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# Sleep Apnea and Glaucoma – Greater Risk for Blacks?

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#### 1. Introduction

Review of the extant literature indicates that both sleep apnea and glaucoma are highly prevalent in the Black population [1,2]. They tend to occur earlier among Blacks and are associated with other metabolic diseases (e.g., obesity and hypertension). that are also highly prevalent in that ethnic group [3,4]. While technology for early detection and evidence-based treatment regimens exist for sleep apnea and glaucoma, sadly Blacks underuse them. Consequently, Blacks in underserved communities continue to bear the burden of those conditions, which have remained largely undiagnosed [5,6].

Whereas prevalence data convincingly show the risks for expressing sleep apnea and glaucoma are higher among Blacks, they are, nevertheless, not as likely to seek medical care as do Whites, even where there is no disparity in adequate medical coverage [7]. Effort should be made to explore the reasons why so few Blacks participate in sleep apnea or ophthalmic screening programs or are receiving timely diagnoses [8,9]. This paper attempts to provide background information supporting greater prevalence of glaucoma and sleep apnea for Blacks in the US. Furthermore, it suggests that if these two conditions were causally associated Blacks would be at greater risk for related comorbidities.

## 2. Prevalence of sleep apnea and glaucoma - Is ethnicity an important factor?

There are no population-based prevalence studies documenting the relationship between glaucoma and sleep apnea. However, clinical and survey data strongly suggest that glaucoma is one of the ophthalmic diseases with a hypothesized link to sleep apnea [10-16]. Below, data supporting the link between sleep apnea and glaucoma are reviewed. However, since no published studies specifically ascertained effects of ethnicity on associations of sleep apnea with glaucoma, we first examined evidence supporting ethnic differences in the prevalence of sleep apnea and glaucoma.

## 3. Epidemiology of sleep apnea

Sleep apnea is a serious, potentially life-threatening condition, characterized by repeated cessation of breathing while sleeping, due mostly to complete or partial pharyngeal obstruction [6,17]. Obstructive sleep apnea, the most prevalent of the sleep-disordered breathing constellation, has several cardio-respiratory features (e.g., loud snoring, loud gasps, and daytime breathlessness). [18-20]. Sleep apnea is also associated with a number of metabolic diseases [21-28], cardiac arrhythmias [18,19], cardiovascular disease [18,20], decreased quality of life [17] and early mortality [18,28]. It causes significant sleep disturbances and excessive daytime sleepiness [18,29], which often lead to road traffic and industrial accidents [18,27,30] as well as cognitive deficits and poor performance [31]. Sleep apnea is also associated with numerous psychiatric comorbid diagnoses including depression (21.8%), anxiety (16.7%), posttraumatic stress disorder (11.9%), psychosis (5.1%), and bipolar disorders (3.3%). [32].

Sleep apnea is thought to be as prevalent as adult diabetes and might affect more than 18 million Americans [6,33]. Others view it as big a public health hazard as smoking [34], in part because of associated residual daytime sleepiness [18,29]. The National Commission on Sleep Disorders Research estimated that sleep apnea is probably responsible for 38,000 cardiovascular deaths yearly, with an associated 42 million dollars spent on related hospitalizations [35]. Evidence shows that sleep-disordered breathing not only increases the risk of cardiovascular related deaths, but increases risk of overall mortality [36].

Using a respiratory disturbance index\* of 10 or greater, the Wisconsin Sleep Cohort Study, an epidemiological study conducted among the U.S. adult population, estimated that sleep apnea affects as much as 15% of men and 5% of women between the ages of 30 and 60 years [25]. Estimates are even higher in this age group when laboratory polysomnographic criteria are used. The largest population-based polysomnographic study conducted in the U.S. revealed that 24% of men and 9% of women had significant sleep apnea [37]. In the clinical setting, the proportion of sleep apnea cases rises to 68% [22]. Sleep researchers and public health advocates have become concerned over the lack of attention paid to ethnic disparities in sleep apnea, as several important epidemiological and clinical findings have shown greater rates for minority groups.

### 4. Sleep apnea - Ethnic variations

Sleep apnea is highly prevalent in the Black population [1]. A community-based study comparing older Blacks and Whites showed that Blacks experienced severe sleep apnea with a relative risk twofold as great as that of their White counterparts [38]. It is noteworthy that ethnicity is associated with the presence of sleep apnea (Respiratory Disturbance Index  $[RDI] \geq 30$ ). independently of age, sex, and body mass index, three of `the main risk factors for sleep apnea [6,39]. Blacks with sleep apnea are often more obese and have significantly greater prevalence of hypertension and glaucoma than their White counterparts [40] (see Table 1 and Figure 1).

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<sup>\*</sup> The apnea-hypopnea index (AHI). or respiratory disturbance index (RDI). refers to the total number of apneas (complete cessation of breathing lasting  $\geq 10$  s). and hypopneas (50% reduction in airflow lasting  $\geq 10$  s, followed by Sa02 desaturations). divided by the patient's total sleep time. The AHI or RDI provides a measure of the severity of sleep apnea.

Ethnicity	1991	1995	1998	2001	2006-8
Black	19.3	22.6	26.9	31.1	35.7
White	11.3	14.5	16.6	19.6	23.7

data obtained from the Center for Disease Control; values represent percent of cases (http://www.cdc.gov/mmwr/PDF/wk/mm5827.pdf)

Table 1. Trends in obesity by ethnicity

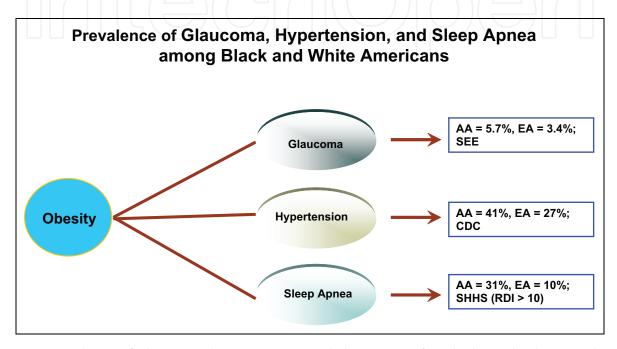


Fig. 1. Prevalence of glaucoma, hypertension, and sleep apnea for Blacks and Whites in the Salisbury Eye Study (SES), Center for Disease Control (CDC), and Sleep Heart Health Study (SHHS). All three conditions are linked to obesity, which is also more prevalent among Blacks (see Table 1)

This ethnic disparity is not observable only among adults who are 40 years old or older. A case-control family study of sleep apnea comparing 225 Blacks and 622 Whites, ages 2 to 86 years, indicated that 31% of Blacks versus 10% of Whites had RDI greater than 10 [1]. Also important in that study was the observation that Blacks may be at risk for sleep apnea at an earlier age. African-Americans with sleep-disordered breathing were younger than Caucasians with sleep-disordered breathing (37.2 +/- 19.5 years vs 45.6 +/- 18.7 years, p < 0.01). [1]. Observed ethnic differences in age of onset and anatomic risk factors for sleep apnea prompted the investigation of a possible racial/ethnic difference in the genetic underpinnings of this condition. Comparing Black and White families, investigators found evidence for segregation of a codominant gene with an allele frequency of 0.14; after adjusting for effects of Body Mass Index (BMI). and age, this accounted for 35% of the total variance in sleep apnea severity [41]. Other analyses by the same research group suggested genetic factors seem to underlie the susceptibility to sleep apnea and obesity among Blacks [42]; they suggest further that the severity of sleep apnea could modulate the genetic determinants of obesity in that ethnic group.

## 5. Epidemiology of glaucoma

Glaucoma is a disease defined by slow progressive loss of vision in association with characteristic signs of damage to the optic nerve. If left untreated, glaucoma leads to blindness, which could lead to sleep disturbances, diminished capacity in activities of daily living, reduced quality of life, and depressed moods [43-46]. Glaucoma is the leading cause of irreversible blindness among Blacks, and the second leading cause for all Americans [47,48]. Of the various forms of glaucoma (e.g., congenital, open-angle, closed-angle, secondary), primary open-angle glaucoma (OAG). is the most common, which affects almost 2.3 million Americans ages 40 and older, or about 1.9% of the U.S. population [49]. Glaucoma increases with age and is more common among Blacks than among Whites. According to data from the Center for Disease Control (CDC), ethnic differences in glaucoma for both men and women widened between 1984 and 1995 (see Figure 2). In the 65-69 age group, prevalence of glaucoma for White females is about 1.6%, while among Black females, prevalence is almost three times higher (4.6%). [49]. The Salisbury Eye Study showed that the prevalence of open-angle glaucoma for Blacks and Whites was 5.7% and 3.4%, respectively [2]. According to the Baltimore Eye Survey, which investigated a randomly selected, stratified, multistage cluster sample of 2395 Blacks and 2913 Whites (40 years of age and older), Whites were more likely to exhibit age-related macular degeneration, whereas Blacks primarily showed open-angle glaucoma [47]. This survey also showed that primary open-angle glaucoma accounted for 19% of all blindness among Blacks; this was six times as frequent among Blacks as among Whites and on average began 10 years earlier [47]. Interestingly, according to a population-based study the prevalence of glaucoma surgery among Blacks was 45% lower than the prevalence for Whites, although glaucoma is four times more prevalent among the former. [43]

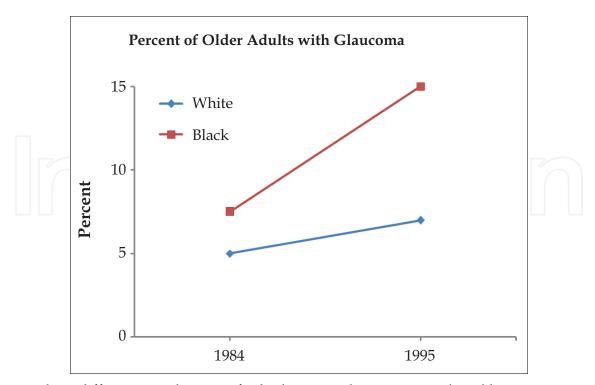


Fig. 2. Ethnic difference in glaucoma for both men and women is widened between 1984 and 1995; adapted from data obtained by the Center for Disease Control

### 6. Impaired regulation of ocular blood flow in glaucoma

The hypothesis that regulation of ocular blood flow might be impaired in glaucoma patients has received much attention since its inception in 1879. Principally, there are two competing theories purporting to explain the pathogenesis of glaucomatous optic neuropathy: the mechanical theory of glaucoma and the vascular theory of glaucoma. Technological advances have provided the impetus for several research studies examining the vascular theory. Essentially, it postulates that glaucomatous optic neuropathy results from inadequate blood flow caused by either increases in intraocular pressure or other risk factors that diminish ocular blood flow supply [50,51]. These two theories do not appear to be mutually exclusive. Both mechanical and vascular factors may converge to effectuate changes in intraocular pressure that might adversely impact perfusion of the retina and the optic nerve head [51,52]. It is equally likely that vascular dysregulations might increase the susceptibility to intraocular pressure (IOP).

Numerous clinical and epidemiologic studies converge to support the argument that deficits in ocular blood flow play a key role in the pathogenesis of glaucoma [50-55]. Indeed, population-based studies show an inverse relationship between ocular blood flow and intraocular pressure (Thessaloniki Eye Study). or associations between glaucoma and perfusion pressure (Barbados Eye Study, Baltimore Eye Study, and Neumarkt Glaucoma Study). [48,55,56]. A 9 year follow up to the Barbados Eye study indicated that lower ocular perfusion pressure [<40mmHg] more than doubled the risk for open angle glaucoma. (RR, 2.6; 95% CI, 1.4-4.6). [51]. With elevation of IOP, a linear and sensitive reduction in circulation through the short posterior ciliary arteries is commonly documented [55]. Some have argued that reduction of ocular blood flow often precedes reperfusion damage, and among glaucoma patients blood flow can also be reduced in other parts of the body.[53] Thus, ischemia and reperfusion damage do not seem to reflect hemodynamic changes only in vascular beds within the eye.

Numerous trials and reviews have discussed vascular dysregulation along with evidence for potential associations with Glaucoma. Dysfunction of both the autonomic nervous system and vascular endothelial cells might be a causal factor [52,54]. The underlying mechanism of the vascular dysregulations observed in glaucoma is not yet fully elucidated. Sleep apnea might also play a key role, as it produces myocardial infarction and/or nocturnal angina due to arterial vasospasm [57].

It is also important to note that even among patients with normal IOP, impaired blood flow may be observed. In addition, vascular compromise may occur in the presence of normal intraocular pressure if the lamina cribrosa, sclera, and cornea are thin [44]. A report by our colleagues at Indiana University indicated that glaucoma patients, who are otherwise characterized by normal pressure, exhibited prolonged retinal arteriovenous passage times in fluorescein angiography and color Doppler imaging, which suggests increased resistance downstream from the central retinal and posterior ciliary arteries [58]. This finding corroborates existing epidemiologic and clinical studies, evidencing that intraocular pressure may not be the only etiological factor in glaucoma [59]. Accumulating evidence points to ocular ischemia as a major factor as well [60]. Indeed, low perfusion pressure constitutes a significant risk factor for open-angle glaucoma, and most clinical studies comparing healthy and glaucoma patients demonstrate a reduction in perfusion pressure among the latter [50]. Authors of that review paper argue that the observed vascular dysregulation may be the principal element causing both low perfusion pressure and

insufficient autoregulation. Newly available technology helps support this theory by allowing us to measure retinal blood flow rate. In a study of retinal blood flow in response to postural changes, patients with OAG were shown to have a very broad range of hemodynamic responses versus controls, suggesting dysregulation or no regulation of the retinal vasculature [54]. Thus, insufficient regulation could lead to low perfusion pressure as well as widely fluctuating perfusion pressures. Chronically low perfusion pressure and unstable, fluctuating pressures may in turn lead to ischemia and reperfusion damage [50].

## 7. Sleep apnea and glaucoma – Is there an association?

The link of sleep apnea to eye disorders has been reviewed recently [61]. Essentially, sleep apnea is linked to glaucoma [10-13], floppy eyelid syndrome [16,62], keratoconus [63], papilledema [64], and optic neuropathy [65]. In the present paper, we focus on glaucoma because it disproportionately affects individuals of the Black ethnicity, offering opportunities for research in its biologic and cultural underpinnings.

Examination of published reports on the link between glaucoma and sleep apnea has indicated that the prevalence of glaucoma among patients with sleep apnea ranges from 2% to 7.2% [11,14,15]. A recent cross-sectional case series suggested that as much as 27% of patients with moderate to severe sleep apnea might have glaucoma [66]. There is a lack of consensus whether the prevalence of glaucoma among patients with sleep apnea is greater than observed in the general population [15]. The discrepancy in reported findings amply demonstrates the need for random and representative, population-based studies to determine whether in fact patients with sleep apnea are at increased risks for developing glaucoma. Results of previous studies have limited generalizability because of selection bias, non-representative sampling, and small sample sizes. A recent Chicago study using a relatively larger sample size of 247 indicated the prevalence of glaucoma among patients with sleep apnea to be 5.7% [10].

Regarding the prevalence of sleep apnea itself among patients with glaucoma, no large-scale representative studies have been undertaken. Available estimates of the prevalence of sleep apnea among patients with glaucoma (ages 45 years and older). range from 20.0% to 57% [12,13]. Within glaucoma subtypes, approximately half of the patients with normal-tension glaucoma and one-third of those with primary open-angle glaucoma exhibit sleep apnea syndrome [67]. As noted previously, these results have not been replicated in the general population. If confirmed, this would support the argument that a sleep history should be recommended for patients with glaucoma [16].

## 8. Complex relationships between sleep apnea and glaucoma

The relationships between glaucoma and sleep apnea are somewhat complex. Several systematic studies are necessary to explicate fully the nature of those relationships. Clinical studies typically show that sleep apnea is associated with several glaucoma indices including intraocular pressure, visual field mean deviation, cup-to-disk ratios, and retinal nerve fiber layer thickness [68-70]. Additionally, evidence from a treatment study using ocular oxymetry recording, a novel tool utilized to measure ocular oxygen tension [71], suggests an association between finger blood flow and optic nerve head blood flow among patients with glaucoma. [72] Other preliminary data show reduction in intraocular pressure among glaucoma patients following a regimen of continuous positive airway pressure [73].

Hence, observational and clinical data converge to support an association between sleep apnea and glaucoma. Nonetheless, systematic studies are needed to establish the causal relationships between these two conditions. Though a direct relationship has not yet been established, data from a recent study makes an effort to imply some correlation. The study splits Sleep apnea patients up into a normal/mild group and a moderate/severe group. The prevalence of Glaucoma in the moderate/severe group was estimated to be 7.1%, significantly higher (p=.033). than the normal/mild group [10]. This study also suggested the severity of obstructive sleep apnea to be inversely correlated with the retinal nerve fiber layer thickness.

Delineating the nature of relations between sleep apnea and ophthalmic diseases remains a challenge. It is worth examining whether there is a direct influence of sleep apnea and glaucoma on ocular blood flow. Conceivably, glaucoma and sleep apnea have an interactive effect on ocular blood flow dysregulations. Preliminary data obtained from 31 patients with sleep apnea undergoing orbital doppler ultrasonography suggests a positive correlation between the ophthalmic artery resistivity index and the mean visual field defect, pointing to the possibility that visual field defects might be due to optic nerve perfusion defects [74]; of note 12.9% of the patients with glaucoma in that study had sleep apnea. These data are consistent with a previous study indicating that blood flow parameters in the orbital vessels were significantly different between patients with sleep apnea and those without the condition [75]. Specifically, among patients with mild sleep apnea, peak systolic velocity and end diastolic velocity in the posterior ciliary arteries were significantly higher than those observed for the control group [75]. In the next two sections, we discuss the effects of hypertension and obesity on the relationships between glaucoma and sleep apnea and the hypothesized effects of sleep apnea on ocular blood flow.

Since available studies do not permit an examination of ethnic effects on associations between sleep apnea and glaucoma, we rely on prevalence data to determine whether Blacks are at greater risk for related comorbidity. Epidemiologic evidence strongly supports the notion that both sleep apnea and glaucoma are highly prevalent among Blacks, and younger Black individuals are particularly more vulnerable [1,40,41]. Although not yet verified, data from two independent lines of clinical investigation have provided support for the idea that ethnicity influences associations between sleep apnea and glaucoma. The first line of study showed that retinal nerve fiber layer is thinner among patients with sleep apnea [69,76,77], which parenthetically generated the hypothesis that reduced ocular perfusion related to hypoxia and vasospasm observed in sleep apnea may cause nerve fiber layer thinning. The second line of investigation showed that retinal nerve fiber layer is typically thinner among Black patients [78]. Plausibly, Blacks with sleep apnea could have even thinner nerve fiber layers. Future large-scale, population-based studies should investigate some of the nuances in the link between glaucoma and sleep apnea and explore the reasons why blacks tend to show worse outcomes for these conditions.

# 9. Sleep apnea and glaucoma - Role of hypertension

One of the complexities permeating relations between glaucoma and sleep apnea relates to the fact that both conditions are potentially characterized by similar pathogenetic mechanisms. Both sleep apnea and glaucoma are linked to hypertension [25,40,79-82], which is more prevalent among Blacks (44% vs. 23%). based on a multi-site study of medically underserved patients [3]. Available data suggests that approximately 40% of patients with

sleep apnea suffer from hypertension, whereas 30% of hypertensive patients have occult sleep apnea [79]. Data from the Wisconsin Sleep Cohort Study, sampling 1060 women and men ages 30 to 60 years showed a dose-response relationship between sleep apnea and blood pressure, independent of several confounding factors [25]. Furthermore, clinical evidence suggests that continuous positive airway pressure treatment for sleep apnea results in a diminution of daytime and nighttime arterial blood pressure [80].

Concerning linkage between glaucoma and hypertension, studies have shown that patients with normal-tension glaucoma exhibited increased variability of night-time blood pressure compared with healthy controls [82]. This is important since increased fluctuation of blood pressure may lead to ocular reperfusion damage and may cause ischemic episodes at the optic nerve head. According to a case-control study, hypertension was significantly more common among patients with glaucoma relative to age- and gender-matched individuals with healthy eyes (OR: 1.29 [81]. Investigators concluded that common pathogenetic mechanisms in ciliary and renal tubular epithelia might explain co-occurrence of glaucoma and systemic hypertension. It is important to mention that a few epidemiologic studies found mixed results. A recent review of studies discussing the association between glaucoma and hypertension acknowledges these studies that found weak or no relationships [52]. The same review acknowledges that blood pressure is likely related to intraocular pressure, but not necessarily the incidence of glaucoma.

## 10. Sleep apnea and glaucoma - Role of obesity

One might also conjecture another viable hypothesis that would suggest that both sleep apnea and glaucoma are caused by a defect in a common pathway potentially resulting from obesity (see Figure 1). Obesity is the strongest predictor of sleep apnea, with estimates suggesting that 60-90% of patients with sleep apnea are obese (defined as BMI >28 kg/m²); data also suggests that a BMI of 28 kg/m² has a sensitivity of 93% and a specificity of 74% for sleep apnea [83]. Data analyzed from the National Health and Nutrition Examination Survey estimated the prevalence of sleep apnea in persons without obesity to be 3% in men and 0.7% in women (p<0.01), while in persons with obesity to be 12.1% in men and 7% in women (p<0.01). [24]. On balance, it is noteworthy that not all patients with sleep apnea are obese, suggesting the involvement of other explanatory factors. Mixed results have been found regarding effects of obesity on intraocular pressure, the widely accepted marker for glaucoma [84]. It may be that body mass index, the most commonly utilized obesity measure, is inadequate when predicting eye disorders [85].

It is likely that sleep apnea and glaucoma represent manifestations of what is referred to as the metabolic syndrome. Metabolic syndrome is defined as a cluster of interrelated risk factors of metabolic origin that increase chances of developing heart disease, stroke, and diabetes. The risk factors include raised blood pressure, dyslipidemia (raised triglycerides and lowered high-density lipoprotein cholesterol), raised fasting glucose, and central obesity. Metabolic syndrome is an emerging public health concern, affecting 25% of adult Americans [86]. According to data from the third National Health and Nutrition Examination Survey of adults (ages  $\geq$  20 years), the age-adjusted prevalence was similar for men (24.0%). and women (23.4%), but Black women had approximately a 57% higher prevalence than did Black men [4]. Individuals with the metabolic syndrome have several co-occurring disorders of the body's metabolism: obesity, hypertension, dyslipidemia, and hypercholesterolemia [87].

A direct link between metabolic syndrome and sleep apnea has not been systematically established. However, preliminary evidence from the Mayo Clinic indicates that the metabolic syndrome might be more prevalent among patients with sleep apnea. Clinical data shows that 60% of patients with sleep apnea had metabolic syndrome, compared with 40% of patients without sleep apnea [23]. Evidently, the components of the metabolic syndrome each correlate highly with sleep apnea [87]. Clinical evidence also suggests that the metabolic syndrome is associated with glaucoma; intraocular pressure is higher among individuals with this disease [88].

If indeed obesity was the final common pathway, this might explain the greater prevalence of sleep apnea and glaucoma among Blacks. Blacks are at greater risk for associated metabolic diseases because they are disproportionately more obese compared with Whites (see Table 1). According to data from the National Center for Health Statistics, about two-thirds of American adults are either overweight (BMI > 25; 33%). or obese (BMI > 30; 31%). [89]. The age-adjusted prevalence of overweight/obesity in ethnic minorities, especially minority women, is higher than in Whites in the U.S., reaching a critical level of greater than two-thirds of the female minority population [90].

### 11. Sleep apnea and ocular blood flow

No conclusive evidence exists for a cause-and-effect relationship between sleep apnea and glaucoma, although it is believed that various physiologic factors produced by sleep apnea may play a significant role in the pathogenesis of glaucoma [91,92]. Sleep apnea is widely recognized for its adverse vascular sequelae: acute myocardial infarction and/or nocturnal angina caused by arterial vasospasm [57]. These may be particularly harmful among patients with glaucoma because at night, ophthalmic artery flow velocities decrease commensurate with reductions in arterial blood pressure[82]. This is considered a vulnerable period when the risk of disease progression is heightened. It should also be noted that intraocular pressure increases, especially in glaucoma patients in the supine position [44] and may further influence the progress of glaucoma.

Optic nerve vascular dysregulation might be secondary to sleep apnea-induced arterial hypertension and arteriosclerosis [93]. Plausibly, impaired optic nerve-head blood flow autoregulation is a sequela of repetitive apnea events [93]. One study suggested that repetitive deep hypoxia, a phenomenon commonly observed during apneic events, might directly damage the optic nerve [13]. It is not certain whether repetitive hypoxia would cause increased intraocular pressure among patients with normal-tension glaucoma, based on data from a case study involving 3 patients [94]. This discrepancy may be explained by age differences in the sample studied; preliminary data suggested that effects of sleep apnea are more pronounced among older patients with normal-tension glaucoma [13]. Investigators argue that both chronic hemodynamic changes and recurring severe hypoxia may contribute to anoxic optic nerve damage observed in glaucoma [67].

Thus, sleep apnea might offer one explanation for the increased prevalence of glaucoma among Blacks. Since sleep apnea and hypertension are worse among Blacks [1,3], this might augur greater impairment of optic arterial blood supply for Blacks. Notwithstanding, the knowledge that Blacks might be at greater risk for morbidity related to untreated sleep apnea and glaucoma, little has been done to investigate the clinical presentation and course of these two diseases in that population. In effect, studies reported to date have only considered group analyses, making it difficult to ascertain racial/ethnic effects on the association between sleep apnea and glaucoma.

## 12. Link among sleep apnea, glaucoma, obesity, hypertension and blood flow

The aforementioned associations do not seem to be fortuitous, judging from the consistency across studies. Whether obesity is the final common pathway has not been convincingly demonstrated, although it is involved in all the disease entities herein discussed (see Figures 1 and 3). Obesity, glaucoma, and hypertension are all associated with sleep apnea, perhaps bi-directionally. This gives rise to the need for empirical studies testing causal models to explain links among obesity, hypertension, sleep apnea, blood flow, and glaucoma. One could imagine the difficulties inherent in performing experimental tests of cause-and-effects relationships of those factors. Such linkage analyses could benefit from the application of path analysis using available national data. Only through costly, systematic, empirical studies can we arrive at definitive explanations of causal models.

To date, no systematic linkage analyses have been performed to elucidate relations between sleep apnea and ocular blood flow dysregulation. If it can be demonstrated that sleep apnea is a mediating factor in the associations between glaucoma and ocular blood flow, this would lead to enhanced strategies to treat glaucoma. Identification and characterization of the relationship between sleep apnea and glaucoma would assist in the diagnosis and treatment of patients with glaucoma whose disease progresses despite medical intervention to lower intraocular pressure.

In formulating a glaucoma diagnosis, the clinician may have to consider the status of the autonomic nervous system in its relations to systemic hemodynamic parameters that might be dysfunctional. In addition, this information will assist the clinician in formulating novel treatment strategies for glaucoma that focus on enhancing end-tissue oxygenation. Since Blacks are at increased risks for developing both glaucoma and sleep apnea, special efforts should be made to target interventions to Blacks in underserved communities.

#### 13. Conclusions

Most of the initial studies reported to date have used relatively small sample sizes, offering little definitive explanation of the link between sleep apnea and glaucoma or whether ethnicity influences such associations. Epidemiologic evidence shows that both glaucoma and sleep apnea are more prevalent among Blacks, and that their onset is earlier in that population. Glaucoma and sleep apnea are potentially characterized by similar pathogenetic mechanisms, as they are both linked to hypertension and obesity. Obesity and hypertension are highly prevalent in the Black population and are widely recognized for their involvement in numerous vascular diseases. Efforts are underway to ascertain whether one condition has a direct effect on the other or whether their co-occurrence engenders worse physiologic and behavioral outcomes among at-risk individuals. Plausibly, individuals with glaucoma show ocular hemodynamic changes and blood flow deficits due to untreated sleep apnea, which is more common among Blacks [7-9]. Systematic studies exploring reasons why Blacks don't participate in screening events or are not receiving timely diagnoses are needed. It may be assumed that the reasons for low participation in screening are probably lack of awareness and occupation with other issues.

Along with further epidemiological investigation, genetic research could also be explored. Genome scanning has already suggested genetic factors linking sleep apnea to obesity, diabetes, and insulin resistance [26,41,42]. More recent analysis of mRNA expression, protein interaction, and results from genome-wide association studies has made an attempt to connect some of the known pathways between these known co-morbidities [16]. This approach could be used in the future to better explain the potential link between sleep apnea and glaucoma.

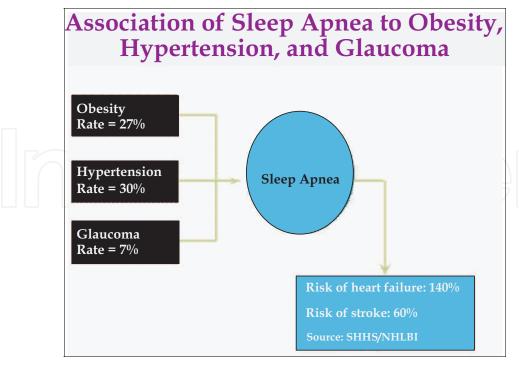


Fig. 3. Prevalence of individuals with obesity, hypertension, and/or glaucoma who also carry a diagnosis of sleep apnea; sleep apnea is itself a strong risk factor for cardiovascular disease

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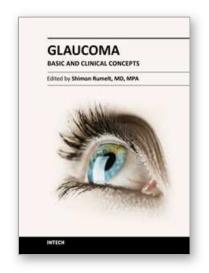
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This book addresses the basic and clinical science of glaucomas, a group of diseases that affect the optic nerve and visual fields and is usually accompanied by increased intraocular pressure. The book incorporates the latest development as well as future perspectives in glaucoma, since it has expedited publication. It is aimed for specialists in glaucoma, researchers, general ophthalmologists and trainees to increase knowledge and encourage further progress in understanding and managing these complicated diseases.

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