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Relationship Levels of Proteinuria and Adverse Perinatal Outcomes among Pre-Eclamptic Mothers Delivering at Fort Portal and Mubende Regional Referral Hospitals, Uganda

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ABSTRACT

Pre-eclampsia, a complex pregnancy disorder, poses significant risks to maternal and fetal well-being. Proteinuria levels, and adverse perinatal outcomes among women with pre-eclamptic patients. A prospective cohort study involving 288 pre-eclamptic women, those done we meticulously collected socio-demographic and obstetric data. Proteinuria levels were categorized (mild, moderate, severe, or massive), while adverse perinatal outcomes (low Apgar score at 5th minute, low birth weight, NICU admission, stillbirth, perinatal death) were assessed. Logistic regression determined associations, with significance set at $p < 0.05$. 51.74% faced adverse perinatal outcomes. those with mild proteinuria were 5.25 times more likely to experience adverse outcomes, 51.74 had adverse perinatal outcomes massive perineuria had 22.50 chance of getting adverse perinatal outcome, severe perineuria had 15.55 times more likely to get adverse perinatal outcomes and massive perineuria waste adverse perinatal outcomes ($p < 0.001$). This study underscores the pivotal role of proteinuria levels in shaping adverse perinatal outcomes in pre-eclamptic women. The link between the severity of pre-eclampsia and ANC attendance with adverse outcomes highlights the multifaceted nature of maternal and fetal health in this population. Tailored interventions, intensified ANC, and robust risk stratification are imperative for enhancing the well-being of both mothers and newborns.

Keywords: Pre-eclampsia, Proteinuria, Adverse Perinatal Outcomes, Antenatal Care (ANC), Logistic Regression Analysis

INTRODUCTION

Pre-eclampsia: Is a multisystemic disease characterized by high blood pressure first detected during pregnancy of systolic value of 140 mmHg or more and diastolic value of 90 mmHg or more during a two-interval period in a previously normotensive mother with proteinuria or without proteinuria after 20 weeks of gestation age [1]. Hypertension, diabetes mellitus, proteinuria, obesity, family history, nulliparity, multiple pregnancies and thrombotic vascular disease contribute as the risk factors for [2]. Preeclampsia is a leading contributor to maternal and neonatal morbidity and mortality, despite the fact that its pathophysiology is not well known [3]. The risk factors align with the pathogenesis of preeclampsia, which involves uteroplacental mismatch, syncytiotrophoblast factors, and an imbalance of angiogenic factors, which lead to maternal systemic endothelial dysregulation and inflammation, a process similar to sepsis [4]. Despite the fact that a number of studies have linked high levels of proteinuria to adverse birth results, The precise effect of proteinuria on birth outcomes is still unknown [5]. The diagnostic criteria for preeclampsia, according to the American College of Obstetricians and Gynecologists, the assessment of hypertensive thresholds is done with either proteinuria (i.e., 300 mg per 24 hours) or without proteinuria (i.e., systolic and diastolic blood pressures of 140 and 90 mmHg, respectively, occurring twice, four hours apart, after 20 weeks) [6]. There are also defined criteria for disease severity and they have been revised over the last decades. Proteinuria levels were evaluated to assess the severity of preeclampsia up to the early 2000s, and a urine protein excretion level of >2 g/24 hours was often the cutoff number for advising pregnancy termination [7]. According to the committee opinion of the American College of Obstetricians and Gynecologists, proteinuria was eliminated from the primary diagnostic criteria for the diagnosis of PE in 2013. The pathological change that takes place in pregnant women with pre-eclampsia is known as systemic arteriolar spasm, which can affect all organs but

is most usually observed in the kidney. Renal arteriolar spasm reduces renal perfusion volume and glomerular filtration rate, damages endothelial cells, increases permeability of the glomerular basement membrane, and causes selective proteinuria. In the revised preeclampsia recommendations published in 2014 by the International Society for the Study of Hypertension in Pregnancy (ISSHP), proteinuria is no longer necessary [8]. In the literature, there are studies showing that massive proteinuria has negative effects especially on fetal outcomes and also on maternal outcomes [9]. Most guidelines recommend oral nifedipine, parenteral labetalol, or parenteral hydralazine.4 as antihypertensive drugs in pre-eclampsia. Magnesium sulfate is effective for the prevention and treatment of preeclampsia, but implementation has been challenging. Antenatal glucocorticoids should be administered according to local gestational age–based guidance for acceleration of fetal pulmonary maturity and prevention of fetal or newborn death, intraventricular hemorrhage, and developmental delay [10].

Previous research has revealed various proteinuria cutoff values that are assumed to be connected to unfavorable preeclampsia outcomes. Uncertainty exists over the efficacy of these criteria in predicting substantial clinical outcomes [7]. This research highlights the relationship between levels of proteinuria and adverse perinatal outcomes and summarize the sociodemographic, obstetric and medical factors like age, marital status, occupation, BMI, gravidity, parity, history of diabetes and HIV status and how they can influence proteinuria among pre-eclamptic pregnant women. Study done in turkey, the results of 230 pregnant women with hypertension were evaluated. Of these, 90 (39.1%) had 24-hour proteinuria ≥300 mg, and 140 (60.9%) had 24- hour proteinuria <300 mg. Of 230 pregnant women, 70 (30.4%) had P/C≥0.3 and 160 (69.6%) had P/C<0.3 [11]. The top limit for normal proteinuria during pregnancy is 300 mg/24 hours, according to international recommendations, however there isn't any proof that this level is associated with bad results. Some authors, including those who wrote the Canadian Hypertension Committee Guidelines for management of hypertensive disorders of pregnancy, believe that a threshold of 300 millimeters per hour (m/24) is a poor predictor of clinical outcome and that a threshold of 500 millimeters per hour (m/24), or a protein/creatinine ratio of 0.5 milligrams per liter, is a better indicator of women who are at risk of unfavorable outcomes [12].

METHODOLOGY

Study Design

A prospective cohort study was used.

Study Setting

The research took place in the maternity labor suite of the FortPortal and Mubende Regional Referral Hospitals, located in western Uganda.The in-patient capacity of FRRH is 350 beds distributed in all departments with 105 beds within the obstetrics and gynecological department. The department has nine Obstetrics and Gynecology specialists, 5 resident doctors, 6 Anesthetists, 2 special grade medical officers, 3 medical officers, 5 intern doctors, and 13 midwives and 12 nurses who work in FRRH Obstetrics and Gynecology department.

Inclusion Criteria and Exclusion Criteria

The study had included all pre-eclamptic women who were in delivered in labor suites of FRRH and MRRH during the study period for delivery services and had given their consent to participate in the study. Mothers with Multiple gestation, known diabetes, known with renal diseases, known with chronic hypertension had excluded from the study

Sample Size Determination

The study was done in Australia by [13]: Proportion of pre-eclamptic mothers who had proteinuria was 75%. The sample size was calculated using the Kish Leslie formula (1965):

$$n = \frac{z^2 p(1-p)}{e^2}$$

([14] reported 10% incidence of perinatal outcomes).

$$n = \frac{(1.96)^2 \times 0.75 \times (1-0.75)}{(0.05)^2} = 288$$

Data Collection Procedure

The lead investigator gathered data, and we taught assistants to use a well-structured, pre-tested, interviewer-administered questionnaire designed to obtain important information following their written informed permission and the ethics review board's ethical approval of the project. When necessary, we used a translator. All consenting preeclamptic moms in the labor suite who met the inclusion criteria were taken into account. The questionnaire was

written in English and then translated into Rutooro, the local language. After the data was collected, each questionnaire's replies were re-translated into English for analysis and reporting. The responses were coded in Excel using the edit command, then exported to SPSS version 25.0 for data analysis.

Ethical Considerations

The department of Obstetrics and Gynecology, the Faculty, and the postgraduate school, as well as the Bishop Staurt University Research and Ethics council (BSU-REC) all approved the study. Before the study was carried out, the approved letter was presented to the hospital administration, and consent/permission was sought from the hospital administration.

Study Flow Process

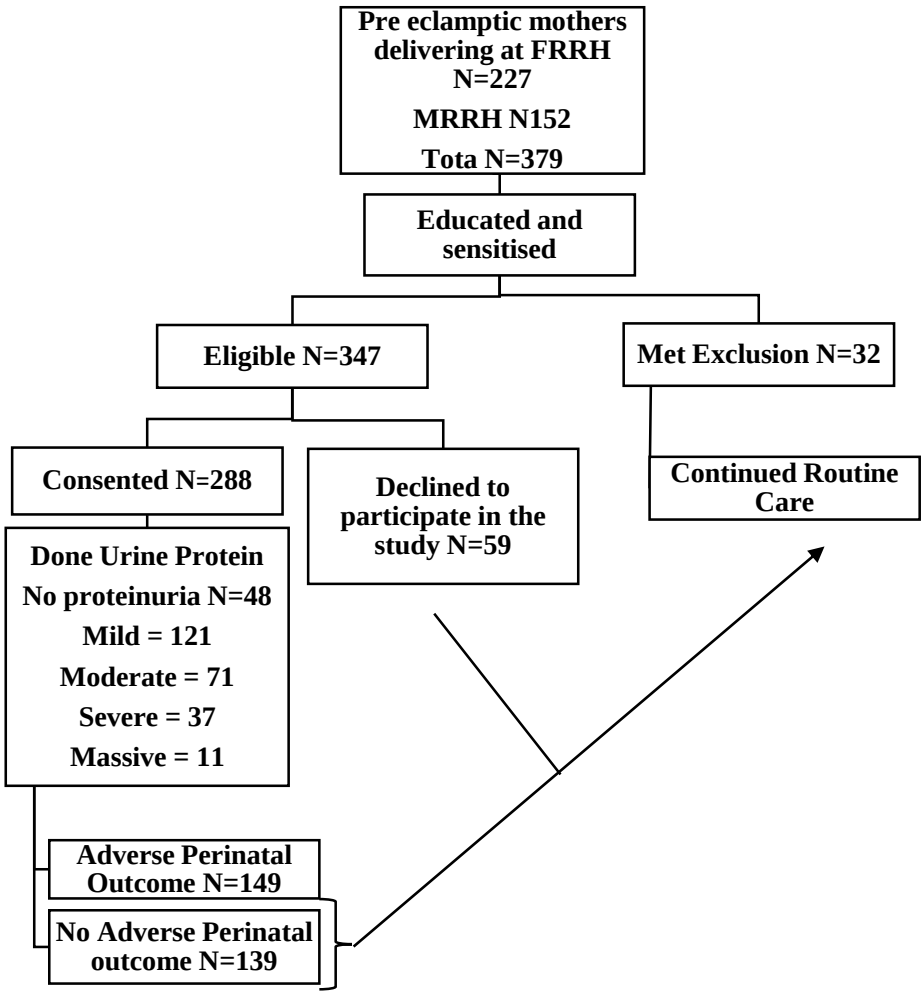

Figure 1 Study Flow Diagram

Table 1: Levels of proteinuria N=288

Level Of Proteinuria	Frequency n	Percentage %	95.0% CI
No proteinuria	48	16.67	12.77 – 21.46
Mild proteinuria	121	42.01	36.41 - 47.83
Moderate proteinuria	71	24.65	19.99 – 29.99
Severe proteinuria	37	12.85	9.43 – 17.25
Massive proteinuria	11	3.82	2.12 - 6.78

The table reveals that among the study participants, the majority (42.01%) had mild proteinuria, while smaller percentages exhibited no proteinuria (16.67%), moderate (24.65%), severe (12.85%), or massive (3.82%) proteinuria, with corresponding 95% confidence intervals provided for each category.

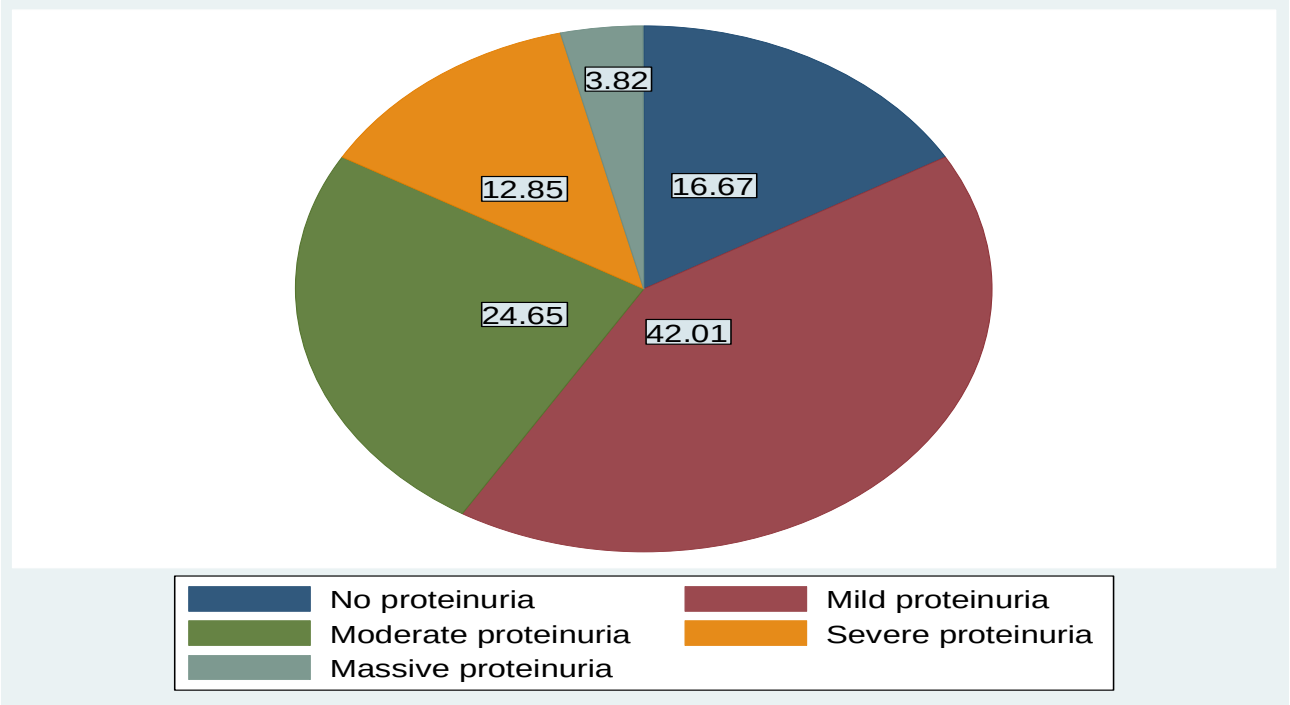

Figure 2: A pie chart showing the distribution of proteinuria levels among study participants.

Table 2: Incidance of adverse perinatal outcomes

Adverse Perinatal Outcome	Frequency n	Percentage %	95.0% CI
No	139	48.26%	(42.53%-54.03%)
Yes	149	51.74%	(45.97%-57.47%)

The findings in Error! Reference source not found. above indicate that 51.74% faced **an** adverse perinatal outcome, with corresponding 95% confidence intervals estimated at (45.97%-57.47%).

Table 3. The proportion of participants with the different adverse perinatal outcomes

Adverse perinatal outcomes		Frequency n	Percent %	95.0% CI
APGAR Score	Less than 7	93	32.3%	(27.1%-37.8%)
	7 or more	195	67.7%	(62.2%-72.9%)
Low Birth Weight	No	191	66.3%	(60.7%-71.6%)
	Yes	97	33.7%	(28.4%-39.3%)
Admission to NICU	No	187	64.9%	(59.3%-70.3%)
	Yes	101	35.1%	(29.7%-40.7%)
Stillbirth	No	257	89.2%	(85.3%-92.4%)
	Yes	31	10.8%	(7.6%-14.7%)
Early neonatal Death	No	269	93.4%	(90.5%-96.3%)
	Yes	19	6.6%	(3.7%-9.46%)

Table 3 displays the frequency distribution of adverse perinatal outcomes, with NICU admission, low birth weight, and low APGAR scores being the most prevalent adverse outcomes.

Table 4 Relationship between Level of Proteinuria and Adverse Perinatal Outcomes

	Adverse Perinatal Outcome		OR (95% CI)	
	No	Yes		
No proteinuria	40	8	Ref	
Mild proteinuria	**59**	**62**	**5.25 (2.27-12.15)**	**<0.001***
Moderate proteinuria	**29**	**42**	**7.24 (2.96 – 17.71)**	**<0.001***
Severe proteinuria	**9**	**28**	**15.55 (5.34 - 45.25)**	**<0.001***
Massive proteinuria	**2**	**9**	**22.50 (4.06 – 124.38)**	**<0.001***

**p<0.05 statistically significant, OR=Odds Ratio, CI=Confidence Interval*

In Table 4 above, we see the odds of experiencing adverse perinatal outcomes in relation to different levels of proteinuria. When compared to the group with no proteinuria (the reference), individuals with mild proteinuria had 5.25 times higher odds of getting adverse outcomes. These odds increased to 7.24 for those with moderate proteinuria, 15.55 for severe proteinuria, and a substantial 22.50 for massive proteinuria. These results were statistically significant ($p < 0.001$), indicating that as the level of proteinuria increases, the risk of adverse perinatal outcomes also increases.

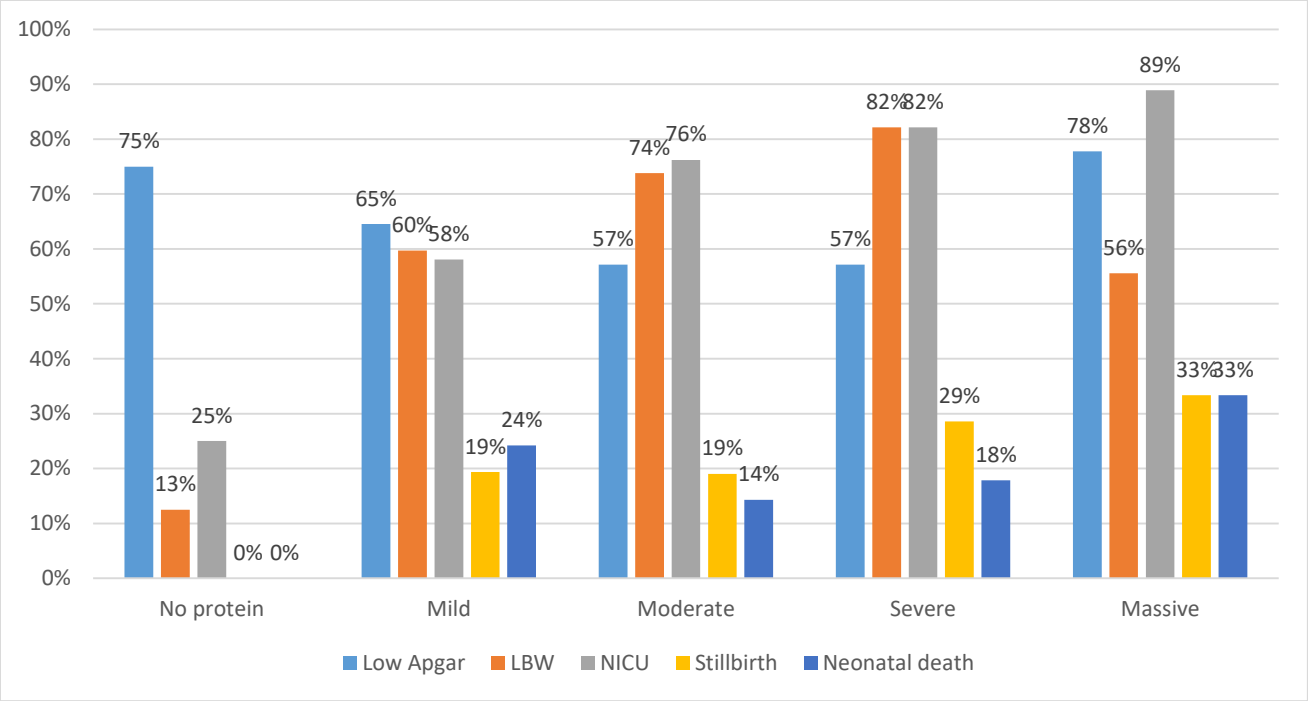

Figure 3 A clustered bar graph showing the relationship between level of proteinuria and adverse perinatal outcomes

This stacked bar graph illustrates the distribution of adverse perinatal outcomes (Yes and No) across different levels of proteinuria, ranging from no proteinuria to massive proteinuria. It shows how the proportion of individuals experiencing adverse outcomes increases as the severity of proteinuria rises, with the highest proportion in the "Massive proteinuria" category.

DISCUSSION

This study unveiled a spectrum of proteinuria levels among preeclamptic mothers, with the majority (42.01%) exhibiting mild proteinuria. These findings resonate with the existing literature, which extensively discusses the connection between proteinuria and pre-eclampsia [15]. Mild proteinuria, defined as 300 mg of protein in a 24-hour urine collection or a urine protein-creatinine ratio of 0.3, has frequently been reported in pre-eclamptic women [16]. It is essential to recognize that mild proteinuria is not indicative of the severity of pre-eclampsia by itself but rather serves as a diagnostic criterion. Our findings align with the established understanding that pre-eclampsia often presents with mild proteinuria [16]. Moderate (24.65%), severe (12.85%), and massive (3.82%) proteinuria were also observed in our study. These findings are consistent with prior research, which underscores the variable nature of proteinuria in pre-eclampsia [17, 15]. The severity of proteinuria in pre-eclampsia can fluctuate, and our study reflects this diversity among the study participants. This study also identified several adverse perinatal outcomes among pre-eclamptic mothers, including low APGAR scores, low birth weight, NICU admission, stillbirth, and early neonatal death. These outcomes mirror the challenges faced by pre-eclamptic mothers during childbirth and align with the existing literature. Apgar scores assessed the overall health and vitality of newborns and are used as an indicator of neonatal well-being (American Academy of Pediatrics, 2015). In this study, approximately one-third of infants had Apgar scores less than 7, indicating a potential need for immediate medical attention. This finding underscores the importance of timely interventions to improve neonatal outcomes, as discussed in the literature [18]. Low birth weight, defined as a birth weight of less than 2500 grams [19], was observed in approximately one-third of infants in our study. This aligns with the literature's emphasis on low birth weight as a risk factor for neonatal morbidity and mortality [19]. Preventing or managing low birth weight in high-risk pregnancies is essential, as discussed in the literature review. Conversely, the majority of infants had scores of 7 or more, suggesting favorable initial health conditions.

The proportion of infants admitted to the Neonatal Intensive Care Unit (NICU) highlights the vulnerability of certain neonates and emphasizes the crucial role of specialized care in improving outcomes for these infants. This

finding aligns with the literature's recognition of the importance of NICU care for preterm or low birth weight infants (American Academy of Pediatrics, 2015). In [19], NICU admission was lower at 49.6%. However, it's important to note that in [19], 65.2% of mothers delivered prematurely, while only 28.8% were preterm in our study. This high number of premature births in [19] could explain the lower NICU admission rate in their study. We found a stillbirth rate of 10.8%, slightly higher than the 9.9% reported in [19]. One possible explanation for this difference is that India, where Chandha & Tayade conducted their study, has a more advanced healthcare system compared to Uganda, where our study took place. The disparity in healthcare infrastructure and access to medical services could contribute to variations in stillbirth rates between the two studies. The low prevalence of stillbirth in the study population is a positive outcome that resonates with global efforts to reduce stillbirth rates [20]. However, the presence of stillbirth emphasizes the ongoing need for comprehensive antenatal care and strategies to mitigate the risks associated with adverse events during pregnancy. It was at 6.6%, which is higher than [19] the proportion of early neonatal deaths signifying the importance of continuous surveillance and timely interventions to prevent neonatal mortality, as highlighted in the literature [21]. Similarly, the lower healthcare in Uganda compared to India could explain this disparity. The study uncovered a compelling relationship between the level of proteinuria and adverse perinatal outcomes, reinforcing the importance of proteinuria assessment as a prognostic tool and guiding clinical practice. These findings have critical implications for the existing literature on the subject. As proteinuria severity increased from mild to massive, we observed a significant escalation in the risk of adverse perinatal outcomes. This relationship is consistent with prior research, which has emphasized the role of proteinuria as a key marker in pre-eclampsia and a predictor of perinatal complications [17]. Specifically, when compared to the reference group with no proteinuria, individuals with mild proteinuria had 5.25 times higher odds of experiencing adverse perinatal outcomes. These odds further increased for those with moderate proteinuria (7.24), severe proteinuria (15.55), and massive proteinuria (22.50). These results were statistically significant ($p < 0.001$), indicating that as the level of proteinuria rises, the risk of adverse perinatal outcomes also rises. This relationship underscores the importance of vigilant monitoring of proteinuria levels in pre-eclamptic mothers. Identifying proteinuria early in pregnancy, monitoring its progression, and responding with appropriate clinical interventions can mitigate the risk of adverse perinatal outcomes. Such interventions may include more frequent antenatal check-ups, specialized maternal and neonatal care, and potentially early delivery in severe cases. These findings align with previous literature that has recognized proteinuria as a key clinical feature in pre-eclampsia management [17]. Moreover, the observed relationship between proteinuria and adverse perinatal outcomes raises questions about the underlying mechanisms that link these variables. Further research into the biological pathways involved in the relationship between proteinuria and adverse outcomes may provide insights into novel therapeutic strategies or interventions aimed at reducing perinatal complications in pre-eclampsia.

CONCLUSION

The majority of preeclamptic mothers exhibited mild to moderate proteinuria, 42.01% and 24.65% respectively. The most common adverse perinatal outcomes included low APGAR scores, low birth weight, and NICU admission. There was a statistically significant association between the level of proteinuria and the likelihood of experiencing adverse perinatal outcomes. The likelihood of adverse outcomes was increasing with the increasing levels of proteinuria.

Recommendation

Based on the study's results, the following recommendations are proposed: A multicenter and wider research should be done on proteinuria among preeclamptic mothers to establish its attributes to adverse neonatal outcomes. Focusing perinatal care strategy for pre-eclampsia mothers, emphasizing early detection and interventions of low APGAR scores, low birth weight, and NICU admissions. Pregnant women should be educated about the potential risks associated with proteinuria and adverse prenatal outcomes.

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