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A study on the Relationship between morning cortisol levels and fasting blood glucose in shift workers exploring the hypothamic-pituitary-adrenal axis Dysregulation

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ABSTRACT

Background: Shift work is associated with disruption of circadian rhythms and hypothalamic–pituitary–adrenal (HPA) axis dysregulation, potentially contributing to metabolic abnormalities. Alterations in cortisol secretion patterns and glucose metabolism among shift workers may increase the risk of early onset metabolic syndrome and type 2 diabetes mellitus.

Objective: To assess the relationship between morning serum cortisol levels and fasting blood glucose among shift workers, exploring the possible contribution of HPA axis dysregulation to early metabolic derangements.

Materials and Methods: This prospective, observational study was conducted at Katuri Medical College and Hospital over six months (October 2023 to March 2024). A total of 100 participants were enrolled, including 70 shift workers and 30 daytime controls. Morning serum cortisol levels and fasting blood glucose levels were measured following overnight fasting. Statistical comparisons between groups were made using the Independent Samples t-test, and the correlation between cortisol and glucose was evaluated using Pearson's correlation coefficient. A p-value < 0.05 was considered statistically significant.

Results: Shift workers exhibited significantly higher mean morning serum cortisol levels (19.5 ± 4.2 µg/dL) compared to controls (15.8 ± 3.6 µg/dL; p = 0.001). Mean fasting blood glucose levels were also elevated among shift workers (101.6 ± 12.5 mg/dL) relative to controls (91.2 ± 10.3 mg/dL; p = 0.002). A moderate positive correlation was found between morning cortisol and fasting blood glucose levels among shift workers (r = +0.41, p = 0.0008).

Conclusion: Morning cortisol levels and fasting blood glucose are significantly elevated among shift workers, with a moderate positive correlation between the two parameters. These findings highlight the early influence of HPA axis dysregulation on glucose metabolism in shift workers and underscore the importance of early screening and preventive strategies to mitigate long-term metabolic risks.

Keywords: Shift work, Morning cortisol, Fasting blood glucose, HPA axis dysregulation, Circadian rhythm, Metabolic risk.

INTRODUCTION

The hypothalamic–pituitary–adrenal (HPA) axis plays a central role in the regulation of stress responses, metabolic homeostasis, and glucose metabolism. Cortisol, the end-product of HPA axis activation, follows a circadian secretion pattern, peaking in the early morning hours and declining progressively throughout the day. Disruptions in this rhythmicity, as observed in shift workers, have been implicated in a wide range of metabolic abnormalities, including impaired glucose tolerance and increased risk of type 2 diabetes mellitus [1,2].

Shift work, characterized by irregular sleep–wake cycles and nocturnal activity, leads to desynchronization of the circadian rhythm. This circadian misalignment contributes to HPA axis dysregulation, potentially resulting in altered cortisol secretion patterns and adverse metabolic outcomes [2,3]. Numerous epidemiological studies have reported an association between shift work, hypercortisolemia, and elevated fasting blood glucose levels, suggesting that HPA axis dysfunction could mediate early metabolic disturbances [1,4].

Morning cortisol measurement serves as an accessible biomarker for evaluating HPA axis function. Alterations in morning cortisol levels have been associated with changes in fasting glucose levels across different populations [2,5].

Furthermore, variations in cortisol reactivity under different metabolic states, such as fasting or glucose loading, can provide additional insights into stress–glucose interactions [3].

Elevated fasting cortisol levels have also been linked to increased cardiovascular risk factors, including ischemic heart disease and type 2 diabetes, highlighting the systemic implications of HPA axis dysregulation [4]. In youth populations with overweight or obesity, perceived stress and elevated morning cortisol have shown positive associations with adverse glycemic measures, emphasizing that these relationships are evident across age groups [5].

Interestingly, even in non-diabetic individuals suffering from chronic conditions like chronic widespread pain, elevations in morning cortisol and fasting glucose have been documented independent of comorbidities such as restless legs syndrome [6], underscoring the broad metabolic influence of HPA axis alterations.

Despite growing evidence, limited research has specifically addressed the relationship between morning cortisol levels and fasting blood glucose among shift workers within the Indian population. Regional differences in work patterns, dietary habits, genetic predispositions, and environmental factors may modulate these associations.

This study, conducted at Katuri Medical College & Hospital, was designed to evaluate the relationship between morning cortisol levels and fasting blood glucose in shift workers compared to controls, with a focus on understanding potential HPA axis dysregulation and its metabolic consequences.

MATERIALS AND METHODS

Study Design and Setting

This was a prospective, observational, comparative study conducted at Katuri Medical College and Hospital, Guntur, over a period of six months, from October 2023 to March 2024.

Study Population

The study included a total of 100 participants, comprising:

- 70 shift workers engaged in night or rotational shifts for at least six months,
- 30 controls comprising individuals working standard daytime hours, matched for age and sex.

Inclusion Criteria

- Individuals aged 20–60 years.
- Shift workers with a minimum shift work exposure of ≥6 months.
- Willingness to participate and provide informed written consent.

Exclusion Criteria

- Known cases of diabetes mellitus, hypertension, or endocrine disorders.
- Use of glucocorticoids or medications affecting cortisol metabolism.
- Pregnancy, lactation, or known psychiatric illnesses.
- Shift workers with less than 6 months of shift exposure.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee of Katuri Medical College and Hospital. Written informed consent was obtained from all participants prior to enrollment.

Data Collection and Methodology

All participants underwent a detailed clinical assessment, including history taking and physical examination. Demographic data such as age and sex, occupational history including shift duration and work pattern, and relevant medical history related to metabolic and endocrine function were documented systematically.

For biochemical assessments, venous blood samples were collected between 7:00 AM and 8:00 AM following an overnight fast of at least 8 hours. Morning serum cortisol levels were estimated using a chemiluminescence immunoassay (CLIA) technique. To ensure consistency and minimize inter-assay variability, all cortisol assays were performed at the same institutional laboratory.

Simultaneously, fasting venous blood samples were analyzed for fasting plasma glucose using an automated glucose oxidase–peroxidase method. Standard operating procedures were followed to maintain sample integrity and accuracy throughout the testing process.

Outcome Measures

- **Primary outcome:** Correlation between morning serum cortisol levels and fasting blood glucose in shift workers.
- **Secondary outcomes:** Comparison of mean cortisol and glucose levels between shift workers and controls.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables, including morning serum cortisol levels and fasting blood glucose, were expressed as mean ± standard deviation (SD). The normality of data distribution was assessed using the Shapiro–Wilk test. Comparisons between shift workers and controls were performed using the Independent Samples t-test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. Correlation between morning cortisol levels and fasting blood glucose was evaluated using the Pearson correlation coefficient for parametric data or the Spearman rank correlation coefficient for non-parametric data. A p-value of less than 0.05 was considered statistically significant.

RESULTS

1. Study Population Characteristics

A total of 100 participants were included, comprising 70 shift workers and 30 control subjects. Shift workers had been engaged in rotational or night shift duties for a mean duration of 4.6 ± 2.1 years. The mean age was 36.8 ± 7.5 years among shift workers and 35.9 ± 8.2 years among controls, with no statistically significant difference between the groups ($p = 0.561$). The gender distribution was comparable, with males constituting 58.6% of the shift workers and 53.3% of the controls ($p = 0.659$). Mean body mass index (BMI) was also similar between the groups (24.7 ± 2.8 kg/m² vs 24.1 ± 2.6 kg/m², $p = 0.324$). Baseline characteristics are summarized in Table 1.

Table1. Baseline characteristics Of The Study Population

Characteristic	Shift Workers (n = 70)	Controls (n = 30)	p-value
Age (years)	36.8 ± 7.5	35.9 ± 8.2	0.561
Male, n (%)	41 (58.6%)	16 (53.3%)	0.659
Female, n (%)	29 (41.4%)	14 (46.7%)	—
BMI (kg/m²)	24.7 ± 2.8	24.1 ± 2.6	0.324
Duration of Shift Work (years)	4.6 ± 2.1	NA	—

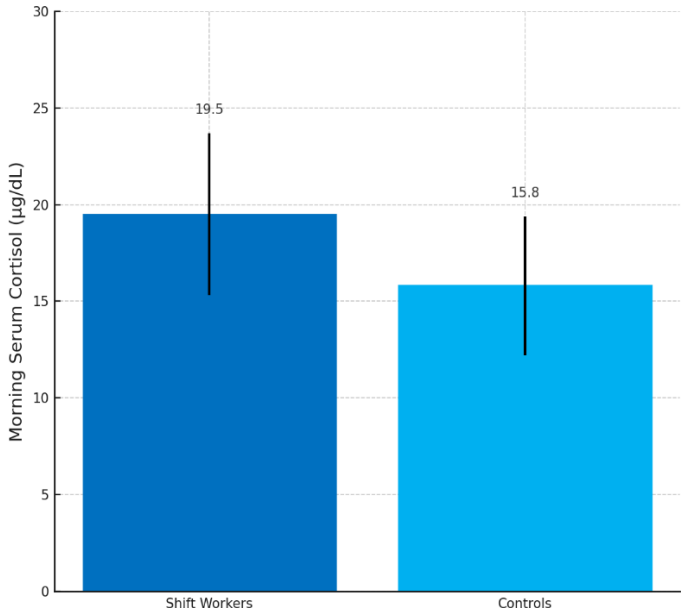
2. Morning Serum Cortisol Levels

The mean morning serum cortisol level among shift workers was 19.5 ± 4.2 µg/dL, significantly higher compared to 15.8 ± 3.6 µg/dL observed in the control group.

The difference was statistically significant ($p = 0.001$), indicating a potential dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis among shift workers.

These findings are graphically represented in Figure 1, illustrating the elevated morning cortisol levels in the shift work group relative to controls.

Figure 1: Comparison of Morning Serum Cortisol Levels



Comparison of mean morning serum cortisol levels between shift workers and controls. Shift workers demonstrated significantly higher morning cortisol levels (19.5 ± 4.2 µg/dL) compared to controls (15.8 ± 3.6 µg/dL) (**p = 0.001**). Error bars represent standard deviations.

3. Fasting Blood Glucose Levels

The mean fasting blood glucose level among shift workers was 101.6 ± 12.5 mg/dL, which was significantly higher compared to the control group, who had a mean fasting glucose of 91.2 ± 10.3 mg/dL. This difference was statistically significant (p = 0.002), suggesting early alterations in glucose metabolism among shift workers, potentially attributable to circadian disruption and hypothalamic–pituitary–adrenal (HPA) axis dysregulation.These findings are summarized alongside cortisol data in Table 2.

Table 2: *Comparison of Morning Serum Cortisol and Fasting Blood Glucose Levels Between Shift Workers and Controls (Mean ± SD).*

Parameter	Shift Workers (n = 70)	Controls (n = 30)	p-value
Morning Serum Cortisol (µg/dL)	19.5 ± 4.2	15.8 ± 3.6	0.001
Fasting Blood Glucose (mg/dL)	101.6 ± 12.5	91.2 ± 10.3	0.002

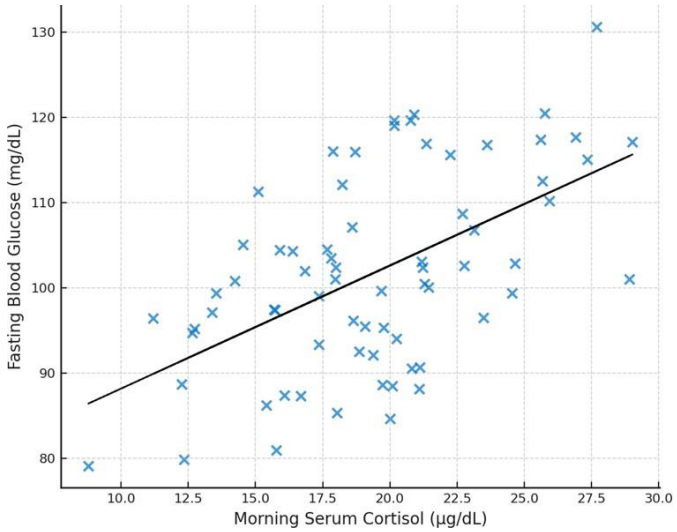
4. Correlation Between Morning Serum Cortisol and Fasting Blood Glucose

Among shift workers, a moderate positive correlation was observed between morning serum cortisol levels and fasting blood glucose levels. The Pearson correlation coefficient (r) was +0.41, indicating a moderate direct relationship, and the correlation was statistically significant (p = 0.0008).

This finding suggests that higher morning cortisol levels may be associated with higher fasting glucose levels among individuals engaged in shift work, supporting the hypothesis of hypothalamic–pituitary–adrenal (HPA) axis dysregulation influencing glucose metabolism.

The relationship between morning cortisol and fasting blood glucose is graphically depicted in Figure 2, illustrating the positive linear association observed.

Figure 2: Correlation between morning serum cortisol and fasting blood glucose levels among shift workers.



A moderate positive correlation was observed ($r = +0.41$, $p = 0.0008$), indicating that higher cortisol levels are associated with higher fasting glucose levels. The dashed line represents the line of best fit.

DISCUSSION

The findings of the present study demonstrate that shift workers exhibit significantly higher morning serum cortisol levels and elevated fasting blood glucose levels compared to controls. Additionally, a moderate positive correlation between morning cortisol and fasting glucose levels was observed among shift workers, suggesting that hypothalamic–pituitary–adrenal (HPA) axis dysregulation may contribute to early metabolic alterations.

Shift work is recognized as a major disruptor of circadian homeostasis, and several studies have highlighted its detrimental impact on metabolic parameters. Padilha et al. [7] reported that early shift work was associated with altered cortisol profiles and impaired glucose metabolism, consistent with the elevated morning cortisol and glucose levels observed in our cohort. This dysregulation may stem from chronic circadian misalignment affecting the HPA axis.

Further supporting these findings, Šušoľiaková et al. [8] demonstrated that early morning shift workers exhibited significantly elevated salivary cortisol levels, reflecting an activated stress response due to disrupted sleep-wake cycles. Burek et al. [9] similarly reported altered synchronization between sleep timing and cortisol profiles among night-shift hospital employees, emphasizing that even subtle shifts in circadian rhythm can have measurable endocrine consequences.

The association between increased cortisol and glucose derangements is further substantiated by Bozic et al. [10], who found that patients with moderate to severe obstructive sleep apnoea, a condition characterized by nocturnal hypoxia and sleep fragmentation, had higher morning cortisol levels and impaired glucose metabolism. Although sleep apnoea was excluded in our study, these parallels reinforce the notion that sleep disruption — whether due to medical conditions or shift work — can significantly alter HPA axis function and glucose regulation.

Mechanistically, cortisol promotes hepatic gluconeogenesis, decreases glucose uptake in peripheral tissues, and exerts lipolytic effects, all of which contribute to hyperglycaemia when cortisol levels are persistently elevated. Raff and Magill [11] reviewed that patients with type 2 diabetes mellitus often exhibit subtle but significant HPA axis hyperactivity, implicating chronic cortisol elevations in the pathogenesis of impaired glucose homeostasis.

Psychiatric comorbidities may also contribute to HPA axis dysregulation. Roy et al. [12] demonstrated that diabetic outpatients exhibited heightened cortisol responses, particularly in the context of psychological stress. While psychiatric disorders were excluded in our population, the overlap between psychological stress, shift work, and metabolic dysregulation warrants further exploration.

Interestingly, Chatzittofis et al. [13] showed that hyperactivation of the HPA axis was not limited to metabolic diseases but also observed in hypersexual disorder, underscoring that chronic stressors — whether psychological, occupational, or social — can impact cortisol regulation.

Beyond glucose metabolism, shift work has been associated with broader metabolic alterations. Arafa and Afify [14] found that shift workers had significantly higher body mass index (BMI) and adverse biochemical profiles compared to day workers. Although BMI was comparable in our cohort, long-term exposure to shift work could progressively contribute to weight gain and worsening metabolic health.

Moreover, long-term shift work has cognitive and neuroendocrine implications. Pavlis [15], in a doctoral study on rotating shift nurses, reported that chronic shift work led to neuroendocrine disruptions affecting both cognitive function and cortisol regulation, reinforcing the systemic impact of circadian disruption.
The strengths of the present study include a focused evaluation of shift workers in a controlled setting, careful exclusion of confounding conditions, and simultaneous assessment of both cortisol and glucose parameters. However, limitations include a relatively modest sample size, the absence of direct assessment of sleep quality or melatonin rhythms, and the cross-sectional nature of the study, which precludes causal inference.

CONCLUSION

Our findings highlight the significant association between morning cortisol levels and fasting blood glucose among shift workers, supporting the role of HPA axis dysregulation in early metabolic disturbances. Given the increasing prevalence of shift work across industries, early identification of endocrine and metabolic alterations is crucial for implementing preventive interventions and minimizing long-term health risks.

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