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Incomplete vs. Complete Testing for HSV in Febrile Neonates

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Research Abstract Title: Incomplete vs. Complete Testing for HSV in Febrile Neonates

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Describe role of Submitting/Presenting Trainee in this project (limit 150 words):

Performed literature searched, developed research protocol and plan identifying primary and secondary outcomes, selected measurable variables to query database, met with biostatistician to determine best statistical analysis, wrote abstract as well as created poster.

Background, Objectives/Goal, Methods/Design, Results, Conclusions limited to 500 words

Background: Neonatal herpes simplex virus (HSV) infection occurs in nearly 1/3,000 births and can result in significant morbidity and mortality. Fever is a common reason for evaluating and/or empirically treating for suspected HSV infection, but current recommendations are based on expert opinion, resulting in variation in clinical practice both in terms of diagnostic testing and acyclovir use.

Objectives/Goal: Our primary objective was to identify clinical factors associated with acyclovir use in the management of febrile infants at our institution. Our secondary objective was to identify HSV diagnostic testing patterns among infants who did/did not receive acyclovir.

Methods/Design: Retrospective chart review of infants 0-28 days of age who were in the inpatient setting for fever was performed. Our primary outcome was acyclovir use on admission. Selected co-variates including initial laboratory testing, clinical history, clinical presentation, and demographic data were analyzed for association with acyclovir use. Infants diagnosed with influenza or respiratory syncytial virus (RSV) at admission or discharged from the ED were excluded.

Results: 509 neonates were included for analysis; 116 received acyclovir at initial presentation (Table 1). When compared to febrile neonates who did not receive acyclovir, infants receiving acyclovir were younger, more often had a positive maternal history of HSV, seizures or skin vesicles at initial presentation, or were febrile in the ED. Age and maternal history of HSV had the

strongest association with HSV use indicating that the presence of either of these covariates will likely frequently be associated with concomitant acyclovir administration. While the isolation of HSV by culture remains the definitive diagnostic method and gold standard of establishing neonatal HSV disease, HSV surface cultures/PCR did not have a significant association with acyclovir administration in our study. No infants who received acyclovir were diagnosed with HSV infection; one neonate who did not receive acyclovir had positive HSV testing.

Table: Acyclovir status for febrile infants 0-28 days of age who were admitted (N=509).

| Factors | Acyclovir Use (n=116) | No Acyclovir (n=393) | P value |
|---|-----------------------|----------------------|---------|
| Ill appearing/septic | 1 (0.9%) | 3/392 (0.8%) | 0.92 |
| Age | 14 (7.5,22.5) | 19 (12,24) | 0.0017 |
| Female | 57 (49%) | 169 (43%) | 0.24 |
| Public Insurance | 77 (66%) | 222 (56%) | 0.057 |
| Risk Status | | | |
| Abnormal Urinalysis | 11/108 (10%) | 50/371 (13%) | 0.37 |
| Abnormal CBC | 34/114 (30%) | 113/382 (30%) | 0.96 |
| Positive Maternal History of HSV | 13/61 (21.3%) | 8/144 (5.6%) | 0.001 |
| Non-white/Multiracial | 37/108 (34%) | 135/360 (38%) | 0.54 |
| Seizures | 3 (2.6%) | 1/391 (0.3%) | 0.04 |
| Skin Vesicles | 3 (2.6%) | 1/392 (0.3%) | 0.04 |
| Abnormal LFTs | 11/72 (15%) | 14/57 (25%) | 0.19 |
| Positive CSF HSV PCR & Surface Viral Cultures Performed | 0/116 (0%) | 1/383 (0.3%) | 1.000 |
| Positive CSF HSV PCR | 0/113 (0%) | 1/75 (1.3%) | 0.40 |
| Surface Viral Cultures Performed | 50/113 (44%) | 11/383 (3%) | <0.001 |
| Caregiver Reported Fever & Fever at Presentation | 66 (57%) | 177 (45%) | 0.02 |
| LOS (days, med [IQR]) | 61.5 (47,83) | 50 (44,63) | 0.0001 |

Values in table presented as frequency (%) or median (IQR). Corresponding p-values for tests of the differences in proportions, χ^2 , Fisher's Exact, and Two-sample Wilcoxon rank-sum (Mann-Whitney) tests between No Acyclovir and Acyclovir Use cohorts are provided.

Conclusions: Acyclovir use was associated with age, maternal history of HSV, seizures, skin vesicles, and fever. The timeliness of acyclovir administration has a direct effect on mortality as early acyclovir use decreases mortality. By identifying these factors associated with acyclovir use, we are able to highlight diagnostic testing patterns and in the future hope to improve judicious use of acyclovir. Diagnostic testing rarely conforms to expert recommendations for children suspected of neonatal HSV infection. Our findings highlight the need to establish a more standardized approach to HSV diagnostic testing and empirical acyclovir use.