.

All our patients had received 3D conformal radiotherapy for curative purposes. It was associated or not with hormone therapy. The time to treatment was defined as the time from the date of diagnosis to the start of radiotherapy.

The median time was 5.7 months (2.3-23) and the mean time was 6.4 months.

Pelvic irradiation was performed in 15 patients (51.72%). The median total dose delivered was 74 Gy, with a mean dose of 73.79 Gy and extremes of 70 Gy for the minimum and 76 Gy for the maximum.

In all our patients, conventional fractionation was used, i.e. 2 Gy per fraction, 5 days a week.

Hormone therapy was combined with radiotherapy in 17 patients (58.62%). All patients in the D'AMICO high-risk group had received long hormonal therapy and 3 patients in the intermediate-risk group had received short hormonal therapy.

The median follow-up after radiotherapy was 56 months (28-66 months). The median follow-up was 63 months (27.5-74.3 months).

Toxicities were assessed according to the RTOG criteria. Acute toxicity was defined as all toxicities occurring during treatment and up to 3 months after the end of treatment and all those occurring beyond 3 months were late. Thus, acute bladder toxicity was found in 7 patients (24.14%) with grade 1 acute toxicity and 1 patient (3.45%) with grade 2 acute toxicity. For acute rectal toxicity, all the patients had tolerated the treatment well in terms of digestion, with grade 1 symptoms in 7 patients (24.14%), then for late bladder toxicity grade 1, we found 5 patients (17.24%), 3 patients (10.34%) for grade 2 and 1 patient for grade 3, i.e. 3.45%. And finally, for late rectal toxicity grade 2, we found 3 patients (10.34%) and 1 patient grade 3.

IV. Discussion

The constant progress of irradiation techniques has mainly allowed an increase in the dose to the target volumes and a reduction of the dose to the organs at risk. Dearnaley et al. in a randomised study reported a reduction in GI toxicity in favour of 3DR compared to conventional radiotherapy with 56% grade 1 rectitis versus 37% and 12% versus 3% for grade 2 [4]. Koper et al, with the same comparison, found less intestinal toxicity, especially in the anus, in patients treated with RC3D [5].

Pelvic irradiation is a much debated topic with conflicting results from several retrospective studies, its toxicity remains quite acceptable [3].

Several randomised studies have shown that the risk of rectal toxicity was greater when a high dose of radiation (78-80 Gy) was delivered to the prostate compared to a standard dose (70 Gy) [6,7].

Regarding urinary toxicity, most randomised studies comparing a "standard" dose (70 Gy) with a high dose (78-80 Gy) did not find a significant increase in urinary toxicity, except for the French Gétug study 06 [6-9]. The lack of a clear conclusion regarding urinary toxicity may have several explanations. The main urinary manifestations seem to be of urethral rather than bladder origin. The urethra is consistently included in the high-dose volume treated and exceptionally delineated as such (10).

The median dose in our series was 74 Gy and 51.72% of patients had received pelvic irradiation.

The radiotherapy was well tolerated by the patients, no acute urinary or digestive toxicity of grade > 2 was noted in our series as in the study by Peeters et al [9]. Indeed, acute urinary toxicity grade 1 and 2 were respectively 24.14% and 3.45% and digestive toxicity was grade 1 in 10 patients (34.48%). These results are lower than those reported by Pollack, Beckendorf, Peeters and Elie Nasr which could be explained by the

small number of patients (8,9,11,12). Late toxicity was relatively lower than in the literature (Table 2-3).

Intensity-modulated conformal radiotherapy significantly reduces late grade 2 GI toxicity without impacting on urinary toxicity with dose escalation [13]. IMRT provides better coverage of the target volume with good sparing of organs at risk, particularly for the rectum according to the study by Pascal Fenoglietto et al [14]. Wang-Chesebro et al. demonstrated with pelvic IMRT a dose reduction in the bladder, V45 Gy (volume receiving 45 Gy) of 90%, 54% for the rectum V45 Gy and 54% of the small bowel V45 Gy compared to three-dimensional conformal radiotherapy [15].

V. Conclusion

Despite the good results obtained with RC3D, intensity modulated radiotherapy (IMRT and VMAT) with rigorous verification of the treatment position is the indicated technique for the treatment of prostate cancers. It allows dose escalation to target volumes with acceptable toxicity.

Table 1: Patient characteristics

Characteristics of patients	Headcount (percent)
Median age (years)	75 (54 - 83)
HTA	23 (79.31%)
Diabetes	12 (41.38%)
Heart disease	3 (10.34%)
CRI	1 (3.45%)
Systematic screening	19 (65.52%)
Urinary signs	10 (34.48%)
Performance status 0 1 2	 20 (69%) 8 (28%) 1 (3%)
TR abnormal	15 (51.72%)
Median PSA (ng/ml)	12 (3.05 - 79)
Gleason -6 (3 + 3) -7 (3 + 4) -7 (4 + 3)	 6 (20.69%) 12 (41.38%) 11 (37.93%)
Classification of D'AMICO -High risk -Low risk -Middle risk	 14 (48.28% 3 (10.34%) 12 (41.38%)

Table 2: Frequency of urinary toxicity in the literature

	Number of patients	Dose (Gy)	Acute urinary toxicity	Median follow-up (month)	Late urinary toxicity
Beckendorf et al (8)	306	70 vs 80	G1 44% vs 42% G2 31% vs 30% G3 5% vs 7%	57	G1 22% vs 27% G2 8% vs 16% G3 2% vs 1%
Pollack et al (11)	301	70 vs 80	G1 43% vs 42% G2 31% vs 23% G3 3% vs 5%	72	≥G2 10% vs 10%
Peeters et al (9)	669	68 vs 78	G1 40% vs 42% G2 13% vs 13%	36 84	≥G2 29% vs 30% ≥G2 41% vs 40%
Elie Nasr(12)	131	66-74	G1 31,3% G2 16,8% G3 2,3%	-	-
Notre étude	29	70-74	G1 24,14% G2 3,45%	56	G1 17,24% G2 10,34% G3 3,45%

Table 3: Frequency of digestive toxicity in the literature

	Number of patients	Dose (Gy)	Acute digestive toxicity	Median follow-up (month)	Toxicité digestive tardive
Beckendorf et al (8)	306	70 vs 80	G1 43% vs 37% G2 27% vs 28% G3 2% vs 2%	57	G1 23% vs 25% G2 12% vs 16% G3 2% vs 6%
Pollack et al (11)	301	70 vs 80	G1 43% vs 39% G2 38% vs 39% G3 2% vs 0%	72	≥G2 12% vs 26%
Peeters et al (9)	669	68 vs 78	G1 41% vs 47% G2 6% vs 4%	36 84	≥G2 23% vs 27% ≥G2 25% vs 35%
Elie Nasr(12)	131	66-74	G1 27,5% G2 9,1%	-	-
Notre étude	29	70-74	G1 24,14%	56	G2 10,34% G3 3,45%

Abbreviations

3D-CRT: 3D conformal radiotherapy

IMRT: intensity modulated conformal radiotherapy

VMAT: volumetric radiotherapy arc therapy

Conflicts of interest: none

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A Novel Homozygous Mutation ABCA3gene: Presented as Sever Respiratory Distress Syndrome in a Term Neonate

By Dr. Samiya Al Hashmi, Dr. Jazel Manarang, Dr. Hussein Al Lawati & Dr. Mujtaba. A. Al Ajmi

Abstract- Congenital surfactant deficiency is a rare condition diagnosed in newborns who present with respiratory distress at birth. We report a case of a term Omani neonate with fatal surfactant protein deficiency who was admitted to the Neonatal Intensive Care Unit (NICU)of the Royal Hospital with respiratory distress syndrome with persistent interstitial infiltrates on serial chest x-ray responsive to intermittent surfactant administration. He underwent a lung biopsy, and immunohistochemistry confirmed the diagnosis of congenital surfactant protein deficiency. However, despite aggressive treatment and supportive measures, his condition rapidly deteriorated, and he succumbed after two months of admission. This case report will highlight and review surfactant deficiency differential diagnoses, management, and complications.

Keywords: surfactant deficiency, term new-born, respiratory distress syndrome, Biopsy.

GJMR-F Classification: NLMC Code: WF 140

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A Novel Homozygous Mutation ABCA3gene: Presented as Sever Respiratory Distress Syndrome in a Term Neonate

Dr. Samiya Al Hashmi [α], Dr. Jazel Manarang [σ], Dr. Hussein Al Lawati [ρ] & Dr. Mujtaba. A. Al Ajmi [ω]

Abstract- **Congenital surfactant deficiency is a rare condition diagnosed in newborns who present with respiratory distress at birth. We report a case of a term Omani neonate with fatal surfactant protein deficiency who was admitted to the Neonatal Intensive Care Unit (NICU)of the Royal Hospital with respiratory distress syndrome with persistent interstitial infiltrates on serial chest x-ray responsive to intermittent surfactant administration. He underwent a lung biopsy, and immunohistochemistry confirmed the diagnosis of congenital surfactant protein deficiency. However, despite aggressive treatment and supportive measures, his condition rapidly deteriorated, and he succumbed after two months of admission. This case report will highlight and review surfactant deficiency differential diagnoses, management, and complications.**

Keywords: surfactant deficiency, term new-born, respiratory distress syndrome, Biopsy.

I. Introduction

In preterm babies, respiratory distress is the most common manifestation of lung immaturity (less than 32 weeks of gestation), which due to deficient surfactant synthesis. Respiratory distress syndrome occurs less frequently to term infants, which may at times to warrant further investigation, especially if with non-improvement to conventional treatment and causing significant morbidity and mortality [1,4]. Pulmonary surfactant is a complex mixture of phospholipids and protein which is produced, stored, and recycled by type II pneumocytes. It found on the alveolar surface, and it functions to prevent alveolar collapsed by lowering its surface tension aiding in normal respiration. Finding respiratory distress syndrome in a term neonate would raise a suspicion of an inherited deficiency in pulmonary surfactant [2,3]. Surfactant protein deficiencies classified according to types; A3 (ABCA), B (SP-B), C (SFTPC), and SP-D. The most common type is Type A3, which was the first recognized inherited pulmonary surfactant disorder and had an autosomal recessive pattern. It is much more common to neonates and carries high mortality and morbidity rates [2,3,5]. Then it followed by surfactant protein C (SFTPC) deficiency in with an autosomal dominant pattern of inheritance and is more associated with interstitial lung disease in older children and adults. Type A3 (ABCA) is similar to Type B (SP-B) in terms of severity. We report this rare case of congenital surfactant deficiency, the first documented case of Oman to the authors' knowledge. The subject, interestingly, had a familial history of the same presentation in a sibling that died within the first few weeks of life and was not thoroughly worked up. This report can assist the clinician regarding the approach to such cases and guide counselling the parents for possible future pregnancies.

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II. Case Description

A full-term (39 weeks) male infant weighing 3120 grams was born to a 31-year-oldgravida four para three mother via spontaneous vaginal delivery. He was born vigorous with APGAR scores 8 and 9 at 1 and 5 minutes, respectively. Mother had gestational diabetes mellitus, diet-controlled with history of premature rupture of membrane two hours prior delivery without any other documented risk of sepsis. The parents are consanguineous (first cousins) and had a previous baby who as well presented with respiratory distress at birth, was admitted to the Neonatal intensive care unit, and died at two weeks of age.

On the second hour of life, the baby started to have respiratory distress, and physical examination revealed tachypnea with chest retractions and grunting. The infant transferred to the NICU for ventilator support, and complete septic workup including chest x-ray and blood gas were facilitated. The infant started on 25% inspired oxygen with flow 1.5L via nasal prongs on which capillary blood gas revealed respiratory acidosis (pH 7.27, PCO_2 55.9,HCO_3 21.8, and BE -0.9).

On admission, the chest radiograph revealed mildly hyperinflated lungs with perihilar interstitial markings (Figure 1). Succeeding chest x-ray on Day 2 showed worsening picture showing reduced lung volume and reticular infiltrations with positive air bronchogram, findings consistent with respiratory distress syndrome (RDS). He eventually required intubation for surfactant administration and was kept on ventilator assist-control mode. The baby's condition momentarily improved but

again had the worsening respiratory condition on the 3rd day of life requiring high-frequency oscillatory ventilation.

This clinical deterioration of cardio respiratory distress and temperature instability prompted repeat septic workup. Blood counts were normal, but C-reactive protein elevated. He initially treated with Cefotaxime and Vancomycin added after culture came positive for coagulase-negative staphylococcus. Repeat chest x-ray again revealed diffuse ground glass appearance for which another dose of surfactant given. Screening functional echocardiography also performed, which showed a small patent ductus arteriosus and a small fenestrated atrial septic defect secundum with mild pulmonary hypertension, which improved with sildenafil and prostaglandin nebulization.

The parents were counseled earlier on the possibility of the same condition as their previous baby and the need for subspecialty involvement. The pulmonology team was involved after the chest CT scan showed diffuse changes highly suggestive of interstitial lung disease (ILD), surfactant deficiency versus alveolar cause. Bronchoalveolar lavage also done to rule out infectious causes, but all turned out equivocal. To complete the workup, blood was sent for the whole-exome sequence together with a lung biopsy, which delayed due to the requirement of high ventilator parameters making him unsuitable for transfer to the operating theatre. In total, the baby received nine doses of surfactant, most of them offered immediate but temporary improvement in clinical status. A course of methylprednisolone and hydroxychloroquine (HCQ) tried but without any dramatic benefit.

The lung biopsy histology showed non-specific interstitial inflammation, which raised the suspicion of surfactant deficiency, and electron microscopy confirmed the diagnosis, revealing interstitial thickening with the proliferation of mesenchymal fibroblastic cells and chronic inflammatory infiltrated of lymphocytes, plasma cells, and scattered eosinophils. The parents received extensive counseling from the concerned subspecialties regarding the poor prognosis and outcome. During most of the patient's admission, the patient required high ventilatory parameters to maintain acceptable oxygen saturations. His condition was complicated with multiple bouts of clinical sepsis and bacteremia ventilated-associated pneumonia, particularly with endotracheal cultures growing *Acinetobacter baumanii* and *Klebsiella pneumonia.* On day 58 of life, despite continuous supportive and humane care, the patient succumbed to respiratory failure.

III. Discussion and Literature Review

Congenital Pulmonary Surfactant Deficiency is a condition that requires a high index of suspicion. In this report, we present a term neonate who developed severe respiratory distress within the first two hours from birth which was progressive until the third day of life. Intermittent surfactant administration offered immediate but temporary improvement of the condition; hence the possibility came into perspective. Respiratory distress syndrome (ARDS) is a common NICU diagnosis. It usually presents in preterm infants but can also occur in term babies, especially those born through a cesarean delivery or from diabetic mothers. The natural course of RDS has been well-studied which typically peaks within the first three days of life before the predictable clinical improvement. Its good response to surfactant therapy, especially those moderate to severe RDS, has also been well established. In this case, the baby presented with an RDS-like picture requiring ventilatory support in the first few days necessitating surfactant administration. However, its course was more progressive than usual, requiring high-frequency oscillatory ventilation and developing pulmonary hypertension. Serial chest radiographs, which initially showed reduced lung volume with air bronchograms, eventually revealed interstitial lung changes. With the history of a previous sibling with the same presentation who died at two weeks of life, a genetic cause suspected. Chest CT scan was requested by pulmonologist, which was suggestive of interstitial lung disease; hence multi-specialty consultation was done by neonatologist to pulmonology, genetic and surgical teams. Bronchoalveolar lavage was done to rule out infectious causes, but finally, lung biopsy confirmed the diagnosis.

Congenital surfactant deficiency is a rare genetic disorder that presents like respiratory distress syndrome but may have different clinical presentations depending on the type. Its incidence is unknown, but in the United States, it estimated at 1 in 1 million live births [1]. Several of causes can present with respiratory distress in newborns and should be excluded before arriving at the diagnosis [2,4,5]. Other differential diagnoses should be ruled out, include sepsis, wet lung, lung malformations as well as non-pulmonary causes of respiratory distress such as congenital heart diseases, among others. One subtype of surfactant protein deficiency is type B (SP-B) which is known to be a clinically progressive disease wherein most the cases lead to fatal hereditary neonatal lung disease. Alveolar capillary dysplasia is another differential diagnosis, a condition that happens due to misalignment of the pulmonary veins (ACD/MPV). It has a similar presentation to congenital surfactant deficiency, that is, occurring in term infants with respiratory distress soon after birth associated with cyanosis and severe pulmonary hypertension despite treatment [6,12]. Radiological appearance and lung biopsy help distinguish disorders of primary surfactant deficiency from other structural causes of lung disease.

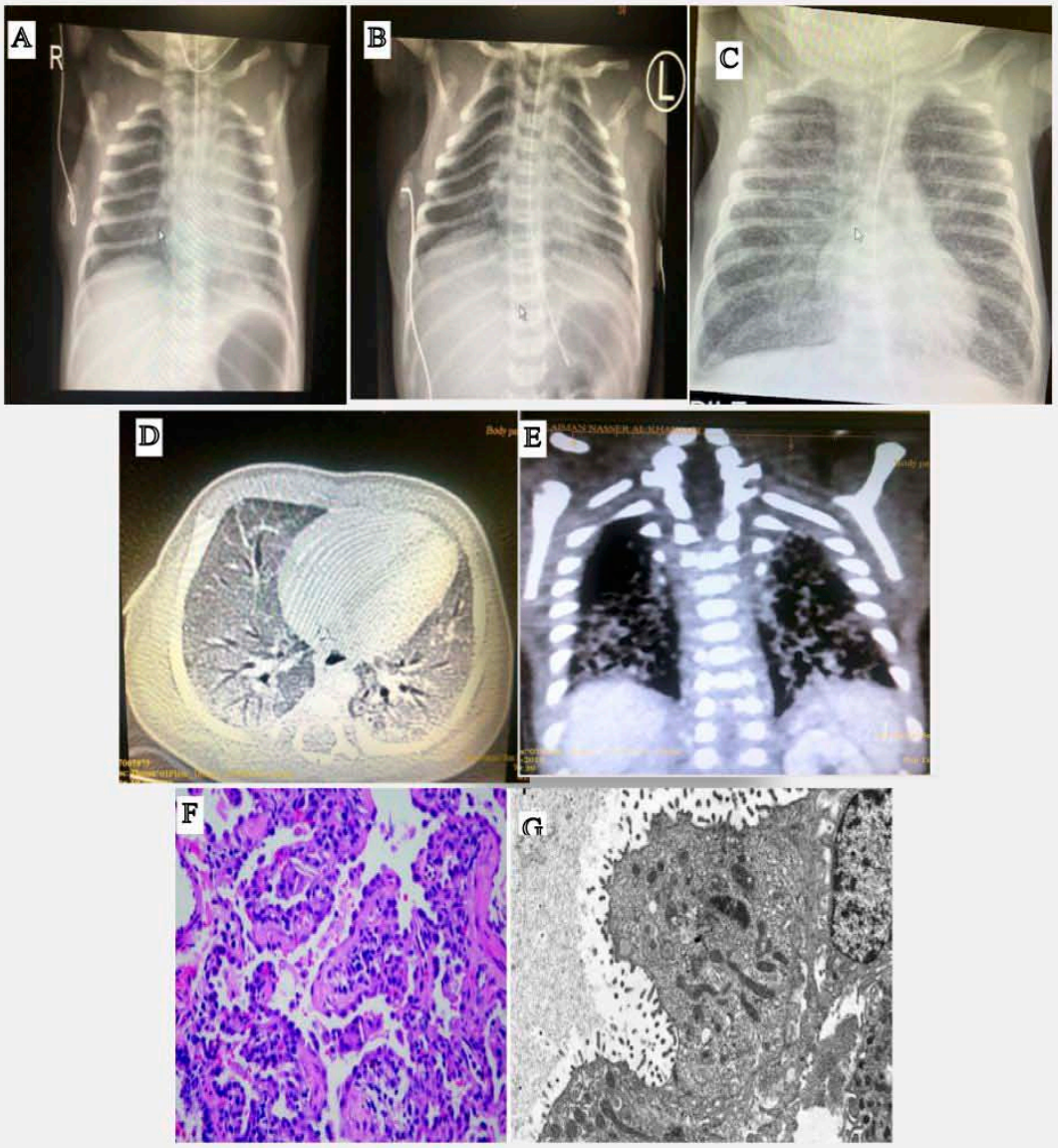

Fig. 1. Serial chest radiographs of neonate with ABCA3 deficiency. (A) At the time of admission 3hrs of age: mildly hyper-inflated lungs and mild perihilar interstitial markings. (**B**) Day 2 of life before receiving surfactant showed reduced lung volume and reticular infiltrations with positive air bronchogram (C). As is typical for the surfactant protein deficiencies, there is a hazy severe diffuse opacification. (D, E) Lung HRCT of the lungs showing patchy areas of ground-glass attenuation with thickening of interlobular septae. Histologic changes in the infant's lung in the surfactant dysfunction mutations ABCA3 -: early lobular remodeling and diffuse alveolar epithelial hyperplasia (F)Electron microscopic features of ABCA3 mutations(G): characteristic abnormal lamellar bodies with distinctive central and eccentric round dense bodies (F&G) picture, **Lee, Cleveland and Langston, 2011)**

Using electron microscopy with its ultrastructural feature provides an important point for diagnosis and helps direct further genetic study and evaluation. Histology, alveolar epithelial hyperplasia is a characteristic of surfactant deficiency in infants. Immunohistochemically, features of SP-B include unrecognizable lamellar bodies and an accumulation of abnormal appearing multivesicular bodies [1,3,6,7,]. In contrast, ABCA3 has tiny lamellar bodies with a prominent dense inclusion. The molecular gene study is providing the direction for genetic counseling among affected families to discuss the risks for future pregnancies. In families in which a mutation has been previously identified, it greatly aids in establishing even antenatal diagnosis. In this case, after confirmation of the diagnosis by lung biopsy and electron microscopy, the surfactant protein deficiency is most likely type B (SP-B), given its clinically progressive course. This definitive diagnosis was confirmed by a genetic study that was sent and reported with pathologic ABCA3 variant C.3253C>T p. (Gln1085) which is associated with autosomal recessive pulmonary surfactant metabolism dysfunction. It is also known as interstitial lung disease due to ABCA3 deficiency.

Among surfactant protein deficiencies, A3 (ABCA3) has been characterized by a variable clinical outcome ranging from fatal respiratory distress syndrome in the neonatal period to chronic interstitial lung disease developing in infancy or childhood. ABCA3 mutations are linked with a higher proportion of cases with significant positive family history the similar conditions [12.13]. Respiratory distress syndrome in term newborns can result from a deficiency in either SP-B or ABCA3 mutations with both genetic mutations having an autosomal recessive pattern of inheritance; whereas chronic ILD during infancy or early childhood can be the manifestation of either SP-C or ABCA3 mutations [11,12.13]. Despite all the supportive measures with ventilation, recurrent surfactant replacement therapy, hydroxychloroquine, and methylprednisolone, there was no improvement in the condition of the infant, and he died at the age of two months. Recurrent surfactant replacement therapy transiently improves the respiratory parameters in patients with surfactant deficiency but is not reported to be effective in the long term [6,7,8]. At present, the only curative option is lung transplantation. However, the procedure itself comes with high rates of complications, mostly with infection, thus the need for lifelong immunosuppressive drugs. [1,6,9]. Other supportive therapies available include sedation, inotropic support, high-dose glucocorticoids, and intravenous gamma globulin, which offer short-term improvement. Mechanical ventilation, HFOV, inhaled nitric oxide, and even extracorporeal membrane oxygenation may be necessary to aid oxygenation. Gene therapy is one area being looked into but yet to be established.

IV. Conclusion

In summary, a term baby presenting with respiratory distress syndrome picture should raise some suspicion of an underlying congenital surfactant deficiency, especially if it presents on a background of positive family history. Congenital surfactant protein ABCA3 deficiency is a fatal type of lung disease that requires intensive management, including ventilatory support, a trial of surfactant administration, and steroids due to its stormy clinical course. It warrants thorough evaluation with immunohistochemical and genetic studies confirming the underlying pathology. Timely establishment of the diagnosis is of utmost importance especially in educating couples on the condition's associated complications, treatment options and its guarded prognosis.

Abbreviations

NICU: Neonatal Intensive care unit: CQ: hydroxychloroquine; ILD: interstitial lung disease; SP-B: surfactant protein B; SFTPC: surfactant protein C gene, ATP-binding cassette transporter protein A3 (ABCA3) respiratory distress syndrome (RDS): HFOV high-frequency oscillatory ventilation.

Conflict of Interests

The authors declare no conflict of interest.

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Adherence to Antihypertensive Medication in a Specialist Led-Hypertension Clinic in Sub-Saharan Africa

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Abstract- Purpose: Hypertension is the biggest single contributing risk factor to global morbidity and mortality burden. Despite worldwide improvement in diagnosis and treatment options for hypertension, poor adherence remains an impediment to improving patients' overall quality of life. This study sought to investigate adherence rates in hypertensive patients and the local factors that contribute to nonadherence.

Methods: This was a hospital-based cross-sectional study conducted at the out-patient department of a hypertension specialist-led clinic in Kumasi-Ghana. The Morisky Medication Adherence Scale 8 was used to measure adherence to antihypertensive medications. Bivariate logistic regression analysis was done to measure the strength of the association between socio-demographic level, BP level, antihypertensive drug used and medication adherence score.

Keywords: hypertension; adherence; specialist-led clinics; blood pressure control; kumasi; Ghana.

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Adherence to Antihypertensive Medications

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Results: Amongst 361 participants recruited, average age was 59.74 years and majority were female (81.99%). Overall, 75.35% of participants had their blood pressures controlled. Our study found a relatively high adherence rate (57.34%) to treatment recommendations according to MMAS-8. Adherence was positively associated with older age, and negatively associated with factors such as comorbidities and the use of calcium channel blockers.

Conclusion: The high prevalence of BP control found in this study can be linked to the relatively high level of adherence found amongst the participants. Specialized-clinics that adopt a holistic and patient-centered care approach such as counseling on diet, exercise and complications of hypertension, may be an important factor in ensuring adherence.

Better adherence leads to better control which ultimately leads to improved outcomes, prolonged survival and reduction in the incidence of end organ damage from hypertension.

Keywords: hypertension; adherence; specialist-led clinics; blood pressure control; kumasi; Ghana.

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I. Introduction

Hypertension is the biggest single contributing risk factor to global morbidity and mortality burden[1]. As a disease entity which affects approximately one-third of adults globally, cardiovascular (CV) disease represents the largest epidemic ever experienced by mankind [1]. According to Lim and colleagues, raised blood pressure (BP) currently causes approximately 9.4 million deaths each year worldwide and this figure is expected to rise, given an expanding and aging global population[1]. Hypertension is defined as having a persistently elevated systolic blood pressure of 130mmHg or above and/or a diastolic of 80mmhg and above. It affects about one billion people worldwide[2]. Several drug classes have been shown to provide cost-effective BP lowering for the prevention of the adverse CV sequelae of raised BP.

Despite the availability of these antihypertensive medications, global data suggest that less than half of those classified as hypertensive are aware of their problem[3]. Furthermore, less than a third of those who are treated for hypertension get their BPs controlled to currently recommended targets[3]. In Ghana, the prevalence of hypertension ranges from 19% to 48% between studies[4]. Old age, over-nutrition and alcohol consumption were some of the factors independently associated with hypertension[4]. According to a 2010 study by Bosu and others, less than one-third of hypertensives were aware of their condition and less than one-tenth had their blood pressures controlled even though there has been a trend towards improved awareness, treatment and control between 1975 and 2005[4]. Due to the asymptomatic nature at onset, diagnosis and adherence to treatment recommendation

is often challenging. Treatment of hypertension requires lifestyle modifications and medications or a combination of both.

Adherence is defined as the extent to which a person's behavior corresponds with agreed recommendations from a health care provider[5]. Adherence to therapies is a primary determinant of treatment success and encompasses numerous health-related behaviours that extend beyond taking prescribed medication[5]. It reflects therapeutic behaviours which include seeking timely medical attention, taking prescribed medication appropriately, attending follow-up appointments, being immunized and adopting recommended behavioural modifications. Good outcomes from chronic disease management such as for hypertension, depends largely on the degree of patient adherence to medication and physician advice.

Despite worldwide improvement in diagnosis and treatment options for chronic diseases, a lack of adherence remains an impediment to improving patients' overall quality of life. A study by Criswell and others in 2010 reported that medication self-efficacy and social support were the most important determinants of medication and lifestyle adherence[6]. The same study also found that non-adherent patients experienced a lower level of social support from people outside their families and patients who were adherent to medication- and lifestyle recommendations reported higher medication self-efficacy as compared to non-adherent patients. There are various means of measuring adherence to chronic medication use in clinical practice, including direct and indirect measures. Direct means include the use of direct assays such as laboratory measurement of biological markers or drug metabolites. Indirect means of measurement include pill-counting, patient self-reporting and the use of modern electronic systems that record medication tablet dispensing[7], [8]. In Ghana, a study conducted at the out-patients department (OPD) of the Korle Bu Teaching Hospital amongst 413 patients found an adherence level of 47% [9]. Another Ghanaian study done in the Komfo Anokye Teaching Hospital between December 2001 and April 2002 found adherence level as low as 7%[10]. A study conducted in Malaysia observed good adherence in 53.4% of the 653 patients sampled[11]. It also found female participants to be more likely to adhere to their medication regime, compared to their male counterparts. Congestive heart failure and the presence of other comorbidities also led to higher adherence rates according to the study by Rao Chythra R. et al[11]. Other factors that had the strongest positive effect on adherence included duration of hypertension (the shorter the duration, the better the adherence) and the use of calcium antagonists, and angiotensin-converting enzyme (ACE). Patients taking two or more drugs and those prescribed more expensive drugs were found to be poorly adherent[11]. Good knowledge of the condition as well as of the medications prescribed has been associated with good adherence to medication in several studies[12]. A study conducted in Northern Ireland by Nazli MuzeyyenSencan found that 9.3% of participants were non-adherent with their antihypertensive medication when assessed using a self-reported adherence scale[13]. The same study also found that 37.9% of respondents had scores indicative of depressive symptoms, a significant comorbidity. It found age as the only significant predictor of medication adherence in that population. Another study conducted in Pennsylvania found the highest rates of adherence were associated with ACE inhibitors and calcium antagonists, and adherence was significantly higher than with diuretics and beta blockers [14]. The study also found poor adherence to be associated with a higher health care cost. Poor adherence to antihypertensive medication is a multifactorial challenge that affects both the patient and the health care system. As a multifactorial problem, adherence is usually influenced by different contextual factors to varying extents. Some of these factors are at the individual level whereas others may operate at the social and health system level.

In spite of the improvement in diagnosis and treatment options for hypertension, poor adherence remains an impediment to reducing end-organ damage and improving patients' overall quality of life especially in sub-Saharan Africa. This study sought to investigate adherence rates and the local factors that contribute to nonadherence amongst hypertensive patients attending a specialist-led clinic in Kumasi-Ghana in order to improve patient outcome.

II. Methods

a) Study design and site

This hospital-based cross-sectional study was conducted at the out-patient clinic of County Hospital, a large privately-owned multi-department urban health facility in Kumasi, Ghana. The specialist-led hypertension clinic caters to a diverse population of patients with different personal and socio-demographic characteristics.

b) Study population

The study involved hypertensive patients, aged 18 years and above and who have been enrolled in the Hypertensive Clinic for at least 12 months. The study was conducted between October 2019 and January 2020.County hospital runs two (2) hypertension clinics per week and sees an average of thirty-five (35) patients per clinic day. The hospital runs a counseling, dietary education session and short fitness exercise for patients on every clinic day.

c) Data collection, Processing and Analysis

Data for the study was collected using an electronic questionnaire developed in open data kit (ODK®). The research team collected data directly from patients and medical records. The electronic questionnaire included variables on sociodemographic characteristics, clinical characteristics such as class of drugs taken by the patients and the Morinsky adherence scale (MMAS) to assess adherence of respondents to their medications.

The MMAS-4 is the original four item scale has a reliability score of 0.61 as a measure of internal consistency [15]. The MMAS-4 has been significantly revised since its introduction in 1986 by Morisky DE, Green LW and Levine DM. A higher MMAS-4 score significantly correlated with the presence of a drug metabolite marker[15]. MMAS- 8 is a modification of MMAS-4 into an 8-item scoring scale and has a higher reliability score of 0.83. The MMAS-8 has proven reliable in indirectly measuring the medication-taking behavior of patients with chronic diseases such as hypertension and diabetes mellitus[16]–[18]. The MMAS-8 was used as a measure of adherence in this study.

d) Assessment of Medication Adherence

The MMAS-8 questionnaire adopted scoring algorithm, where negative response for each item was coded as 1, except for the question asking if the patient took their medications yesterday (where a positive response was coded as 1). The total MMAS-8 score was calculated by summing the values from all the 8 question items. Adherence was defined as having a MMAS-8 score more than 6 out of a total of 8 scores. Cronbach's alpha test of internal consistency was calculated at 0.79 for the 8 items in MMAS-8 score.

e) Data analysis

The data was analyzed using Stata/SE 14.0 statistical software (StataCorp. 4905 Lakeway Drive Station, Texas 77845, USA). Descriptive statistics was performed for all variables and expressed as means and standard deviation for continuous variables.

Bivariate analysis (logistic regression) was done to measure the strength of the association between socio-demographic, BP level, antihypertensive drug used and medication adherence score. These were presented as crude (unadjusted) Odds ratio. Multivariate logistics regression model was fitted using forward stepwise approach to adjust for the effect of other confounding factors in order to unravel the true factors associated with medication adherence score. The regression models controlled or adjusted for age, gender, educational level, occupation, cigarette smoking and family history of hypertension.

All statistical analysis was done at a 95% significance level with p values < 0.05 considered as statistically significant. Cronbach's alpha test of internal consistency was calculated at 0.79 for the 8 items in MMAS-8 score.

f) Operational definitions

Three seated Blood Pressure (BP) measurements were obtained at 5-minute intervals from each participant. An average was calculated for each of the three systolic and diastolic measurements taken. Hypertension was defined as an average systolic BP (SBP) $\geq$140 mm Hg and/or an average diastolic BP (DBP) $\geq$ 90 mm Hg. Controlled hypertension was defined as having an average SBP $<$140 mm Hg and/or an average DBP $<$ 90 mm Hg, whilst on medication.

III. Ethical Considerations

Participation Informed Consent Forms (ICF) were designed based on the principles of Good Clinical Practice (GCP). The content of the ICF were clearly explained to the understanding of the potential participants. Literate participants were allowed to write and sign the ICF while non-literate participants thumb printed their consent, assisted by a third party, preferrably an accompanying relative (as witness) who countersigned the ICF. Ethical approval was obtained from the Committee on Human Research Publication and Ethics (CHRPE) from the Kwame Nkrumah University of Science and Technology after administrative approval from County Hospital.

This study posed minimal or no anticipated risks to participants since it was a non-invasive study, with no identifying information collected. There was no cost to the participant nor was there compensation to participate in this study

IV. Results

a) Sociodemographic of the hypertensive patients

The study involved 361 patients who consented to participate in the study. All participants were included in the analysis of the study. Out of this, 296 (81.99%) were females and 65 (18.01%) were males, giving a female-male ratio of 4.6:1.More than half of the patients (n=219; 60.66%) were over 55 years old with a mean age of 59.74. The majority (n=296; 81.99%) of respondents had some level of education but only 11% had achieved tertiary education. Further details of participant socio-demographics can be found in Table 1.

Table 1: Socio-demographic of study participants

Variables	Frequency (n=361)	Percentage (%)
Gender		
- Male	65	18.01
- Female	296	81.99
Age (years)		
- Middle age (36-55)	142	39.34
- Older age (>55)	219	60.66
Mean (SD)	59.74 (±10.91)	
Educational level		
- No formal education	65	18.01
- Basic education	119	32.96
- Secondary education	135	37.40
- Tertiary education	42	11.63
Occupational status		
- Unemployed	140	38.78
- Unskilled	171	47.37
- Skilled	27	7.48
- Professional	23	6.37
Religion		
- Christian	326	90.30
- Muslim	33	9.14
- Traditionalist	2	0.56
Enrolled on NHIS		
- No	2	0.55
- Yes	359	99.45
Smoke cigarette		
- No	343	95.01
- Yes	18	4.99

b) Clinical Characteristics of Participants

Out of the 361 hypertensive patients, more than half 234 (64.32%) reported a family history of hypertension. Almost half (n=167; 46.26%) of participants reported a comorbidity, out of which 82.63% were Diabetic. A little over three quarters (n=272; 75.35%) had controlled blood pressure (optimal blood pressure) with a mean systolic and diastolic pressure of 125.25/75.54mmHg.

More than half (n=207; 57.34%) were adherent (MMAS-8 score 6 to 8) to antihypertensive medication prescribed (Table 2).

Table 2: Clinical Characteristics of Hypertensive Patients

Variables	Frequency (n=361)	Percentage (%)
Diagnosis		
- HPT	223	61.77
- Both HPT and Diabetes	138	38.23
Family history of HPT		
- No	95	26.32
- Yes	234	64.32
- Do not know	32	8.66
Comorbidity		
- No	194	53.74
- Yes	167	46.26
Blood pressure		
- Controlled	272	75.35
- Uncontrolled	89	24.65
Mean (SD)	125.25 (±15.15)	
Comorbidity(n=167)		
- Diabetes	138	82.63
- Others	29	17.37
Medication adherence		
- Non-adherent	154	42.66
- Adherent	207	57.34

c) *Class of Antihypertensive Drugs used among the Hypertensive Patients*

The most common class of drugs prescribed for participants were calcium channel blockers (n=244; 67.59%) and angiotensin receptor blockers (n=238; 65.93%). Other classes of medications prescribed included statins (30.47%), beta-blockers (26.04%), ACE inhibitors (10.53%) and diuretics (8.31%). (Table 3).

Table 3: Class of Antihypertensive Drugs used among the Hypertensive Patients

Variables	Frequency (n=361)	Percentage (%)
Calcium channel blockers		
- No	117	32.41
- Yes	244	67.59
Diuretics		
- No	331	91.69
- Yes	30	8.31
Beta-blockers		
- No	267	73.96
- Yes	94	26.04
Angiotensin converting enzyme inhibitors		
- No	323	89.47
- Yes	38	10.53
Angiotensin receptor blockers		
- No	123	34.07
- Yes	238	65.93
Centrally acting		
- No	322	89.20
- Yes	39	10.80
Statins		
- No	251	69.53
- Yes	110	30.47

d) *Factors Influencing Medication Adherence among Hypertensive Patients*

Bivariate analysis of medication adherence and patient demographic factors, clinical characteristics and drug classes taken was performed. Significant association was demonstrated between age of patient, existence of other comorbidities and certain classes of antihypertensive medications. Older patients (> 55 years) were more likely (aOR=2.74, CI=1.60- 4.68; p<0.000) to adhere to their antihypertensive medications compared to their younger counterparts (<55 years). Having a comorbid condition was associated with reduced likelihood to adhere to antihypertensive drugs (aOR=0.30, CI=0.13-0.71, p=0.006). Similarly, being on calcium channel blockers was associated with a 46% less likelihood to adhere, compared to other classes of antihypertensive drugs (aOR=0.54, CI=0.33-0.91, p=0.020). (Table 4).

Table 4: Factors affecting medication adherence

Variable	OR (95%CI)	p-value	aOR (95%CI)	p-value
Gender				
- Male	1.00		1.00	
- Female	0.95 (0.55-1.63)	0.840	1.46 (0.70-3.06)	0.310
Age				
- Middle age	1.0		1.00	
- Older age	2.18 (1.41-3.36)	<0.000*	2.74 (1.60-4.68)	<0.000*
Smoke cigarette				
- No	Ref		1.00	
- Yes	0.58 (0.22-1.50)	0.261	0.36 (0.11-1.16)	0.088
Family history of HPT				
- No	1.00		1.00	
- Yes	1.09 (0.69-1.77)	0.722	1.13 (0.65-1.97)	0.666
- Do not know	0.67 (0.30-1.50)	0.329	0.00 (0.13-1.26)	0.118

Family history of diabetes				
- No	1.00		1.00	
- Yes	1.05 (0.51-2.14)	0.897	1.21 (0.71-2.07)	0.488
- Do not know	1.15 (0.54-2.42)	0.723	1.73 (0.61-4.90)	0.301
Comorbidity				
- No	1.0		1.00	
- Yes	0.42 (0.19-0.93	0.031*	0.30 (0.13-0.71)	0.006*
Waist-to-height				
- Normal	1.00		1.00	
- Abnormal	0.96 (0.30-3.08)	0.944	0.89 (0.24-3.30)	0.861
Blood pressure level				
- Uncontrolled	1.00		1.00	
- Controlled	0.94 (0.58-1.52)	0.799	0.80 (0.45-1.42)	0.447
Calcium channel blockers				
- No	1.0		1.00	
- Yes	0.73 (0.47-1.15)	0.180	0.54 (0.33-0.91)	0.020*
Diuretics				
- No	1.0		1.00	
- Yes	1.13 (0.53-2.41)	0.759	1.17 (0.49-2.80)	0.718
Beta-blockers				
- No	Ref		Ref	
- Yes	1.36 (0.84-2.20)	0.217	1.25 (0.71-2.20)	0.432
Angiotensin converting enzyme inhibitor				
- No	1.00		Ref	
- Yes	1.16 (0.58-2.30)	0.675	1.73 (0.73-4.08)	0.212
Angiotensin receptor blockers				
- No	Ref		Ref	
- Yes	1.03 (0.66-1.59)	0.905	1.23 (0.70-2.17)	0.478
Centrally acting				
- No	Ref		Ref	
- Yes	0.96 (0.49-1.87)	0.901	1.05 (0.48-2.31)	0.906

(*)=Statistically Significant

V. Discussion

a) *Blood pressure control*

Blood pressure control amongst respondents was optimum. Most of our study participants had their blood pressures controlled with a mean systolic and diastolic of 125.25mmHg and 75.54mmHg amongst hypertensives who had been on treatment for at least a year. This is in contrast to a systematic review by Bosu and colleagues which found that less than ten percent (10%) of hypertensives had their blood pressures controlled according to most Ghanaian studies[4]. This could be due to the effective management by cardiology specialists and the relatively high adherence of most patients to treatment recommendations. Our study site also runs a counselling, dietary session and short fitness exercise for patients on every clinic day. Also, our study was conducted in an urban setting and this might contribute to the better control of hypertension similar to a study by Chow and others which found increased awareness, treatment, and control of hypertension in urban communities compared to rural communities[3]. In addition, this could it be due to the nature of people who may opt for care in private clinics, they may have better socioeconomic profile, be better motivated or may be more likely to have better support systems.

b) *Adherence rates*

The overall adherence rate found in this study falls within 52% to 92% reported from western studies[19]. It is similar to that reported by an Ethiopian study [20] even though it is considerably less than the adherence rate of 82.2% reported by a Malaysian study[21]. Previous studies conducted on adherence in Ghana found lower rates of 47% in Korle Bu[9] and 7% in Komfo Anokye Teaching Hospital[10]. The rates of good adherence to antihypertensive medications may vary due to a host of factors such as the study design and population, method of adherence measurements, biases, scoring systems used etc. Population wise, adherence rates may vary due to perception of orthodox medications, poverty, cost of medications, insurance policies, self-care attitudes and social support systems in place. Our study site is a specialist led clinic and this might explain the reason for a high adherence rate comparable to that of developed countries. Our clinic setting employs a patient-centered care approach which focuses on true partnership between patients and healthcare staff. It involves counselling and education

on hypertension and its end-organ damage, diet and exercise. In addition, patient communal coping in our clinic setting might also be a contributing factor to the relatively high adherence rate observed in this study.

c) Factors affecting medication adherence

Worldwide, there are several studies that have associated several factors to medication adherence. Medication adherence has been associated with a host of factors such as demography, psychological factors as well as disease and medication-taking behaviors[22]. Based on the results of our study, adherence to antihypertensive medication is influenced by factors such as older age, significant comorbidities and the use of calcium channel blockers.

As found in other studies[22], younger adults had lower adherence rates compared to older adults. Older people are more accepting of their diagnosis and hence may be more inclined to follow through with their medications. Also, younger people have more distractions in terms of work and meeting responsibilities compared to those over 55 who may be retired, have less work commitments or may be settled into a more routine life.

The presence of other comorbidities such as atrial fibrillation, diabetes mellitus and glaucoma were found to be significantly associated with poorer adherence amongst hypertensives. Comorbidities can lead to a higher pill burden which can negatively influence adherence to medications. This finding is however in contrast to studies by Rao Chythra R. and others who found congestive heart failure and the presence of other comorbidities led to higher adherence rates [11]. Perhaps, one can reason that the presence of severe life-threatening comorbidities tend to increase reliance on medications for survival and hence may make patients somewhat more adherent. The conflicting evidence with regards to comorbidities and medication adherence suggests a more nuanced relationship that requires further contextual examination.

The use of calcium channel blockers was associated with lower rates of adherence amongst hypertensive patients. This could be as a result of the side effects of pedal edema and headaches. This was also in contrast with a Pennsylvanian study which found the highest rates of adherence were associated with ACE inhibitors and calcium antagonists, significantly higher than with diuretics and beta blockers[14].

VI. Conclusion

From our study, blood pressure control among respondents at the specialist led clinic was optimum. Our study also found a relatively high adherence rate to medications which was positively associated with older age, and negatively associated with factors such as comorbidities and the use of calcium channel blockers. The relatively high level of adherence found in this study can be attributed to our specialist-led setting which uses a patient-centered care approach involving adequate counseling and education of patients and communal coping mechanisms used by patients. The high prevalence of BP control found in this study can be linked to the relatively high level of adherence found amongst the participants. Better adherence leads to better control which ultimately leads to improved outcomes, prolonged survival and reduction in the incidence of end organ damage from hypertension. The extent to which such adherence is influenced by attendance by specialist physicians in the local context should be the subject of further enquiry.

What is already known about this topic

- Worldwide and particularly in sub-Saharan Africa there is an increasing prevalence of hypertension and its complications;
- In spite of increasing availability of modern treatment options for hypertension, adherence to treatment modalities remain an impediment to the control of hypertension;
- Poor adherence to antihypertensive medications is multifactorial and affects not only the patient but the entire health care system.

What this study adds

- A relatively high level of adherence was found amongst hypertensive patients being managed at a specialist-led clinic
- Specialized-clinics that adopt a holistic and patient-centered care approach such as counseling on diet, exercise and complications of hypertension, may be an important factor in ensuring adherence
- Relatively high levels of adherence to antihypertensives correlate with achieving optimum blood pressure targets, which could in turn lead to improved patient outcomes.

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Conflict of interest

All authors declare no conflict of interest

Author's contribution

All authors contributed in idea generational, data collection, analysis, writing and proofreading of this case report and are in agreement with its content before submission.

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A Rare Case of Purtscher's Retinopathy Seen in RTA Patient

By Aye Myat Mon, Yogita Rajbhandari, Sudeep Rajbhandari & Sanyam Bajimaya

Introduction- Purtscher's retinopathy was described by German Ophthalmologist Otmar Purtscher in 1910. It is an occlusive microvascular retinopathy caused by trauma such as head injury, thoracic compressive injury or long bone fractures.[1] Without history of trauma, it can also be due to systemic disease like acute pancreatitis, renal failure, lymphoproliferative disorder, valsalva maneuver, fat embolism syndrome or autoimmune diseases and they present with similar retinal findings and it is called Purtscher like retinopathy.[2]

Patients usually come with reduced visual acuity following injury. Clinical findings commonly seen in retina include cotton wool spots, retinal haemorrhage, areas of retina whitening (Purtscher flecken) or optic disc oedema. And 60% of cases have bilateral involvement.[3] Purtscher flecken, pathognomonic of Purtscher's retinopathy, are typically seen in posterior pole sparing the perivascular areas.[4,5]

GJMR-F Classification: NLMC Code: WW 270, WW 168

Strictly as per the compliance and regulations of:

A Rare Case of Purtscher's Retinopathy Seen in RTA Patient

Aye Myat Mon [α], Yogita Rajbhandari [σ], Sudeep Rajbhandari [ρ] & Sanyam Bajimaya [ω]

I. Introduction

Purtscher's retinopathy was described by German Ophthalmologist Otmar Purtscher in 1910. It is an occlusive microvascular retinopathy caused by trauma such as head injury, thoracic compressive injury or long bone fractures.[1] Without history of trauma, it can also be due to systemic disease like acute pancreatitis, renal failure, lymphoproliferative disorder, valsalva maneuver, fat embolism syndrome or autoimmune diseases and they present with similar retinal findings and it is called Purtscher like retinopathy.[2]

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We report a case of Purtscher's retinopathy following Road Traffic Accident (RTA).

II. Case Presentation

A 35 year old male patient came with chief complaint of painless diminution of vision in both eyes for 10 days following road traffic accident (RTA). He had history of loss of consciousness for 1 hour but he denied any history of nausea, vomiting or bleeding from nose and ears. He was admitted in a general hospital where he underwent repair of his lip laceration and open reduction and internal fixation of his both upper limbs. He was discharged from the hospital after nine days stay.

Regarding his general examination, he was well oriented but ill-appearing. The sutures were noted on his lip. There was POP cast with arm slings on his both upper limbs. On ocular examination, his unaided visual acuity was 6/24 in right eye and counting fingers at 3m in left eye. Extraocular motility was full in both duction and version movements. Lid and adnexa were normal in both eyes. Anterior segment examination revealed sub-conjunctival haemorrhage in RE. Cornea was clear in both eyes. Anterior chamber was normal in depth and was quiet. The pupillary reaction was sluggish in both eyes and relative afferent pupillary defect (RAPD) could not be properly accessed. Lens was clear in both eyes.

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On dilated fundus examination with clear vitreous media, optic disc was pink with well-defined margin and cup disc ratio of 0.3 with healthy neuroretinal rim in both eyes. There were multiple cotton wool spots around peripapillary region, few Purtscher fleckens and sub-retinal haemorrhage in BE while macula was healthy. Intraocular pressure was 12 mm Hg in both eyes.

Provisional diagnosis of BE Purtscher's retinopathy with traumatic optic neuropathy was made. Color vision, Humphrey 30-2 visual field test and macula OCT were sent to confirm the diagnosis. He was started on oral prednisolone 60mg (1mg/kg BW) OD for 1 week, oral Pantoprazole 40mg OD for 1 week and topical Ketorolac QID for 2 weeks and was called for follow-up with reports.

His color vision was normal in RE but abnormal in LE and visual field deficit in HVF 30-2 was detected in LE. Macula OCT was normal in both eyes.

The final diagnosis was made as BE Purtscher's retinopathy with LE traumatic optic neuropathy. Patient was asked to continue oral prednisolone in tapering dose and was called for follow up in one month.

At 1month follow-up, his unaided visual acuity was 6/6 in RE and 6/24 in LE. Sub-conjunctival haemorrhage had resolved. On dilated fundus examination with clear vitreous media, optic disc of RE was normal in appearance while mild temporal pallor of disc was noted in LE. About 50% of cotton wool spots had resolved in BE.

Regarding treatment, oral prednisolone was continued along with a multivitamin capsule. Patient was advised to follow up in 1 month.

III. Discussion

Pathogenesis of Purtscher's retinopathy has been assumed due to microembolization of retinal vessels either from fat emboli in patient with long bone fractures or disseminated pancreatic proteases in acute pancreatitis. The possible emboli in Purtscher's retinopathy may include air, fat, leucocyte aggregates, platelets and fibrin. It causes arteriolar precapillary occlusion and retinal nerve fiber layer infarction presenting with cotton-wool spots.[4,6]In other words, it is a kind of retinal vasculitis induced by lipase after systemic injury which leads to thrombosis and vascular occlusion.[4] The pathognomonic sign is Purtscher

flecken and they can be found in inner retina between the retinal arterioles and venules. And the reason why Purtscher flecken were confined to the posterior pole can be explained because it is prone to get embolic occlusion due to less anastomoses and less arterioles in that area.[4,5] In our case, the patient had fractures in both upper limbs, making fat emboli a likely cause.

The commonest clinical signs of the disease mentioned in one study were cotton wool spots (93%), retinal haemorrhages (65%) and Purtscher flecken (63%).[2]It was relevant with our case because there were all three significant clinical signs in BE. In 4% of patients with long bone fracture, there may be only cotton-wool spots and retinal haemorrhages but not Purtscher flecken.[4] Other ocular findings which can be seen are optic atrophy, decreased color vision, RPE changes and dilated and tortuous retinal vessels.

Few diagnostic criteria for Purtscher retinopathy have been defined in literatures. Our diagnosis was based on criteria given by Miguel el at[2] who had defined it with presence of at least three of the following criteria: Purtscher flecken, cotton-wool spots confined to the posterior pole, retinal haemorrhage, relevant etiology and complementary investigations compatible with diagnosis.

There is no standard treatment mentioned in the literatures. Most of the patients recover without any treatment.[7] But the vision improvement was well noted in some studies after giving intravenous methyl prednisolone and oral prednisolone after initial trauma. In the study by Atabay et al[8], intravenous methyl prednisolone was given to a Purtscher's retinopathy patient 3 weeks after the initial trauma but visual acuity improved by more than 3 lines after 3 months. In Wang et al[9], the patient with the history of trauma received 1 g of intravenous methylprednisolone for 3 days followed by oral steroids for 3 weeks and the improvement of vision from CF to 6/12 was noted. Normalization of fundus was 40% after 2 months in Miguel's study.[2] In our case, visual acuity improved from CF3m to 6/24 with oral prednisolone (1mg/kg) at 1 month follow up.

IV. Conclusion

Purtcher's retinopathy is a rare condition in our practice but it can be diagnosed clinically with its significant clinical signs and the relevant history of trauma or other associated diseases. And treatment with oral corticosteroid can improve the visual acuity.

Consent

The patient has no objection to use his photos in academic and research work.

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Conflict of interest
None.

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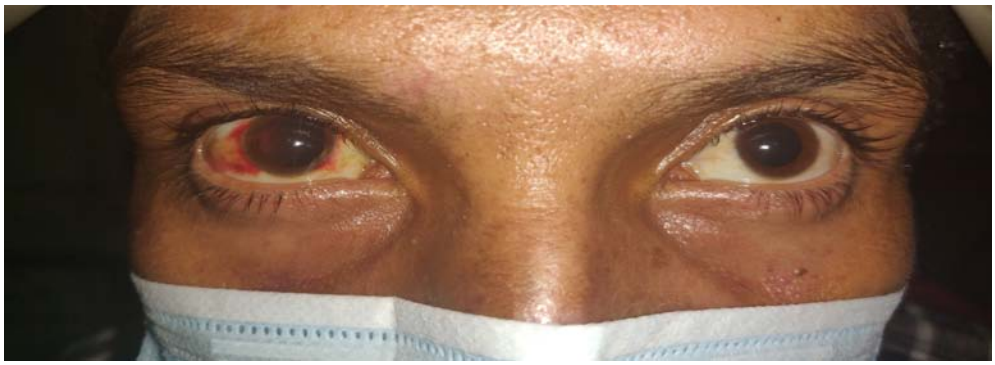

Figure 1: Photo showing RE subconjunctival hemorrhage

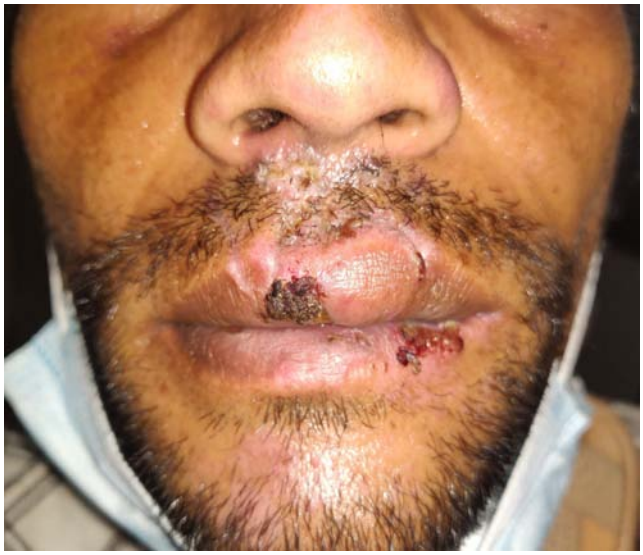

Figure 2: Photo showing facial injury

Figure 3: Patient presenting with arm slings after surgery of bilateral forehands fracture

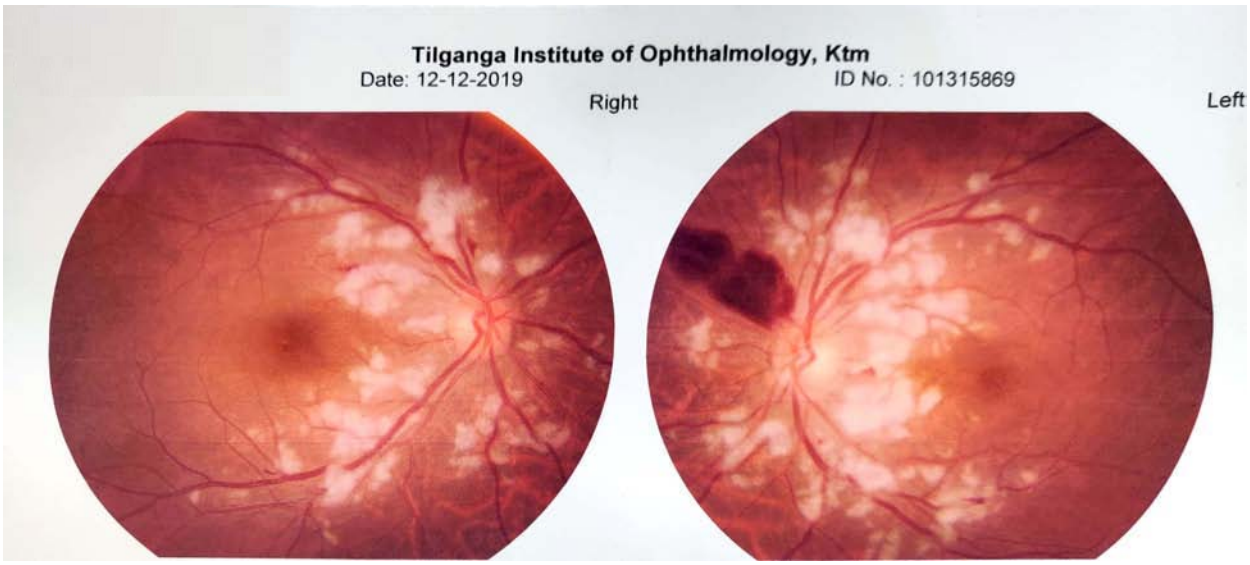

Figure 4: Fundus photo of both eyes at the time of presentation showing cotton wool spots, Purtscher's flecken and retinal hemorrhages

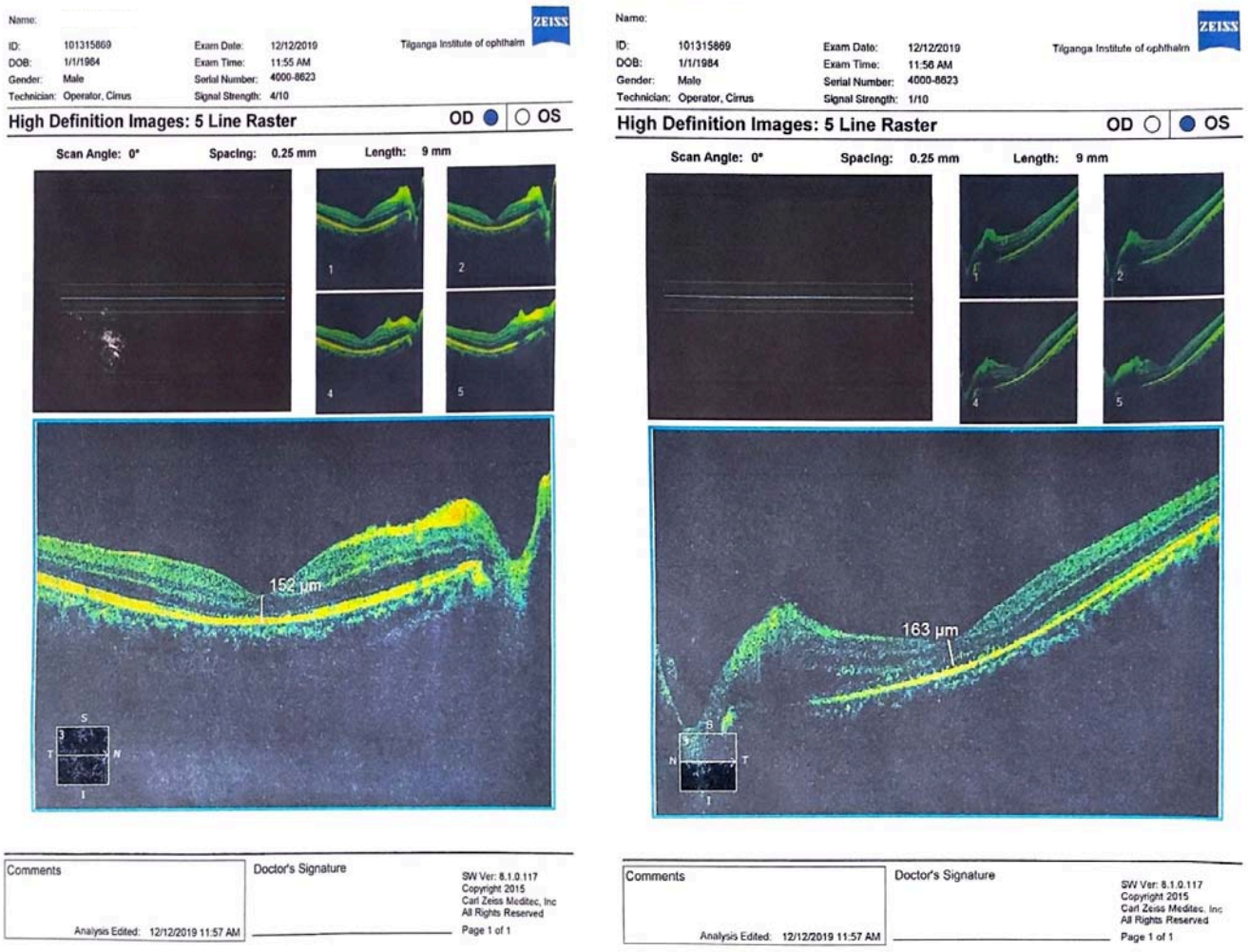

Figure 5: Macula OCT of both eyes showing normal macula contouro

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Memberships

Fellows/Associates of Medical Research Council

FMRC/AMRC Memberships

Introduction

FMRC/AMRC is the most prestigious membership of Global Journals accredited by Open Association of Research Society, U.S.A (OARS). The credentials of Fellow and Associate designations signify that the researcher has gained the knowledge of the fundamental and high-level concepts, and is a subject matter expert, proficient in an expertise course covering the professional code of conduct, and follows recognized standards of practice. The credentials are designated only to the researchers, scientists, and professionals that have been selected by a rigorous process by our Editorial Board and Management Board.

Associates of FMRC/AMRC are scientists and researchers from around the world are working on projects/researches that have huge potentials. Members support Global Journals' mission to advance technology for humanity and the profession.

FMRC

Fellow of Medical Research Council

FELLOW OF MEDICAL RESEARCH COUNCIL is the most prestigious membership of Global Journals. It is an award and membership granted to individuals that the Open Association of Research Society judges to have made a 'substantial contribution to the improvement of computer science, technology, and electronics engineering.

The primary objective is to recognize the leaders in research and scientific fields of the current era with a global perspective and to create a channel between them and other researchers for better exposure and knowledge sharing. Members are most eminent scientists, engineers, and technologists from all across the world. Fellows are elected for life through a peer review process on the basis of excellence in the respective domain. There is no limit on the number of new nominations made in any year. Each year, the Open Association of Research Society elect up to 12 new Fellow Members.

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We accept the manuscript submissions in any standard (generic) format.

We typeset manuscripts using advanced typesetting tools like Adobe In Design, CorelDraw, TeXnicCenter, and TeXStudio. We usually recommend authors submit their research using any standard format they are comfortable with, and let Global Journals do the rest.

Alternatively, you can download our basic template from https://globaljournals.org/Template

Authors should submit their complete paper/article, including text illustrations, graphics, conclusions, artwork, and tables. Authors who are not able to submit manuscript using the form above can email the manuscript department at submit@globaljournals.org or get in touch with chiefeditor@globaljournals.org if they wish to send the abstract before submission.

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Authors must ensure the information provided during the submission of a paper is authentic. Please go through the following checklist before submitting:

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2. Authors must accept the privacy policy, terms, and conditions of Global Journals.
3. Ensure corresponding author's email address and postal address are accurate and reachable.
4. Manuscript to be submitted must include keywords, an abstract, a paper title, co-author(s') names and details (email address, name, phone number, and institution), figures and illustrations in vector format including appropriate captions, tables, including titles and footnotes, a conclusion, results, acknowledgments and references.
5. Authors should submit paper in a ZIP archive if any supplementary files are required along with the paper.
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7. Manuscript submitted *must not have been submitted or published elsewhere* and all authors must be aware of the submission.

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It is required for authors to declare all financial, institutional, and personal relationships with other individuals and organizations that could influence (bias) their research.

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Plagiarism is not acceptable in Global Journals submissions at all.

Plagiarized content will not be considered for publication. We reserve the right to inform authors' institutions about plagiarism detected either before or after publication. If plagiarism is identified, we will follow COPE guidelines:

Authors are solely responsible for all the plagiarism that is found. The author must not fabricate, falsify or plagiarize existing research data. The following, if copied, will be considered plagiarism:

- Words (language)
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- Findings
- Writings
- Diagrams
- Graphs
- Illustrations
- Lectures

- Printed material
- Graphic representations
- Computer programs
- Electronic material
- Any other original work

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1. Substantial contributions to the conception and acquisition of data, analysis, and interpretation of findings.
2. Drafting the paper and revising it critically regarding important academic content.
3. Final approval of the version of the paper to be published.

Changes in Authorship

The corresponding author should mention the name and complete details of all co-authors during submission and in manuscript. We support addition, rearrangement, manipulation, and deletions in authors list till the early view publication of the journal. We expect that corresponding author will notify all co-authors of submission. We follow COPE guidelines for changes in authorship.

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Unless specified in the notification, the Editorial Board's decision on publication of the paper is final and cannot be appealed before making the major change in the manuscript.

Acknowledgments

Contributors to the research other than authors credited should be mentioned in Acknowledgments. The source of funding for the research can be included. Suppliers of resources may be mentioned along with their addresses.

Declaration of funding sources

Global Journals is in partnership with various universities, laboratories, and other institutions worldwide in the research domain. Authors are requested to disclose their source of funding during every stage of their research, such as making analysis, performing laboratory operations, computing data, and using institutional resources, from writing an article to its submission. This will also help authors to get reimbursements by requesting an open access publication letter from Global Journals and submitting to the respective funding source.

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Authors can submit papers and articles in an acceptable file format: MS Word (doc, docx), LaTeX (.tex, .zip or .rar including all of your files), Adobe PDF (.pdf), rich text format (.rtf), simple text document (.txt), Open Document Text (.odt), and Apple Pages (.pages). Our professional layout editors will format the entire paper according to our official guidelines. This is one of the highlights of publishing with Global Journals—authors should not be concerned about the formatting of their paper. Global Journals accepts articles and manuscripts in every major language, be it Spanish, Chinese, Japanese, Portuguese, Russian, French, German, Dutch, Italian, Greek, or any other national language, but the title, subtitle, and abstract should be in English. This will facilitate indexing and the pre-peer review process.

The following is the official style and template developed for publication of a research paper. Authors are not required to follow this style during the submission of the paper. It is just for reference purposes.

Manuscript Style Instruction (Optional)

- Microsoft Word Document Setting Instructions.
- Font type of all text should be Swis721 Lt BT.
- Page size: 8.27" x 11'", left margin: 0.65, right margin: 0.65, bottom margin: 0.75.
- Paper title should be in one column of font size 24.
- Author name in font size of 11 in one column.
- Abstract: font size 9 with the word "Abstract" in bold italics.
- Main text: font size 10 with two justified columns.
- Two columns with equal column width of 3.38 and spacing of 0.2.
- First character must be three lines drop-capped.
- The paragraph before spacing of 1 pt and after of 0 pt.
- Line spacing of 1 pt.
- Large images must be in one column.
- The names of first main headings (Heading 1) must be in Roman font, capital letters, and font size of 10.
- The names of second main headings (Heading 2) must not include numbers and must be in italics with a font size of 10.

Structure and Format of Manuscript

The recommended size of an original research paper is under 15,000 words and review papers under 7,000 words. Research articles should be less than 10,000 words. Research papers are usually longer than review papers. Review papers are reports of significant research (typically less than 7,000 words, including tables, figures, and references)

A research paper must include:

a) A title which should be relevant to the theme of the paper.
b) A summary, known as an abstract (less than 150 words), containing the major results and conclusions.
c) Up to 10 keywords that precisely identify the paper's subject, purpose, and focus.
d) An introduction, giving fundamental background objectives.
e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition, sources of information must be given, and numerical methods must be specified by reference.
f) Results which should be presented concisely by well-designed tables and figures.
g) Suitable statistical data should also be given.
h) All data must have been gathered with attention to numerical detail in the planning stage.

Design has been recognized to be essential to experiments for a considerable time, and the editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned unrefereed.

i) Discussion should cover implications and consequences and not just recapitulate the results; conclusions should also be summarized.
j) There should be brief acknowledgments.
k) There ought to be references in the conventional format. Global Journals recommends APA format.

Authors should carefully consider the preparation of papers to ensure that they communicate effectively. Papers are much more likely to be accepted if they are carefully designed and laid out, contain few or no errors, are summarizing, and follow instructions. They will also be published with much fewer delays than those that require much technical and editorial correction.

The Editorial Board reserves the right to make literary corrections and suggestions to improve brevity.

Format Structure

It is necessary that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.

All manuscripts submitted to Global Journals should include:

Title

The title page must carry an informative title that reflects the content, a running title (less than 45 characters together with spaces), names of the authors and co-authors, and the place(s) where the work was carried out.

Author details

The full postal address of any related author(s) must be specified.

Abstract

The abstract is the foundation of the research paper. It should be clear and concise and must contain the objective of the paper and inferences drawn. It is advised to not include big mathematical equations or complicated jargon.

Many researchers searching for information online will use search engines such as Google, Yahoo or others. By optimizing your paper for search engines, you will amplify the chance of someone finding it. In turn, this will make it more likely to be viewed and cited in further works. Global Journals has compiled these guidelines to facilitate you to maximize the web-friendliness of the most public part of your paper.

Keywords

A major lynchpin of research work for the writing of research papers is the keyword search, which one will employ to find both library and internet resources. Up to eleven keywords or very brief phrases have to be given to help data retrieval, mining, and indexing.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy: planning of a list of possible keywords and phrases to try.

Choice of the main keywords is the first tool of writing a research paper. Research paper writing is an art. Keyword search should be as strategic as possible.

One should start brainstorming lists of potential keywords before even beginning searching. Think about the most important concepts related to research work. Ask, “What words would a source have to include to be truly valuable in a research paper?” Then consider synonyms for the important words.

It may take the discovery of only one important paper to steer in the right keyword direction because, in most databases, the keywords under which a research paper is abstracted are listed with the paper.

Numerical Methods

Numerical methods used should be transparent and, where appropriate, supported by references.

Abbreviations

Authors must list all the abbreviations used in the paper at the end of the paper or in a separate table before using them.

Formulas and equations

Authors are advised to submit any mathematical equation using either MathJax, KaTeX, or LaTeX, or in a very high-quality image.

Tables, Figures, and Figure Legends

Tables: Tables should be cautiously designed, uncrowned, and include only essential data. Each must have an Arabic number, e.g., Table 4, a self-explanatory caption, and be on a separate sheet. Authors must submit tables in an editable format and not as images. References to these tables (if any) must be mentioned accurately.

Figures

Figures are supposed to be submitted as separate files. Always include a citation in the text for each figure using Arabic numbers, e.g., Fig. 4. Artwork must be submitted online in vector electronic form or by emailing it.

Preparation of Eletronic Figures for Publication

Although low-quality images are sufficient for review purposes, print publication requires high-quality images to prevent the final product being blurred or fuzzy. Submit (possibly by e-mail) EPS (line art) or TIFF (halftone/ photographs) files only. MS PowerPoint and Word Graphics are unsuitable for printed pictures. Avoid using pixel-oriented software. Scans (TIFF only) should have a resolution of at least 350 dpi (halftone) or 700 to 1100 dpi (line drawings). Please give the data for figures in black and white or submit a Color Work Agreement form. EPS files must be saved with fonts embedded (and with a TIFF preview, if possible).

For scanned images, the scanning resolution at final image size ought to be as follows to ensure good reproduction: line art: >650 dpi; halftones (including gel photographs): >350 dpi; figures containing both halftone and line images: >650 dpi.

Color charges: Authors are advised to pay the full cost for the reproduction of their color artwork. Hence, please note that if there is color artwork in your manuscript when it is accepted for publication, we would require you to complete and return a Color Work Agreement form before your paper can be published. Also, you can email your editor to remove the color fee after acceptance of the paper.

Tips for writing a good quality Medical Research Paper

1. Choosing the topic: In most cases, the topic is selected by the interests of the author, but it can also be suggested by the guides. You can have several topics, and then judge which you are most comfortable with. This may be done by asking several questions of yourself, like "Will I be able to carry out a search in this area? Will I find all necessary resources to accomplish the search? Will I be able to find all information in this field area?" If the answer to this type of question is "yes," then you ought to choose that topic. In most cases, you may have to conduct surveys and visit several places. Also, you might have to do a lot of work to find all the rises and falls of the various data on that subject. Sometimes, detailed information plays a vital role, instead of short information. Evaluators are human: The first thing to remember is that evaluators are also human beings. They are not only meant for rejecting a paper. They are here to evaluate your paper. So present your best aspect.

2. Think like evaluators: If you are in confusion or getting demotivated because your paper may not be accepted by the evaluators, then think, and try to evaluate your paper like an evaluator. Try to understand what an evaluator wants in your research paper, and you will automatically have your answer. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

3. Ask your guides: If you are having any difficulty with your research, then do not hesitate to share your difficulty with your guide (if you have one). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work, then ask your supervisor to help you with an alternative. He or she might also provide you with a list of essential readings.

4. Use of computer is recommended: As you are doing research in the field of medical research then this point is quite obvious. Use right software: Always use good quality software packages. If you are not capable of judging good software, then you can lose the quality of your paper unknowingly. There are various programs available to help you which you can get through the internet.

5. Use the internet for help: An excellent start for your paper is using Google. It is a wondrous search engine, where you can have your doubts resolved. You may also read some answers for the frequent question of how to write your research paper or find a model research paper. You can download books from the internet. If you have all the required books, place importance on reading, selecting, and analyzing the specified information. Then sketch out your research paper. Use big pictures: You may use encyclopedias like Wikipedia to get pictures with the best resolution. At Global Journals, you should strictly follow here.

6. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right? It is a good habit which helps to not lose your continuity. You should always use bookmarks while searching on the internet also, which will make your search easier.

7. Revise what you wrote: When you write anything, always read it, summarize it, and then finalize it.

8. Make every effort: Make every effort to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in the introduction—what is the need for a particular research paper. Polish your work with good writing skills and always give an evaluator what he wants. Make backups: When you are going to do any important thing like making a research paper, you should always have backup copies of it either on your computer or on paper. This protects you from losing any portion of your important data.

9. Produce good diagrams of your own: Always try to include good charts or diagrams in your paper to improve quality. Using several unnecessary diagrams will degrade the quality of your paper by creating a hodgepodge. So always try to include diagrams which were made by you to improve the readability of your paper. Use of direct quotes: When you do research relevant to literature, history, or current affairs, then use of quotes becomes essential, but if the study is relevant to science, use of quotes is not preferable.

10. Use proper verb tense: Use proper verb tenses in your paper. Use past tense to present those events that have happened. Use present tense to indicate events that are going on. Use future tense to indicate events that will happen in the future. Use of wrong tenses will confuse the evaluator. Avoid sentences that are incomplete.

11. Pick a good study spot: Always try to pick a spot for your research which is quiet. Not every spot is good for studying.

12. Know what you know: Always try to know what you know by making objectives, otherwise you will be confused and unable to achieve your target.

13. Use good grammar: Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice.

Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

14. Arrangement of information: Each section of the main body should start with an opening sentence, and there should be a changeover at the end of the section. Give only valid and powerful arguments for your topic. You may also maintain your arguments with records.

15. Never start at the last minute: Always allow enough time for research work. Leaving everything to the last minute will degrade your paper and spoil your work.

16. Multitasking in research is not good: Doing several things at the same time is a bad habit in the case of research activity. Research is an area where everything has a particular time slot. Divide your research work into parts, and do a particular part in a particular time slot.

17. Never copy others' work: Never copy others' work and give it your name because if the evaluator has seen it anywhere, you will be in trouble. Take proper rest and food: No matter how many hours you spend on your research activity, if you are not taking care of your health, then all your efforts will have been in vain. For quality research, take proper rest and food.

18. Go to seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

19. Refresh your mind after intervals: Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.

20. Think technically: Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

21. Adding unnecessary information: Do not add unnecessary information like "I have used MS Excel to draw graphs." Irrelevant and inappropriate material is superfluous. Foreign terminology and phrases are not apropos. One should never take a broad view. Analogy is like feathers on a snake. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Never oversimplify: When adding material to your research paper, never go for oversimplification; this will definitely irritate the evaluator. Be specific. Never use rhythmic redundancies. Contractions shouldn't be used in a research paper. Comparisons are as terrible as clichés. Give up ampersands, abbreviations, and so on. Remove commas that are not necessary. Parenthetical words should be between brackets or commas. Understatement is always the best way to put forward earth-shaking thoughts. Give a detailed literary review.

22. Report concluded results: Use concluded results. From raw data, filter the results, and then conclude your studies based on measurements and observations taken. An appropriate number of decimal places should be used. Parenthetical remarks are prohibited here. Proofread carefully at the final stage. At the end, give an outline to your arguments. Spot perspectives of further study of the subject. Justify your conclusion at the bottom sufficiently, which will probably include examples.

23. Upon conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print for the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects of your research.

Informal Guidelines of Research Paper Writing

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form which is presented in the guidelines using the template.
- Please note the criteria peer reviewers will use for grading the final paper.

Final points:

One purpose of organizing a research paper is to let people interpret your efforts selectively. The journal requires the following sections, submitted in the order listed, with each section starting on a new page:

The introduction: This will be compiled from reference matter and reflect the design processes or outline of basis that directed you to make a study. As you carry out the process of study, the method and process section will be constructed like that. The results segment will show related statistics in nearly sequential order and direct reviewers to similar intellectual paths throughout the data that you gathered to carry out your study.

The discussion section:

This will provide understanding of the data and projections as to the implications of the results. The use of good quality references throughout the paper will give the effort trustworthiness by representing an alertness to prior workings.

Writing a research paper is not an easy job, no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record-keeping are the only means to make straightforward progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear: Adhere to recommended page limits.

Mistakes to avoid:

- Insertion of a title at the foot of a page with subsequent text on the next page.
- Separating a table, chart, or figure—confine each to a single page.
- Submitting a manuscript with pages out of sequence.
- In every section of your document, use standard writing style, including articles ("a" and "the").
- Keep paying attention to the topic of the paper.
- Use paragraphs to split each significant point (excluding the abstract).
- Align the primary line of each section.
- Present your points in sound order.
- Use present tense to report well-accepted matters.
- Use past tense to describe specific results.
- Do not use familiar wording; don't address the reviewer directly. Don't use slang or superlatives.
- Avoid use of extra pictures—include only those figures essential to presenting results.

Title page:

Choose a revealing title. It should be short and include the name(s) and address(es) of all authors. It should not have acronyms or abbreviations or exceed two printed lines.

Abstract: This summary should be two hundred words or less. It should clearly and briefly explain the key findings reported in the manuscript and must have precise statistics. It should not have acronyms or abbreviations. It should be logical in itself. Do not cite references at this point.

An abstract is a brief, distinct paragraph summary of finished work or work in development. In a minute or less, a reviewer can be taught the foundation behind the study, common approaches to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Use comprehensive sentences, and do not sacrifice readability for brevity; you can maintain it succinctly by phrasing sentences so that they provide more than a lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study with the subsequent elements in any summary. Try to limit the initial two items to no more than one line each.

Reason for writing the article—theory, overall issue, purpose.

- Fundamental goal.
- To-the-point depiction of the research.
- Consequences, including definite statistics—if the consequences are quantitative in nature, account for this; results of any numerical analysis should be reported. Significant conclusions or questions that emerge from the research.

Approach:

- Single section and succinct.
- An outline of the job done is always written in past tense.
- Concentrate on shortening results—limit background information to a verdict or two.
- Exact spelling, clarity of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else.

Introduction:

The introduction should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable of comprehending and calculating the purpose of your study without having to refer to other works. The basis for the study should be offered. Give the most important references, but avoid making a comprehensive appraisal of the topic. Describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will give no attention to your results. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here.

The following approach can create a valuable beginning:

- Explain the value (significance) of the study.
- Defend the model—why did you employ this particular system or method? What is its compensation? Remark upon its appropriateness from an abstract point of view as well as pointing out sensible reasons for using it.
- Present a justification. State your particular theory(-ies) or aim(s), and describe the logic that led you to choose them.
- Briefly explain the study's tentative purpose and how it meets the declared objectives.

Approach:

Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done. Sort out your thoughts; manufacture one key point for every section. If you make the four points listed above, you will need at least four paragraphs. Present surrounding information only when it is necessary to support a situation. The reviewer does not desire to read everything you know about a topic. Shape the theory specifically—do not take a broad view.

As always, give awareness to spelling, simplicity, and correctness of sentences and phrases.

Procedures (methods and materials):

This part is supposed to be the easiest to carve if you have good skills. A soundly written procedures segment allows a capable scientist to replicate your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order, but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt to give the least amount of information that would permit another capable scientist to replicate your outcome, but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section.

When a technique is used that has been well-described in another section, mention the specific item describing the way, but draw the basic principle while stating the situation. The purpose is to show all particular resources and broad procedures so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step-by-step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

Materials may be reported in part of a section or else they may be recognized along with your measures.

Methods:

- Report the method and not the particulars of each process that engaged the same methodology.
- Describe the method entirely.
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures.
- Simplify—detail how procedures were completed, not how they were performed on a particular day.
- If well-known procedures were used, account for the procedure by name, possibly with a reference, and that's all.

Approach:

It is embarrassing to use vigorous voice when documenting methods without using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result, when writing up the methods, most authors use third person passive voice.

Use standard style in this and every other part of the paper—avoid familiar lists, and use full sentences.

What to keep away from:

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings—save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part as entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Use statistics and tables, if suitable, to present consequences most efficiently.

You must clearly differentiate material which would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matters should not be submitted at all except if requested by the instructor.

Content:

- Sum up your conclusions in text and demonstrate them, if suitable, with figures and tables.
- In the manuscript, explain each of your consequences, and point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation of an exacting study.
- Explain results of control experiments and give remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or manuscript.

What to stay away from:

- Do not discuss or infer your outcome, report surrounding information, or try to explain anything.
- Do not include raw data or intermediate calculations in a research manuscript.
- Do not present similar data more than once.
- A manuscript should complement any figures or tables, not duplicate information.
- Never confuse figures with tables—there is a difference.

Approach:

As always, use past tense when you submit your results, and put the whole thing in a reasonable order.

Put figures and tables, appropriately numbered, in order at the end of the report.

If you desire, you may place your figures and tables properly within the text of your results section.

Figures and tables:

If you put figures and tables at the end of some details, make certain that they are visibly distinguished from any attached appendix materials, such as raw facts. Whatever the position, each table must be titled, numbered one after the other, and include a heading. All figures and tables must be divided from the text.

Discussion:

The discussion is expected to be the trickiest segment to write. A lot of papers submitted to the journal are discarded based on problems with the discussion. There is no rule for how long an argument should be.

Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implications of the study. The purpose here is to offer an understanding of your results and support all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of results should be fully described.

Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact, you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved the prospect, and let it drop at that. Make a decision as to whether each premise is supported or discarded or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."

Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work.

- You may propose future guidelines, such as how an experiment might be personalized to accomplish a new idea.
- Give details of all of your remarks as much as possible, focusing on mechanisms.
- Make a decision as to whether the tentative design sufficiently addressed the theory and whether or not it was correctly restricted. Try to present substitute explanations if they are sensible alternatives.
- One piece of research will not counter an overall question, so maintain the large picture in mind. Where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

When you refer to information, differentiate data generated by your own studies from other available information. Present work done by specific persons (including you) in past tense.

Describe generally acknowledged facts and main beliefs in present tense.

The Administration Rules

Administration Rules to Be Strictly Followed before Submitting Your Research Paper to Global Journals Inc.

Please read the following rules and regulations carefully before submitting your research paper to Global Journals Inc. to avoid rejection.

Segment draft and final research paper: You have to strictly follow the template of a research paper, failing which your paper may get rejected. You are expected to write each part of the paper wholly on your own. The peer reviewers need to identify your own perspective of the concepts in your own terms. Please do not extract straight from any other source, and do not rephrase someone else's analysis. Do not allow anyone else to proofread your manuscript.

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Please note that following table is only a Grading of "Paper Compilation" and not on "Performed/Stated Research" whose grading solely depends on Individual Assigned Peer Reviewer and Editorial Board Member. These can be available only on request and after decision of Paper. This report will be the property of Global Journals.

Topics	Grades		
	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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